ONTARIO HEALTH TECHNOLOGY ASSESSMENT SERIES

Ablative Technologies for Thyroid Nodules

A Health Technology Assessment

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Ontario Health

Key Messages

What Is This Health Technology Assessment About?

Thyroid nodules are common. Most are benign (i.e., not cancerous) and do not need to be treated. However, treatment may be needed when larger nodules lead to compressive symptoms (e.g., difficulty breathing or trouble swallowing) or when the nodules themselves produce thyroid hormone (called "autonomously functioning thyroid nodules" or AFTNs). Papillary thyroid cancer is the most common type of thyroid cancer, and it may also need to be treated if there is a risk of the cancer growing or spreading.

Surgery is the usual treatment for thyroid nodules and papillary thyroid cancer, but it is invasive and comes with risks of complications. Ablative technologies (including radiofrequency, microwave, laser, and high-intensity focused ultrasound ablation) use high temperature, chemicals, or electricity to shrink or remove the nodule. They do not require general anesthesia, a surgical incision, or removal of the thyroid gland, and they could be alternatives to surgery.

This health technology assessment looked at how safe, effective, and cost-effective ablative technologies are for adults with symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer. It also looked at the budget impact of publicly funding ablative technologies and at the experiences, preferences, and values of patients with thyroid nodules.

What Did This Health Technology Assessment Find?

Ablative technologies (radiofrequency, microwave, laser, and high-intensity focused ultrasound ablation) may be as effective as surgery for patients with symptomatic benign thyroid nodules or small, low-risk papillary thyroid cancer, but the evidence is of low to very low quality. Radiofrequency ablation may be as effective as ethanol ablation in reducing nodule volume and improving symptoms in patients with cystic thyroid nodules. Radiofrequency ablation may reduce nodule volume, improve symptoms, and normalize thyroid-stimulating hormone levels in patients with AFTNs. Compared with surgery, thermal ablations may provide better postprocedural outcomes in patients with small, low-risk papillary thyroid cancer. Ablative technologies are reasonably safe, may not result in hypothyroidism, and may lead to fewer adverse events than surgery.

In economic modelling, radiofrequency ablation is the optimal strategy compared to standard care in patients with symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer. Compared to surgery, radiofrequency ablation is less costly and leads to better overall health outcomes (offering similar effectiveness with fewer complications). Compared to active surveillance, radiofrequency ablation may also be cost-effective for patients with small, low-risk papillary thyroid cancer. We estimate that publicly funding radiofrequency ablation for patients with symptomatic benign thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer in Ontario over the next 5 years would save $5.42 million, $0.62 million, and $4.03 million, respectively.

Evidence related to physician and patient preferences for the treatment of thyroid nodules showed that both physicians and patients rated effectiveness as the top criterion. Physicians preferred interventions that were safe and effective, and patients placed more value on quality of life after the intervention. In patients with papillary thyroid cancer, preferences were driven by concerns about complications. The people we interviewed saw surgery as invasive and associated it with scarring, longer recovery, and the potential need for lifelong medication. They valued radiofrequency ablation because it is minimally invasive, has a short recovery time, has less scarring, and is largely pain-free.

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The statements, conclusions, and views expressed in this report do not necessarily represent the views of those we consulted.

Citation

TBD

Abstract

Background

Thyroid nodules are common, but most are benign and do not require treatment. However, intervention is warranted in people who experience compressive symptoms or hyperthyroidism, or based on risk of malignancy. Ablative technologies may offer a minimally invasive option for those in whom surgery is being considered. We conducted a health technology assessment of ablative technologies for adults with symptomatic benign thyroid nodules, cystic thyroid nodules, autonomously functioning thyroid nodules (AFTNs), or small, low-risk papillary thyroid cancer, which included an evaluation of effectiveness, safety, cost-effectiveness, the budget impact of publicly funding ablative technologies, and patient preferences and values.

Methods

We performed a systematic literature search of the clinical evidence to retrieve systematic reviews; we then complemented the chosen systematic reviews with a literature search to identify primary studies published from January 2022. We assessed the risk of bias of each included study using the Risk of Bias in Systematic Reviews tool for systematic reviews and the Cochrane Risk-of-Bias Tool 2 for primary studies. We assessed the quality of the body of evidence according to the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group criteria. We performed a systematic economic literature search and conducted cost–utility analyses with a lifetime horizon from a public payer perspective. We also analyzed the budget impact of publicly funding radiofrequency ablation (RFA) in adults with symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer in Ontario. To contextualize the potential value of RFA, we spoke with people who had thyroid nodules.

Results

We included 4 systematic reviews and 1 randomized controlled trial in the clinical evidence review. In patients with symptomatic benign thyroid nodules, thermal ablations (including RFA, microwave ablation, and high-intensity focused ultrasound ablation) may be as effective as surgery in reducing nodule volume and improving symptoms, and they may result in better quality of life (GRADEs: Very low to Low). In patients with cystic thyroid nodules, RFA may be as effective as ethanol ablation in reducing nodule volume and improving symptoms (GRADEs: Low). In patients with AFTNs, RFA may reduce nodule volume, improve symptoms, and normalize thyroid-stimulating hormone levels (GRADEs: Low). In patients with small, low-risk papillary thyroid cancer, thermal ablations may be as effective as surgery in terms of tumour disappearance but have a lower tumour recurrence rate; they may require less surgical time and a shorter length of hospital stay, and they may be associated with less postprocedural pain and better postprocedural quality of life than surgery (GRADEs: Low to Very low). The effectiveness of the different thermal ablations may be similar, but the evidence is very uncertain. Compared with surgery, thermal ablations may not result in hypothyroidism and may lead to fewer adverse events (GRADEs: Low to Very low). Thermal ablations are reasonably safe, and their safety profiles are comparable (GRADEs: Low to Very low).

In patients with symptomatic benign thyroid nodules and AFTNs, RFA is more effective and less costly than surgery. In patients with small, low-risk papillary thyroid cancer, RFA is more effective and less

costly than surgery and cost-effective compared with active surveillance at an incremental cost-effectiveness ratio of $1,574 per QALY gained. Publicly funding RFA for patients with symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer in Ontario would lead to cost savings of $5.42 million, $0.64 million, and $4.03 million over 5 years, respectively.

The quantitative preference evidence demonstrated that physicians preferred interventions that were safe and effective, and patients placed more value on quality of life after interventions. Patient preferences for interventions for papillary thyroid microcarcinoma were driven by aversion to complications rather than by interest in a particular treatment pathway. The people we interviewed noted their preference for minimally invasive options such as RFA for the treatment of thyroid nodules. Those who had experience with RFA noted benefits such as improvement of their symptoms, shorter recovery time, and less scarring.

Conclusions

Ablative technologies may be as effective as surgery for patients with symptomatic benign thyroid nodules or small, low-risk papillary thyroid cancer, and they may also be safer. Effectiveness and safety among the different ablative technologies may be similar, but the evidence was inconclusive. In patients with symptomatic thyroid nodules and AFTNs, RFA is more effective and less costly than surgery. In patients with small, low-risk papillary thyroid cancer, RFA is more effective and less costly than surgery and cost-effective compared with active surveillance. We estimate that publicly funding RFA for patients with symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer in Ontario would result in cost savings of $5.42 million, $0.64 million, and $4.03 million over the next 5 years, respectively. Thyroid nodules have a negative impact on people's physical and emotional well-being, affecting daily activities, work, and overall quality of life. The people we interviewed expressed a preference for minimally invasive treatment options such as RFA, noting benefits such as shorter recovery times and less reliance on lifelong medication as a result of preserved thyroid function.

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Objective

This health technology assessment evaluates the effectiveness, safety, and cost-effectiveness of ablative technologies for the treatment of symptomatic benign thyroid nodules, cystic thyroid nodules, autonomously functioning thyroid nodules (AFTNs), or small, low-risk papillary thyroid cancer in adults. It also evaluates the budget impact of publicly funding ablative technologies and the experiences, preferences, and values of adults with symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer.

Background

Health Condition

Thyroid nodules are solid or fluid-filled lumps that form in the thyroid gland, a small gland that sits at the base of the neck, just above the breastbone. Thyroid nodules are common; they may be identified based on symptoms, as part of a physical examination, or incidentally during radiographic imaging of the neck or chest.[1] Their clinical importance is related to the need to exclude thyroid cancer and, in some cases, to treat nodule-related compressive symptoms (e.g., difficulty breathing or swallowing) or excessive thyroid hormone production.[2]

Most thyroid nodules are benign and do not require intervention. The long-term risk of thyroid cancer after an initial negative biopsy result is low, but clinical surveillance of symptomatic benign thyroid nodules continues indefinitely.[3] Intervention can be necessary for compressive symptoms from enlarged thyroid nodules with different compositions (i.e., solid, cystic, or mixed) or for hyperthyroidism from AFTNs (i.e., benign nodules that produce excessive thyroid hormone without stimulation from the pituitary gland).[4]

Intervention for thyroid nodules may also be indicated based on the risk of malignancy. Thyroid cancer occurs in 7% to 15% of thyroid nodules.[2] Papillary thyroid cancer is the most prevalent type, and papillary thyroid microcarcinoma (with a tumour diameter of 10 mm or less) is a subgroup of this type.[5]

Clinical Need and Population of Interest

Thyroid nodules have a prevalence of up to 67% of adults in the general population, depending on the mode of detection (e.g., palpation, ultrasound, or autopsy).[6] Over 90% of thyroid nodules are clinically insignificant and do not require treatment after they have been confirmed to be benign based on imaging characteristics (i.e., sonography) or biopsied cell analysis (i.e., cytology).[7] The cumulative risk of being diagnosed with thyroid cancer after a negative thyroid biopsy result is 4.6% after 10 years and 7.5% after 24 years.[3]

In 2022, there were 3,461 new cases of thyroid cancer in Ontario (2,457 in women and 1,004 in men).[8] Well-differentiated papillary thyroid cancer and follicular thyroid cancer account for about 84% and 4% of all thyroid cancers, respectively.[1]

The incidences of thyroid nodules and thyroid cancer have been increasing steadily in Canada, largely because of improved and more frequent medical imaging.[9] However, the increased detection of incidental nodules has raised concerns about overdiagnosis and overtreatment.

Current Treatment Options

Benign Thyroid Nodules

Clinical surveillance is recommended for most asymptomatic benign thyroid nodules.[10] For large symptomatic benign thyroid nodules or AFTNs, surgery (i.e., partial or total thyroidectomy) is the conventional treatment.[7] Radioactive iodine is also a treatment option for AFTNs. Surgery carries a risk of complications such as bleeding, infection, and nerve paresis. Radioactive iodine can result in local radiation-induced toxicity and is contraindicated for those who are pregnant or lactating. Both treatments may also cause hypothyroidism, and some may require lifelong replacement of thyroid hormones and laboratory monitoring as a result.[11,12] Aspiration (i.e., using a needle to drain fluids from cysts) may relieve symptoms from benign cystic thyroid nodules, but recurrence rates are high.[13]

Papillary Thyroid Cancer

Surgery is the most common treatment for thyroid cancer. Compared to total thyroidectomy, partial thyroidectomy has shown similar survival outcomes and lower complication rates.[14] Radioactive iodine treatment after surgery improves overall survival in patients who are at high risk of recurrence.[1]

A number of international clinical practice guidelines recommend active surveillance as an alternative to immediate surgery for low-risk papillary thyroid cancer.[15] This approach involves monitoring with ultrasound and physical examination over time. However, although active surveillance is a feasible treatment option, it carries the risk of cancer progression. Therefore, selecting appropriate patients is crucial, based on tumour characteristics such as size, location, number, and ultrasound findings, as well as on patient factors such as age and family history.

Health Technology Under Review

Multiple ultrasound-guided ablation technologies have been developed that harness the power of extreme temperature, chemicals, or electricity. These minimally invasive procedures could be alternatives to surgery for thyroid nodules because they do not require general anesthesia, surgical incision, or removal of the thyroid gland.[16] Based on evidence of low certainty, the 2025 American Thyroid Association management guidelines for adults with differentiated thyroid cancer conditionally recommended that ultrasound-guided percutaneous ablation may be considered as an alternative to active surveillance or surgery for select patients with low-risk papillary thyroid carcinoma.[17]

Thermal Ablation

Thermal ablation causes coagulative necrosis in the tissue by generating extreme hyperthermic conditions (> 50–60°C or > 120–140°F).[18] Thermal ablation techniques are differentiated by how they generate heat, and they include radiofrequency, microwave, laser, and high-intensity focused ultrasound (HIFU) ablation. Because ablation does not allow for definitive histologic analysis of the nodule, benign status must be confirmed by at least 2 biopsies (fine-needle or core-needle) or clear

benign characteristics on ultrasound and clinical history to minimize the risk of overlooking malignant lesions, particularly in the case of large lesions.

Radiofrequency ablation (RFA) is performed percutaneously using an electrode to generate a high-frequency alternating current (200–1200 kHz) that agitates the ions in the tissue, resulting in ionic excitation that causes heat production.[18] The heat is then transmitted to the adjacent tissue by conduction, causing further ablation. RFA is indicated for the following: people with compressive symptoms from a single or dominant solid thyroid nodule; people with AFTNs that are causing subclinical or overt hyperthyroidism; or people with low-risk papillary thyroid cancer.[19-21]

Laser ablation uses single or multiple optical fibres to deliver a focused beam of light energy to the tissue; photons transfer kinetic energy to the atoms, generating heat.[18] Compared to other thermal ablative technologies, laser ablation delivers less total energy, which may confer greater safety in critical areas.[20]

Microwave ablation involves the creation of an electromagnetic field using microwaves of frequencies from 900 to 2500 MHz, which are emitted from a needle-like antenna.[18] This leads to the oscillation of polar water molecules and generation of frictional heat. With multiple antennae producing an exponential increase in heating, microwave ablation delivers more thermal energy in a shorter time. This reduction in treatment time may be valuable for treating large tumours.[20]

HIFU ablation directs ultrasound waves to a specific target location with resulting vibration of atoms, leading to the generation of frictional heat at the focal point.[18] It does not require insertion of needles or probes into the thyroid. Focused ultrasound allows for precise targeting of the nodule, which minimizes damage to surrounding healthy tissues.[22] However, it requires a longer treatment time to scan and ablate the entire nodule volume, especially for larger nodules.[23]

Chemical Ablation

Chemical ablation causes coagulative necrosis through cell dehydration and ischemia by forming a thrombus in the small vessels.[18] It is indicated for cystic thyroid nodules. Ethanol is the agent used most often in chemical ablation. Ethanol ablation involves injecting 95% to 99% dehydrated alcohol into the target cystic thyroid nodule, which can be left in situ or aspirated out after a certain dwell time.

Nanosecond Pulsed-Field Ablation

Nanosecond pulsed-field ablation delivers ultrafast, nonthermal electrical pulses that create transient micropores in cell membranes and intracellular organelles, leading to apoptosis (programmed cell death) in unwanted thyroid tissues.[24] Unlike thermal ablation, nanosecond pulsed-field ablation affects only the targeted soft tissues of the nodule without damaging surrounding tissues.

Regulatory Information

The Viva Combo Radiofrequency Generator, manufactured by STARmed Co. Ltd (Seoul, Korea) and distributed by Southmedic Inc. (Barrie, Ontario), is licensed by Health Canada as a Class 3 device (licence no. 108949) for RFA. No technology for laser, microwave, HIFU, or nanosecond pulsed-field ablation is licensed by Health Canada for thyroid ablation.

The ethanol used in chemical ablation is not subject to Health Canada regulatory approval.

Ontario, Canadian, and International Context

In Ontario, focal tumour ablation – which directly applies thermal (e.g., RFA or microwave ablation) or chemical (e.g., ethanol ablation or transcatheter arterial chemoembolization) therapies to specific tumours and surrounding areas – is publicly funded for cancers of the liver, lung, and kidney.[25] RFA for symptomatic benign thyroid nodules and papillary thyroid cancer is not publicly funded. Outside Ontario, RFA for thyroid conditions is being offered in British Columbia, Quebec, and Nova Scotia, but it is not publicly funded.

We are aware of 4 centres in Ontario that currently offer RFA for symptomatic benign thyroid nodules and/or AFTNs.[26] Of these 4 centres, 3 also offer ethanol ablation for benign cystic thyroid nodules and 2 offer RFA for small (< 2 cm) papillary thyroid cancer. These procedures are funded from philanthropy sources, research grants, or self-pay. Laser, microwave, HIFU, and nanosecond pulsed-field ablation are not being used in Ontario or other Canadian provinces.

Radiofrequency ablation for thyroid nodules is performed by head and neck surgeons, endocrine surgeons, endocrinologists, and interventional radiologists who are experienced in ultrasound-guided procedures and have specialized training in ablation techniques. Procedures are conducted under local anesthesia on an outpatient basis. During the procedure, a small needle electrode is inserted into the thyroid nodule under ultrasound guidance to deliver radiofrequency energy from a radiofrequency generator to ablate the targeted tissues. Patients can expect to go home the same day after RFA. The ablation procedure takes about 1 hour on average, but the actual duration depends on clinical indications, patient factors, and the skill level of the interventionist. The frequency of follow-up also varies based on clinical indications and response to the ablation procedure. Patient eligibility and indications for ablative technologies for thyroid nodules or papillary thyroid cancer are based primarily on clinical practice guidelines from the American Thyroid Association.[17,18]

A number of international clinical practice guidelines provide recommendations on the use of ablative technologies for symptomatic benign thyroid nodules and papillary thyroid cancer, including patient eligibility, preprocedural assessment, standard techniques, and postprocedural evaluation (see Appendix 1, Table A1). Overall, these guidelines recommend that thermal ablation should be considered for people with symptomatic benign thyroid nodules or certain low-risk papillary thyroid cancers and metastatic neck lymphadenopathy who are ineligible for surgery or who do not want surgery.

Equity Context

We used the PROGRESS-Plus framework[27] to help explicitly consider health equity in our health technology assessments. PROGRESS-Plus is a health equity framework used to identify population and individual characteristics across which health inequities may exist. These characteristics include place of residence; race or ethnicity, culture or language; gender or sex; disability; occupation; religion; education; socioeconomic status; social capital; and other key characteristics (e.g., age) that stratify health opportunities and outcomes.

Access to RFA for people with symptomatic benign thyroid nodules and/or small, low-risk papillary thyroid cancer is currently limited to several centres in Ontario (specifically in the Greater Toronto Area) that have adopted the technologies. Public funding may improve equity in access to these treatments, because it would incentivize surgeons to become trained in the procedure. Courses are available

for training in ablative techniques, and many surgeons specialized in thyroid diseases are already well trained in ultrasound-guided interventions, such as needle biopsies.

Expert Consultation

We engaged with experts in the specialty areas of head and neck surgery, endocrine surgery, and interventional radiology to help inform the development and refinement of the research questions, review methods, and review results, as well as to contextualize the evidence on RFA for thyroid nodules to Ontario.

PROSPERO Registration

This health technology assessment has been registered in PROSPERO, the international prospective register of systematic reviews (CRD #420251006858), available at crd.york.ac.uk/PROSPERO.

Clinical Evidence

Research Question

What are the effectiveness and safety of ablative technologies compared with surgery, active surveillance, or other ablative technologies for the treatment of symptomatic benign thyroid nodules, cystic thyroid nodules, autonomously functioning thyroid nodules (AFTNs), or small, low-risk papillary thyroid cancer in adults?

Methods

Review Approach

To leverage existing evidence, we first searched for recent systematic reviews of high methodological quality that addressed our research questions. We based our selection of the systematic reviews on the recency of the evidence, the rigorous selection of included studies, a risk-of-bias assessment, and the comprehensiveness of outcomes reported. Then, we ran a systematic literature search starting from the end date of the search of the selected systematic review published earliest to identify any relevant randomized controlled trials that had been published since that search was conducted.

Clinical Literature Search

We performed a clinical literature search on February 19, 2025, using a methodological filter to retrieve systematic reviews, meta-analyses, and health technology assessments published from database inception until the search date. We used the Ovid interface in the following databases: MEDLINE, Embase, the Cochrane Database of Systematic Reviews, and the National Health Service Economic Evaluation Database (NHS EED).

After the systematic reviews had been selected, we updated our search starting from the end date of the search from the earliest systematic review. We performed a clinical literature search on June 9, 2025, using the same search strategy with a methodological filter to retrieve randomized controlled trials published from January 1, 2022, until the search date. We used the Ovid interface in the following databases: MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, and the National Health Service Economic Evaluation Database (NHS EED).

A medical librarian developed the search strategies using controlled vocabulary (e.g., Medical Subject Headings) and relevant keywords. The final search strategy was peer-reviewed using the PRESS Checklist.[28]

We created database auto-alerts in MEDLINE and Embase for both searches and monitored them until October 31, 2025. We also performed a targeted grey literature search of the International HTA Database, the websites of health technology assessment organizations and regulatory agencies, and clinical trial and systematic review registries, following a standard list of sites developed internally. See Appendix 2 for our literature search strategies, including all search terms.

Eligibility Criteria

Studies

Inclusion Criteria

- Systematic reviews
  - English-language full-text publications
  - Studies published from database inception until February 19, 2025
  - Systematic reviews, meta-analyses, and health technology assessments that reported outcomes separately for each ablative technology (e.g., radiofrequency, microwave), rather than for ablative technologies as a class (e.g., thermal ablation)
- Primary studies
  - English-language full-text publications
  - Studies published from January 1, 2022, to June 9, 2025
  - Randomized controlled trials (RCTs)

Exclusion Criteria

- Systematic reviews
  - Animal and in vitro studies
  - Nonsystematic reviews, narrative reviews, abstracts, editorials, letters, case reports, and commentaries
- Primary studies
  - Animal and in vitro studies
  - Observational studies, reviews, abstracts, editorials, letters, case reports, and commentaries

Participants

Inclusion Criteria

- Adults with symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer (tumours < 2 cm maximum diameter)

Exclusion Criteria

- Children (< 18 years of age)
- Pregnant people

Interventions

Inclusion Criteria

- Thermal ablation, including radiofrequency ablation (RFA), microwave ablation, laser ablation, and high-intensity focused ultrasound (HIFU) ablation
- Chemical ablation, including ethanol
- Nanosecond pulsed-field ablation

Exclusion Criteria

- Nonablative technologies

Comparators

Inclusion Criteria

- Surgery
- Active surveillance
- Other ablative technologies (e.g., RFA vs. microwave ablation)

Exclusion Criteria

- One versus multiple treatments with the same ablative technology (e.g. 1 vs. 2 RFA sessions)
- One versus multiple treatments with different ablative technologies (e.g., RFA vs. RFA and microwave ablation)

Outcome Measures

- Nodule volume reduction
- Symptom improvement
- Cosmetic appearance improvement
- Thyroid function
- Need for repeated ablative or operative treatment
- Return to work
- Heath service use (e.g., surgical time, length of hospital stay)
- Pain
- Quality of life
- Nodule recurrence rate
- Complications (e.g., recurrent laryngeal nerve palsy or voice change)
- Adverse events
- Specific to papillary thyroid cancer:
  - Tumour disappearance rate

  - Thyroglobulin
  - Overall survival
  - Disease recurrence

Timing

- 6 to 12 months for short-term outcomes (e.g., nodule volume reduction, pain)
- 3 to 5 years for long-term outcomes (e.g., overall survival, disease recurrence)

Setting

- Outpatient

Literature Screening

Two reviewers screened titles and abstracts to assess the eligibility of a sample of 100 citations to validate the inclusion and exclusion criteria. A single reviewer then screened all remaining citations using Covidence[29] and obtained the full texts of studies that appeared eligible for review according to the inclusion criteria. The same reviewer then examined the full-text articles and selected studies eligible for inclusion. The reviewer also examined reference lists and consulted content experts for any additional relevant studies not identified through the search.

Data Extraction

For the systematic reviews, we extracted data on populations, interventions, comparators, outcomes, the literature search, and risk of bias assessment to guide selection of the systematic reviews with the best quality. From the chosen systematic reviews, we extracted data on study characteristics, type of ablative technologies, study design, outcome results, and follow-up duration for each included study.

For the primary studies, we extracted data on study characteristics, type of ablative technologies, populations, interventions, comparators, and outcomes.

Equity Considerations

From diagnosis and treatment to outcomes, there are disparities in thyroid care based on gender, age, race or ethnicity, and rural versus urban access.[30] Thyroid nodules are approximately 4 times more common in women than in men, and prevalence increases with age.[31,32] Non-White people are less likely to receive appropriate and timely treatment than White people.[33] Rural populations and people who live farther from treatment centres experience more advanced disease as a result of access issues.[34] As well, people from high-poverty areas are associated with more loss to follow-up for thyroid nodules.[35] In Ontario, a population-based prospective cohort study showed that immigrants from Southeast and East Asia had a statistically significant higher incidence of thyroid cancer than non-immigrants.[36]

Without public funding, specific factors related to age, sex and gender, race or ethnicity, geographic location, socioeconomic status, or financial barriers may further limit access to advances in thyroid care, including ablative technologies.

Equity considerations relevant to the use of ablative technologies for thyroid nodules and papillary thyroid cancer across different populations are reported to the extent that the information was available in the included studies.

Statistical Analysis

Due to the heterogeneity of the study populations and outcomes reported in the included systematic reviews and primary study, we did not perform a meta-analysis. Instead, we have reported all statistical analyses as they were presented in the selected studies.

Critical Appraisal of Evidence

We assessed risk of bias using the Risk of Bias in Systematic Reviews (ROBIS) tool[37] for the selected systematic reviews; we reported risk of bias as originally reported for the studies included in the systematic reviews (Appendix 3). We assessed risk of bias using the Cochrane Risk-of-Bias Tool 2[38] for the selected primary study.

We evaluated the quality of the body of evidence for each outcome according to the *Grading of Recommendations Assessment, Development, and Evaluation* (GRADE) *Handbook*.[39] The body of evidence was assessed based on the following considerations: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The overall rating reflects our certainty in the evidence.

Results

Clinical Literature Search

Systematic Reviews

The clinical literature search for systematic reviews yielded 520 citations, including grey literature results and after removing duplicates, published from database inception to February 19, 2025. We identified no additional eligible studies from other sources, including database alerts (monitored until October 31, 2025). In total, we identified 76 systematic reviews that met our inclusion criteria. See Appendix 4 for a list of selected studies excluded after full-text review. Figure 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the clinical literature search for systematic reviews.

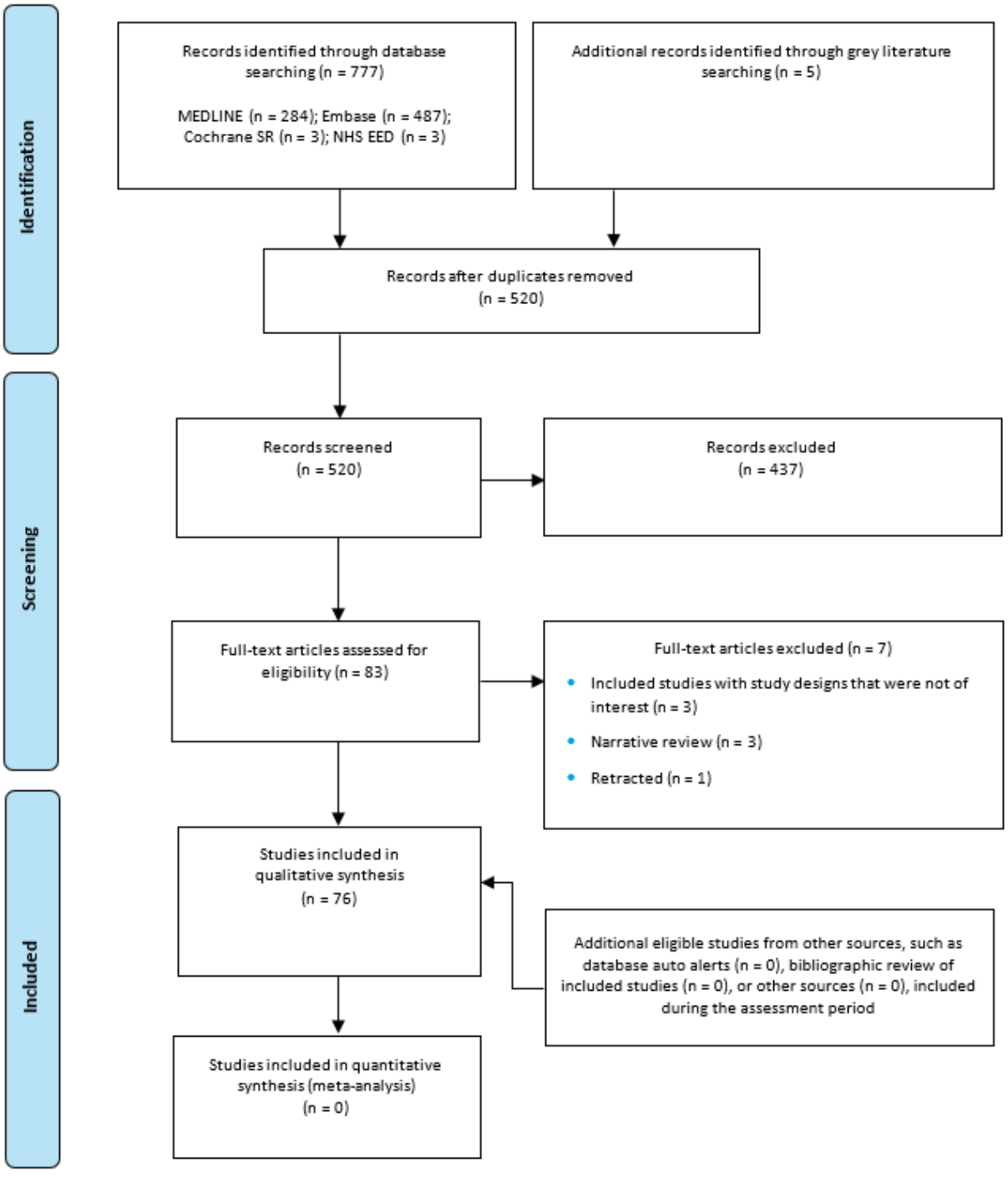

Figure 1: PRISMA Flow Diagram – Clinical Search for Systematic Reviews

PRISMA flow diagram showing the clinical search for systematic reviews. The clinical search yielded 520 citations, including grey literature results and after removing duplicates, published between database inception and February 19, 2025. We screened the abstracts of the 520 identified studies and excluded 437. We assessed the full text of 83 articles and excluded a further 7. In the end, we included 76 articles in the qualitative synthesis. Note: The purpose of the search for systematic reviews was to identify recent high-quality systematic reviews that addressed the clinical research question to leverage existing evidence; we did not subject the included systematic reviews to meta-analysis.
Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.
Source: Adapted from Page et al.[40]

Primary Studies

The clinical literature search for primary studies yielded 148 citations, including grey literature results and after removing duplicates, published between January 1, 2022, and June 9, 2025. We identified no additional eligible studies from other sources, including database alerts (monitored until October 31, 2025). In total, we identified 1 study (RCT) that met our inclusion criteria. See Appendix 4 for a list of selected studies excluded after full-text review. Figure 2 presents the PRISMA flow diagram for the clinical literature search for primary studies.

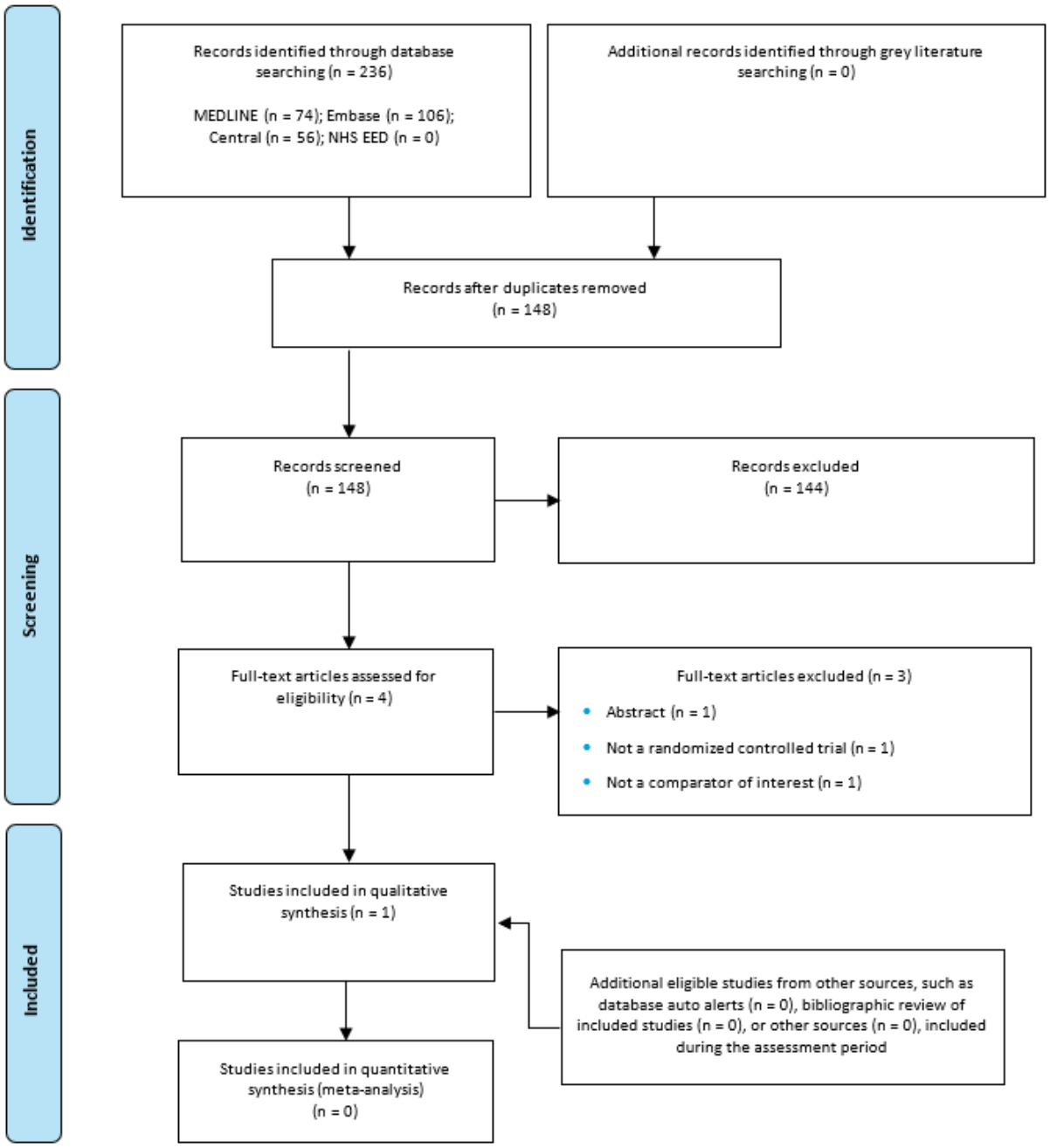

Figure 2: PRISMA Flow Diagram – Clinical Search for Primary Studies

PRISMA flow diagram showing the clinical search for primary studies. The clinical search yielded 148 citations, including grey literature results and after removing duplicates, published between January 1, 2022, and June 9, 2025. We screened the abstracts of the 148 identified studies and excluded 144. We assessed the full text of 4 articles and excluded a further 3. In the end, we included 1 article in the qualitative synthesis.

Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Source: Adapted from Page et al.[40]

Characteristics of Included Studies

Systematic Reviews

Seventy-six systematic reviews[23,41-115] met our eligibility criteria, published between 2014 and 2025. See Appendix 3, Table A2, for risk-of-bias assessments using the ROBIS tool. After excluding 45 systematic reviews with a high risk of bias,[23,44-46,49,52,54-58,60-62,65-67,71,72,75,76,79-83,86,88,89,91-96,99,100,102-105,109,110,112,114] we considered 31 systematic reviews with low risk of bias for inclusion: 15 on symptomatic benign thyroid nodules,[41-43,47,48,50,53,59,64,68,85,87,98,111,115] 2 on cystic thyroid nodules,[77,108] 2 on AFTNs,[70,74] and 12 on papillary thyroid cancer.[51,63,69,73,78,84,90,97,101,106,107,113]

For our analysis, we selected 4 of the above systematic reviews: 1 on symptomatic benign thyroid nodules by Nicolopoulos et al (Austrian Institute for Health Technology Assessment)[85] published in 2024 (with a literature search end date of December 2023); 1 on cystic thyroid nodules by Leon-Salas et al[77] published in 2023 (with a literature search end date of July 2022); 1 on AFTNs by Javid et al[70] published in 2024 (with a literature search end date of January 2024); and 1 on papillary thyroid cancer by Nguyen et al[84] published in 2025 (with a literature search end date of March 2024). Table 1 describes the characteristics of the included systematic reviews.

Table 1: Characteristics of the Included Systematic Reviews

Author, year Literature search end date	Population	Interventions	Comparators	Outcomes	Designs of included studies
Nicolopoulos et al, 2024[85] December 2023	Adults with symptomatic benign thyroid nodules	Thermoablation, including radiofrequency, ultrasound-guided percutaneous laser, microwave, HIFU	Thyroidectomy, radioiodine	Nodule volume reduction, symptom reduction, cosmetic appearance improvement, thyroid function, health-related quality of life, nodule recurrence rate, adverse events, severe adverse events	RCTs Retrospective, propensity-score-matched, nonrandomized studies of intervention
Leon-Salas et al, 2023[77] July 2022	Patients of all ages with thyroid nodular pathology or metastatic cervical adenopathies	Ultrasound-guided percutaneous ethanol injection	Surgery, percutaneous thermal ablation (laser, radiofrequency, or microwave)	Outcomes for safety or effectiveness (i.e., volume reduction, symptom score, cosmetic score, therapeutic success, major complications)	RCTs
Javid et al, 2024[70] January 2024	Adults with AFTNs	RFA	NA	Volume reduction rate, normalization of TSH, symptom score, cosmetic score, complications	Noncomparative after vs. before studies
Nguyen et al, 2025[84] March 2024	Adults with small, low-risk papillary thyroid cancer	RFA, microwave ablation, laser ablation, surgery	Network meta-analysis comparing RFA, microwave ablation, laser ablation, and surgery	Tumour volume reduction rate, tumour disappearance rate, tumour recurrence rate, surgical outcomes (surgical time, length of hospital stay), postprocedural outcomes (pain, recurrent laryngeal nerve palsy, overall complications)	Nonrandomized comparative studies Noncomparative after vs. before studies

Abbreviations: AFTN, autonomously functioning thyroid nodule; HIFU, high-intensity focused ultrasound; NA, not applicable; RCT, randomized controlled trial; RFA, radiofrequency ablation; TSH, thyroid-stimulating hormone.

The systematic review by Nicolopoulos et al (Austrian Institute for Health Technology Assessment)[85] had a robust review methodology, a recent literature search, and a vigorous study selection of higher-quality evidence (i.e., RCTs and propensity-matched nonrandomized studies). It reported comprehensive literature search strategies and provided detailed information about the included study designs, the characteristics of study populations, and outcomes. It also focused on comparisons between thermal ablation technologies and thyroid surgery (current standard care in Ontario). Although the review considered all thermal ablations as a class from a policy perspective, most outcomes were reported separately for each ablative technology.

We did not find any systematic reviews of studies comparing ablative technologies with surgery for cystic thyroid nodules, but we did identify 2 systematic reviews[77,108] on benign cystic and predominantly cystic thyroid nodules. The systematic review by Yang et al[108] included RCTs and observational studies; the systematic review by Leon-Salas et al[77] included only RCTs. We selected the systematic review by Leon-Salas et al[77] because it included a registered review protocol and had a more recent literature search.

We did not find any systematic reviews of studies comparing ablative technologies with surgery for AFTNs. The systematic review by Javid et al[70] included noncomparative studies that investigated the efficacy of RFA in people with AFTNs. We selected this review because it had a registered review protocol and a recent literature search.

The systematic review by Nguyen et al[84] focused on the efficacy and safety of thermal ablations (including RFA, microwave ablation, and laser ablation) and surgery in people with small, low-risk papillary thyroid cancer. It explored direct and indirect evidence for the 3 thermal ablative technologies and their comparison with surgery. It also provided detailed information about the characteristics of study populations and outcomes, and it had a recent literature search.

Studies From the Selected Systematic Reviews

Nicolopoulos et al (Austrian Institute of Health Technology Assessment) included 4 RCTs[116-119] and 5 retrospective, propensity-score-matched, nonrandomized studies[23,120-123] in their systematic review of thermal ablation for symptomatic benign thyroid nodules. Three[117-119] of the RCTs compared microwave ablation with thyroidectomy. The remaining RCT[116] compared laser ablation with radioactive iodine, but because radioactive iodine was not a predefined comparator of interest for this clinical evidence review, we did not extract data from this RCT. The RCT by Jin et al[117] included RFA and microwave ablation as interventions; although most outcomes were reported for thermal ablation as a class, the authors did report volume rate reduction and procedural outcomes stratified by ablation technique. Among the 5 nonrandomized studies, 1 was on microwave ablation and RFA,[120] 1 was on microwave ablation,[121] 1 was on HIFU ablation,[23] and the remaining 2 were on RFA.[122,123] The study by Bo et al[120] did not report outcomes for each ablative technology separately, so we did not extract data from this study. All included studies were conducted in China. The follow-up duration ranged from 48 hours to 15 months. Sample sizes were 52 to 450 patients for the RCTs and 98 to 216 patients for the nonrandomized studies after propensity matching.

The systematic review by Leon-Salas et al[77] included 3 RCTs[124-126] that compared percutaneous ethanol injection with RFA in patients with thyroid nodular pathology. Two of the RCTs[125,126] evaluated patients with predominantly cystic thyroid nodules and 1 RCT[124] evaluated patients with solid nodules. Given the scope of our review, we extracted data only from the studies in cystic thyroid nodules. Both RCTs were conducted in Korea and had a follow-up duration of 6 months. Sample sizes were 46 to 50 patients.

The systematic review by Javid et al[70] included 10 noncomparative studies[127-136] that evaluated the efficacy of RFA in patients with AFTNs. Among these, 4 were prospective[129,132,134,136] and 6 were retrospective.[127,128,130,131,133,135] Six of the studies were conducted in Italy; the others were conducted in Korea, Austria, and Vietnam. Follow-up duration ranged from 6 to 24 months, and sample sizes were 9 to 44 patients.

The systematic review and network meta-analysis by Nguyen et al[84] included 2 prospective comparative studies,[137,138] 19 retrospective comparative studies,[118,122,139-155] 8 prospective noncomparative studies,[156-163] and 32 retrospective noncomparative studies[164-195] exploring direct and indirect comparisons of RFA (38.80%), microwave ablation (38.78%), laser ablation (3.86%), and surgery (18.56%) for patients with small, low-risk papillary thyroid cancer. Of the total, 47 studies included only patients with papillary thyroid microcarcinoma, and 14 studies included patients with papillary thyroid microcarcinoma or papillary thyroid cancer with a maximum tumour diameter of 2 cm. Among the 61 included studies, 55 (> 90%) were conducted in China; the rest were conducted in Korea and Italy. Follow-up durations ranged from 12 to 94 months for comparative studies and 9 to 130 months for noncomparative studies. Sample sizes ranged from 81 to 725 patients for comparative studies and from 6 to 1,278 patients for noncomparative studies.

Appendix 5, Table A21, summarizes the design and characteristics of the studies included in the selected systematic reviews.

Primary Study

One prospective, multicentre RCT[196] met our inclusion criteria, comparing RFA with microwave ablation in patients who had predominantly solid symptomatic benign thyroid nodules. Eligible patients were recruited consecutively in outpatient clinics at 5 institutions between August 2019 and November 2020. A random number table was generated by statisticians using statistical software, and an independent investigator used the table to assign patients to receive RFA or microwave ablation at a 1:1 ratio.

Appendix 5, Table A22, describes the patient characteristics from the selected RCT.

Risk of Bias in the Included Studies

Details of our findings with respect to quality of evidence from the included studies can be found in Appendix 3.

In the systematic review by Nicolopoulos et al (Austrian Institute of Health Technology Assessment),[85] the authors assessed risk of bias using the Cochrane Risk-of-Bias 2 tool[38] for RCTs and the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool[197] for nonrandomized studies. The authors considered the overall risk of bias for the RCTs to be high because of deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. They considered the overall risk of bias for the nonrandomized studies to be moderate to serious because of confounding, classification of intervention, missing data, measurement of outcomes, and selection of reported results. Using GRADE methodology,[39] the authors considered the strength of evidence from the RCTs and nonrandomized studies for all outcomes to be Very low. The authors' evidence-based conclusion was that there was no evidence or inconclusive evidence to demonstrate an additional benefit for thermal ablation in symptomatic benign thyroid nodules.

In the systematic review by Leon-Salas et al,[77] the authors assessed the risk of bias for RCTs of percutaneous ethanol injection versus RFA using the Cochrane Risk-of-Bias 2 tool.[38] The overall risk of bias from the included RCTs was unclear because no information about the randomization process was provided, and no trial protocol could be checked to determine the prespecified outcomes of the studies. Using GRADE methodology,[39] the authors considered the overall quality of evidence for outcomes comparing ethanol ablation with RFA to be Moderate, downgraded due to imprecision.

In the systematic review by Javid et al,[70] the authors assessed the risk of bias for noncomparative studies of RFA in AFTNs using the ROBINS-I tool[197] and found that all included studies were at risk of confounding and selection bias, and several studies were at risk of bias due to missing data. This review did not use GRADE to assess the overall certainty of evidence.

In the systematic review by Nguyen et al,[84] the authors used the Methodological Index for Non-Randomized Studies (MINORS) tool[198] to assess the overall quality of the included studies in papillary thyroid cancer. The authors included only studies of fair or high quality. This review did not use GRADE to assess the overall certainty of evidence.

In the recently published RCT by Chen et al,[196] we assessed the risk of bias to be high using the Cochrane Risk-of-Bias 2 tool[38] because of concerns about allocation concealment and a lack of blinding of outcome assessors and participants with respect to randomization assignment.

We used the risk of bias assessments from the selected systematic reviews as a guide to determine the GRADE quality of the evidence for each outcome.

Ablative Technologies for Symptomatic Benign Thyroid Nodules

We extracted outcomes from 7 studies[117-119,121-123,199] included in the systematic review by Nicolopoulos et al (Austrian Institute of Health Technology Assessment),[85] which compared ablative technologies with surgery for symptomatic benign thyroid nodules. We extracted outcomes from the RCT by Chen et al,[196] which compared RFA with microwave ablation.

Nodule Volume Reduction

Table 2 summarizes the results for nodule volume reduction.

Table 2: Nodule Volume Reduction, Symptomatic Benign Thyroid Nodules

Author, year	Study design	Results
RFA vs. thyroidectomy		
Jin et al, 2021[117]	RCT	VRR (mean ± SD) 1 month: RFA 15.4% ± 7.2%, thyroidectomy NR 3 months: RFA 48.2% ± 11.3%, thyroidectomy NR 6 months: RFA 68.1% ± 8.1%, thyroidectomy NR 12 months: RFA 80.1% ± 1.8%, thyroidectomy NR
Yan et al, 2023[122]	Nonrandomized study	VRR (median [IQR]) 1 month: RFA 55.0% (35.9%), thyroidectomy 100% 3 months: RFA 75.9% (18.8%), thyroidectomy 100% 6 months: RFA 84.6% (26.2%), thyroidectomy 100% 12 months: RFA 92.7% (27.5%), thyroidectomy 100% 24 months: RFA 94.1% (15.0%), thyroidectomy 100%
Microwave ablation vs. thyroidectomy		
Jin et al, 2021[117]	RCT	VRR (mean ± SD) 1 month: MWA 15.3% ± 7.1%, thyroidectomy NR 3 months: MWA 47.9% ± 10.2%, thyroidectomy NR 6 months: MWA 67.8% ± 7.9%, thyroidectomy NR 12 months: MWA 79.3% ± 3.2%, thyroidectomy NR
Zhi et al, 2018[119]	RCT	VRR (mean) 3 months: MWA 75.9%, thyroidectomy NR 6 months: MWA 88.4%, thyroidectomy NR 12 months: MWA 95.2%, thyroidectomy NR
Jin et al, 2018[121]	Nonrandomized study	VRR (mean ± SD) 1 month: MWA 15.2% ± 2.3%, thyroidectomy NR 3 months: MWA 47.6% ± 3.6%, thyroidectomy NR 6 months: MWA 67.2% ± 6.8%, thyroidectomy NR 12 months: MWA 79.6% ± 10.2%, thyroidectomy NR
HIFU ablation vs. lobectomy		
Lang et al, 2019[199]	Nonrandomized study	VRR (mean ± SD) 3 months: HIFU 50% ± 22%, lobectomy NR 6 months: HIFU 64% ± 26%, lobectomy NR
RFA vs. microwave ablation		
Chen et al, 2024[196]	RCT	VRR (mean ± SD) 6 months: RFA 65% ± 31%, MWA 59% ± 20% 2 years: RFA 83% ± 24%, MWA 80% ± 18% Noninferiority test[a] VRR at 6 months: −5.6% (95% CI −12.5% to ∞); P = .01 VRR at 2 years: −2.4% (95% CI −8.0% to ∞); P < .001 Change of VRR over time between RFA and MWA Mean difference: 6.9% (95% CI −0.5% to 13.9%); P = .73

Abbreviations: CI, confidence interval; HIFU, high-intensity focused ultrasound; IQR, interquartile range; MWA, microwave ablation; NR, not reported; RCT, randomized controlled trial; RFA, radiofrequency ablation; SD, standard deviation; VRR, volume reduction ratio.

[a] The predetermined noninferiority margin was −13%.

RFA Versus Thyroidectomy

One RCT by Jin et al[117] and 1 nonrandomized study by Yan et al[122] compared RFA with total thyroidectomy and demonstrated a trend in decreasing nodule volume with RFA from 1-month to 24-month follow-up. Both studies also showed a volume reduction of greater than 50% with RFA from 6-month follow-up onward, which was considered to be therapeutic success.[200] The RCT did not report volume reduction rate in the thyroidectomy group because the entire thyroid gland was removed; the nonrandomized study reported a 100% volume reduction rate for the thyroidectomy group across all follow-ups.

Based on 1 RCT and 1 nonrandomized study, the GRADE quality of the evidence for nodule volume reduction comparing RFA with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A4).

Microwave Ablation Versus Thyroidectomy

Two RCTs (Jin et al and Zhi et al)[117,119] and 1 nonrandomized study (Jin et al)[121] compared microwave ablation with thyroidectomy and showed a downward trend in nodule volume for patients who received microwave ablation from 1- to 12-month follow-up. These studies showed a volume reduction of greater than 50% at 6-month follow-up and beyond. Volume reduction rates in the thyroidectomy groups were not reported because the entire thyroid gland was removed.

Based on 2 RCTs and 1 nonrandomized study, the GRADE quality of the evidence for nodule volume reduction comparing microwave ablation with thyroidectomy was Low to Very low, downgraded due to risk of bias and imprecision (Appendix 3, Table A5).

HIFU Ablation Versus Lobectomy

One nonrandomized study by Lang et al[199] compared HIFU ablation with lobectomy and reported a volume reduction of 50% or greater after HIFU ablation at 3- and 6-month follow-up. Volume reduction in the lobectomy group was not reported.

Based on 1 nonrandomized study, the GRADE quality of the evidence for nodule volume reduction comparing HIFU ablation with lobectomy was Very low, downgraded due to risk of bias and imprecision (Appendix 3, Table A6).

RFA Versus Microwave Ablation

In an RCT by Chen et al,[196] the change in volume reduction rate was similar for RFA and microwave ablation at 6-month and 2-year follow-up. An infinity at the upper confidence interval for the difference in volume rate reduction (relative to the predetermined noninferiority margin of −13%) established noninferiority between RFA and microwave ablation but with limited precision, and showed that the true difference in treatment effect was unknown.[201]

Based on 1 RCT, the GRADE quality of the evidence for nodule volume reduction comparing RFA with microwave ablation was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A7).

Symptom Improvement

Table 3 summarizes the results for symptom improvement.

Table 3: Symptom Improvement, Symptomatic Benign Thyroid Nodules

Author, year	Study design	Results
RFA vs. thyroidectomy		
Yan et al, 2023[122]	Nonrandomized study	Symptom reduction score (median [IQR]) Baseline: RFA 3 (2),[a] thyroidectomy 5 (4)[b] 12-month follow-up: RFA 1 (1),[a] thyroidectomy 2 (2)[b]
Microwave ablation vs. thyroidectomy		
Zhi et al, 2018[119]	RCT	Nodule-related symptoms at baseline: MWA 10/28 (35.7%), thyroidectomy 11/24 (45.8%) Remission of nodule-related symptoms: MWA 10/28 (35.7%), thyroidectomy 11/24 (45.8%)
Jin et al, 2018[121]	Nonrandomized study	Symptom score by 10 cm VAS (mean ± SD) Baseline before propensity matching: MWA 4.1 ± 1.4, surgery 4.5 ± 1.3; *P* = .011 Baseline after propensity matching: MWA 4.3 ± 1.4, surgery 4.5 ± 1.3; *P* = .389 Follow-up: NR
HIFU ablation vs. lobectomy		
Lang et al, 2019[199]	Nonrandomized study	Symptom improvement score at 6 months No improvement: HIFU 4 (5%), lobectomy 10 (13%) Slight improvement: HIFU 20 (26%), lobectomy 15 (20%) Moderate improvement: HIFU 30 (39%), lobectomy 33 (43%) Significant improvement: HIFU 23 (30%), lobectomy 19 (25%)
RFA vs. microwave ablation		
Chen et al, 2024[196]	RCT	Symptom score by 10 cm VAS (mean ± SD) at 2 years RFA: 0.06 ± 0.29 MWA: 0.06 ± 0.26 Mean difference < 0.001 (95% CI −0.1 to 0.1); *P* = .99

Abbreviations: CI, confidence interval; HIFU, high-intensity focused ultrasound; IQR, interquartile range; MWA, microwave ablation; NR, not reported; RCT, randomized controlled trial; RFA, radiofrequency ablation; SD, standard deviation; VAS, visual analog scale.

[a] RFA change from baseline to 12 months (*P* = .001).

[b] Surgery change from baseline to 12 months (*P* < .001).

RFA Versus Thyroidectomy

The nonrandomized study by Yan et al[122] compared RFA with thyroidectomy and reported a statistically significant improvement in symptom reduction score, measured by a 10 cm visual analog scale (scores 0 to 10), at 12-month follow-up in both the RFA (*P* = .001) and thyroidectomy groups (*P* < .001).

Based on 1 nonrandomized study, the GRADE quality of the evidence for symptom improvement comparing RFA with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A4).

Microwave Ablation Versus Thyroidectomy

In the RCT by Zhi et al,[119] 10 patients in the microwave ablation group and 11 patients in the thyroidectomy group reported nodule-related symptoms at baseline. Both groups reported remission of all nodule-related symptoms at 12-month follow-up. The nonrandomized study by Jin et al[121] did not report symptom reduction at follow-up.

Based on 1 RCT and 1 nonrandomized study, the GRADE quality of the evidence for symptom improvement comparing microwave ablation with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A5).

HIFU Ablation Versus Lobectomy

The nonrandomized study by Lang et al[199] reported a similar proportion of moderate or significant improvement in nodule-related symptoms for patients who received HIFU ablation (69%) and those who received lobectomy (68%).

Based on 1 nonrandomized study, the GRADE quality of the evidence for symptom improvement comparing HIFU ablation with lobectomy was Low, downgraded due to risk of bias (Appendix 3, Table A6).

RFA Versus Microwave Ablation

In the RCT by Chen et al,[196] there was no difference in symptom score between RFA and microwave ablation at 2-year follow-up.

Based on 1 RCT, the GRADE quality of the evidence for symptom improvement comparing RFA with microwave ablation was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A7).

Cosmetic Appearance Improvement

Table 4 summarizes the results for cosmetic appearance improvement.

Table 4: Cosmetic Appearance Improvement, Symptomatic Benign Thyroid Nodules

Author, year	Study design	Results
RFA vs. thyroidectomy		
Yan et al, 2023[122]	Nonrandomized study	Symptom score (median [IQR]) Baseline: RFA 3 (1.5),[a] thyroidectomy 4 (2)[b] 12-month follow-up: RFA 1 (1),[a] thyroidectomy: 0 (0)[b]
Microwave ablation vs. thyroidectomy		
Zhi et al, 2018[119]	RCT	Cosmetic concerns prior to treatment: MWA 28/28 (100%), thyroidectomy 24/24 (100%) Excellent cosmetic results after intervention: MWA 28/28 (100%), thyroidectomy 20/24 (83.3%)
Jin et al, 2018[121]	Nonrandomized study	Cosmetic score (mean ± SD) Baseline before propensity matching: MWA 3.2 ± 0.8, thyroidectomy 2.9 ± 0.8; *P* = .002 Baseline after propensity matching: MWA 3.2 ± 0.8, thyroidectomy 3.0 ± 1.9; *P* = .478 Follow-up: "A better cosmetic effect in the ultrasound-guided MWA group compared to the conventional thyroidectomy group"
RFA vs. microwave ablation		
Chen et al, 2024[196]	RCT	Cosmetic score (mean ± SD) at 2 years RFA: 1.1 ± 0.49 MWA: 1.2 ± 0.54 Mean difference 0.1 (95% CI −0.1 to 0.2); *P* = .44

Abbreviations: CI, confidence interval; IQR, interquartile range; MWA, microwave ablation; NR, not reported; RCT, randomized controlled trial; RFA, radiofrequency ablation; SD, standard deviation.

[a] RFA change from baseline to 12 months (*P* = .001).

[b] Surgery change from baseline to 12 months (*P* = .001).

RFA Versus Thyroidectomy

The nonrandomized study by Yan et al[122] showed statistically significant improvement in cosmetic appearance from baseline to 12-month follow-up in both the RFA (*P* = .001) and thyroidectomy (*P* = .001) groups.

Based on 1 nonrandomized study, the GRADE quality of the evidence for cosmetic appearance improvement comparing RFA with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A4).

Microwave Ablation Versus Thyroidectomy

In the RCT by Zhi et al,[119] all patients in the microwave ablation and thyroidectomy groups reported cosmetic concerns prior to the intervention. At 12-month follow-up, excellent cosmetic results were reported in 100% of patients in the microwave ablation group and 83% in the thyroidectomy group. In a nonrandomized study, Jin et al[121] narratively reported that better cosmetic effect was observed in the microwave ablation group compared with the thyroidectomy group.

Based on 1 RCT and 1 nonrandomized study, the GRADE quality of the evidence for cosmetic appearance improvement comparing microwave ablation with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A5).

RFA Versus Microwave Ablation

In the RCT by Chen et al,[196] there was no difference in cosmetic score between RFA and microwave ablation at 2-year follow-up.

Based on 1 RCT, the GRADE quality of the evidence for cosmetic appearance improvement comparing RFA with microwave ablation was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A7).

Thyroid Function

Table 5 summarizes the results for thyroid function.

Table 5: Thyroid Function, Symptomatic Benign Thyroid Nodules

Author, year	Study design	Results
RFA vs. thyroidectomy		
Yan et al, 2023[122]	Nonrandomized study	Hypothyroidism after interventions Before propensity matching: RFA 0 (0%), surgery 50 (27.6%); *P* < .001 After propensity matching: RFA 0 (0%), surgery 10 (20.4%); *P* = .001
Microwave ablation vs. thyroidectomy		
Zhi et al, 2018[119]	RCT	Serum TSH, µU/mL (mean ± SD) Baseline: MWA 1.85 ± 1.17, thyroidectomy 1.76 ± 0.83 1 month[a]: MWA 1.82, thyroidectomy 3.94 6 months[a]: MWA 1.96, thyroidectomy 3.59 12 months[a]: MWA 2.10, thyroidectomy 2.81
Jin et al, 2018[121]	Nonrandomized study	"Radionuclide scan of the thyroid showed that the residual thyroid function of all of the subjects in this study was normal"
HIFU ablation vs. lobectomy		
Lang et al, 2019[199]	Nonrandomized study	Hypothyroidism at 6-month follow-up: RFA 0 (0%), surgery 4 (5.2%)

Abbreviations: HIFU, high-intensity focused ultrasound; MWA, microwave ablation; RCT, randomized controlled trial; RFA, radiofrequency ablation; SD, standard deviation; TSH, thyroid-stimulating hormone.

[a] Standard deviation not reported.

RFA Versus Thyroidectomy

In their nonrandomized study, Yan et al[122] reported that thyroid function was well maintained in patients treated with RFA, whereas 27.6% of patients in the thyroidectomy group (20.4% after propensity matching) developed hypothyroidism and needed thyroid hormone replacement.

Based on 1 nonrandomized study, the GRADE quality of the evidence for thyroid function comparing RFA with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A4).

Microwave Ablation Versus Thyroidectomy

In the RCT by Zhi et al,[119] microwave ablation did not affect thyroid function: serum thyroid-stimulating hormone remained stable throughout the 12-month follow-up period. In a nonrandomized study by Jin et al,[121] radionuclide scans of the thyroid gland showed normal thyroid function in all patients.

Based on 1 RCT and 1 nonrandomized study, the GRADE quality of the evidence for thyroid function comparing microwave ablation with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A5).

HIFU Ablation Versus Lobectomy

In their nonrandomized study, Lang et al[199] reported that no patients in the HIFU ablation group developed hypothyroidism, and 5% patients in the lobectomy group had hypothyroidism at 6-month follow-up.

Based on 1 nonrandomized study, the GRADE quality of the evidence for thyroid function comparing HIFU ablation with lobectomy was Low, downgraded due to risk of bias (Appendix 3, Table A6).

Quality of Life

Table 6 summarizes the results for quality of life.

Table 6: Quality of Life, Symptomatic Benign Thyroid Nodules

Author, year	Study design	Results
RFA vs. thyroidectomy		
Yue et al, 2016[123]	Nonrandomized study	SF-36 dimension score after propensity matching, RFA vs. surgery: baseline / 6 months Physical function: 87.5 ± 10.8 vs. 87.1 ± 13.2 / 89.17 vs. 87.9 Role–physical: 91.7 ± 12.8 vs. 90.3 ± 10.2 / 93.47 vs. 93.06 Bodily pain: 92.9 ± 12.8 vs. 94.1 ± 11.1 / 94.44 vs. 94.31 General health: 65.3 ± 15.6 vs. 64.9 ± 16.2 / 68.5[a] vs. 66.7 Vitality: 69.4 ± 15.3 vs. 69.1 ± 17.4 / 71.3 vs. 67.5 Social functioning: 92.5 ± 17.8 vs. 92.5 ± 16.7 / 93.89 vs. 93.33 Role–emotional: 91.7 ± 15.8 vs. 91.0 ± 15.5 / 96.6[b] vs. 94.4[c] Mental health: 75.3 ± 16.3 vs. 76.0 ± 15.7 / 80.9[d] vs. 79.3[e] EQ-5D-3L, RFA vs. surgery at baseline Mobility (*P* = .09) No problems: 108 (78.8%) vs. 229 (85.5%) Some problems: 29 (21.2%) vs. 38 (14.2%) Confined to bed: 0 (0%) vs. 0 (0%) Self-care (*P* = .095) No problems: 131 (95.6%) vs. 263 (98.5%) Some problems: 6 (4.4%) vs. 4 (1.5%) Unable to: 0 (0%) vs. 0 (0%) Usual activities (*P* = .042) No problems: 110 (80.3%) vs. 188 (70.4%) Some problems: 27 (19.7%) vs. 79 (29.6%) Extreme: 0 (0%) vs. 0 (0%) Pain discomfort (*P* = .054) None: 86 (62.8%) vs. 193 (72.3%) Moderate: 51 (37.2%) vs. 74 (27.7%) Extreme: 0 (0%) vs. 0 (0%) Anxiety/depression (*P* = .004) None: 85 (62%) vs. 119 (44.6%) Moderate: 50 (36.5%) vs. 144 (53.9%) Extreme: 2 (1.5%) vs. 4 (1.5%) Patients in perfect health state: 40 (29.2%) vs. 61 (22.8%)
Microwave ablation vs. thyroidectomy		
Zhi et al, 2018[119]	RCT	SF-36 score, MWA vs. surgery; 6 months / 12 months Physical function: 88.15 vs. 87.69 / 88.61 vs. 87.82 Role–physical: 92.40 vs. 91.95 / 92.56 vs. 92.09 Bodily pain: 92.86 vs. 95.14 / 92.72 vs. 94.94 General health: 66.57 vs. 65.20 / 66.61 vs. 65.35 Vitality: 70.97 vs. 70.67 / 71.04 vs. 70.89 Social functioning: 94.07 vs. 92.71 / 93.67 vs. 92.56 Role–emotional: 93.71 vs. 92.71 / 93.35 vs. 92.56 Mental health: 76.60 vs. 74.92 / 77.06 vs. 75.47

Abbreviations: MWA, microwave ablation; NR, not reported; RCT, randomized controlled trial; RFA, radiofrequency ablation.

[a] Significantly improved from baseline (*P* = .012).
[b] Significantly improved from baseline (*P* = .007).
[c] Significantly improved from baseline (*P* = .049).
[d] Significantly improved from baseline (*P* = .002).
[e] Significantly improved from baseline (*P* = .011).

RFA Versus Thyroidectomy

The nonrandomized study by Yue et al[123] reported that general health, assessed by the SF-36 health survey, showed a statistically significant improvement at 6-month follow-up compared with baseline in the RFA group. Role–emotional and mental health showed statistically significant improvements in both RFA and thyroidectomy groups.

Based on 1 nonrandomized study, the GRADE quality of the evidence for quality of life comparing RFA with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A4).

Microwave Ablation Versus Thyroidectomy

The RCT by Zhi et al[119] concluded that compared to patients who underwent thyroidectomy, those who underwent microwave ablation had better general health and mental health scores as measured by the SF-36 health survey at 6- and 12-month follow-up.

Based on 1 RCT, the GRADE quality of the evidence for quality of life comparing microwave ablation with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A5).

Nodule Recurrence Rate

RFA Versus Thyroidectomy

In their nonrandomized study comparing RFA with thyroidectomy, Yan et al[122] did not detect any nodule regrowth. Six ablated nodules (12.2%) disappeared during the follow-up period and had not recurred beyond 12 months.

Based on 1 nonrandomized study, the GRADE quality of the evidence for nodule recurrent rate comparing RFA with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A4).

Adverse Events

Table 7 summarizes the results for adverse events.

Table 7: Adverse Events, Symptomatic Benign Thyroid Nodules

Author, year	Study design	Results
RFA vs. thyroidectomy		
Yan et al, 2023[122]	Nonrandomized study	Treatment-related complications, before propensity matching Any: RFA 0/49 (0%), thyroidectomy 16/181 (8.8%); *P* < .001 Transient recurrent laryngeal nerve palsy: RFA 0 (0%), thyroidectomy 4 (2.2%) Transient hypoparathyroidism: RFA 0 (0%), thyroidectomy 3 (1.7%) Fever: RFA 0 (0%), thyroidectomy 3 (1.7%) Wound infection: RFA 0 (0%), thyroidectomy 4 (2.2%) Respiratory dysfunction: RFA 0 (0%), thyroidectomy 1 (0.6%) Loss of consciousness: RFA 0 (0%), thyroidectomy 1 (0.6%) Treatment-related complications, after propensity matching Any: RFA 0/49 (0%), thyroidectomy 3/49 (6.1%); *P* < .001 Transient recurrent laryngeal nerve palsy: RFA 0 (0%), thyroidectomy 1 (2%) Transient hypoparathyroidism: RFA 0 (0%), thyroidectomy 1 (2%) Fever: RFA 0 (0%), thyroidectomy 1 (2%) Wound infection: RFA 0 (0%), thyroidectomy 0 (0%) Respiratory dysfunction: RFA 0 (0%), thyroidectomy 0 (0%) Loss of consciousness: RFA 0 (0%), thyroidectomy 0 (0%)
Microwave ablation vs. thyroidectomy		
Yan et al, 2018[118]	RCT	Hypercalcemia: MWA 0 (0%), thyroidectomy 1 (2%) Tetany: MWA 0 (0%), thyroidectomy 1 (2%) Cervical hematoma: MWA 0 (0%), thyroidectomy 0 (0%) Recurrent laryngeal nerve injury: MWA 0 (0%), thyroidectomy 0 (0%) Secondary open surgery: MWA 0 (0%), thyroidectomy NR
Zhi et al, 2018[119]	RCT	Numbness: MWA 0 (0%), thyroidectomy 2 (8%) Hoarseness: MWA 1 (4%), thyroidectomy 2 (8%) Postprocedural pain: MWA 2 (28%), thyroidectomy 22 (24%) Postprocedural fever: MWA 0 (0%), thyroidectomy 0 (0%) Postprocedural infection: MWA 0 (0%), thyroidectomy 0 (0%) Skin burn: MWA 0 (0%), thyroidectomy 0 (0%) Neck damage: MWA 0 (0%), thyroidectomy 0 (0%)
Jin et al, 2018[121]	Nonrandomized study	Treatment related complications: MWA 2/106 (1.9%), thyroidectomy 7/106 (6.6%) Paralysis of vocal cords: MWA 1 (0.94%), thyroidectomy 7 (6.6%) Skin burn: MWA 1 (0.94%), thyroidectomy 0 (0%)
HIFU ablation vs. lobectomy		
Lang et al, 2019[199]	Nonrandomized study	Any treatment-related complications: HIFU 4/77 (5.2%), lobectomy 4/77 (5.2%) Vocal cord palsy: HIFU 3 (3.9%), lobectomy 3 (3.9%) Homer's syndrome: HIFU 1 (1.3%), lobectomy 0 (0%) Bleeding: HIFU 0 (0%), lobectomy 1 (1.3%) Infection: HIFU 0 (0%), lobectomy 0 (0%)
RFA vs. microwave ablation		
Chen et al, 2024[196]	RCT	Transient hypertension: RFA 17%, MWA 9.2%; *P* = .11

Abbreviations: HIFU, high-intensity focused ultrasound; MWA, microwave ablation; RCT, randomized controlled trial; RFA, radiofrequency ablation.

RFA Versus Thyroidectomy

In their nonrandomized study, Yan et al[122] reported that no patients who underwent RFA had any adverse events. Patients who underwent thyroidectomy had a statistically significant higher number of adverse events (including transient recurrent laryngeal nerve palsy, transient hypoparathyroidism, and fever) compared with those who underwent RFA (*P* < .001).

Based on 1 nonrandomized study, the GRADE quality of the evidence for adverse events comparing RFA with thyroidectomy was Low, downgraded due to risk of bias (Appendix 3, Table A4).

Microwave Ablation Versus Thyroidectomy

Two RCTs (Yan et al and Zhi et al)[118,119] and 1 nonrandomized study by Jin et al[121] reported adverse events comparing microwave ablation with thyroidectomy. Overall, adverse events (including hypercalcemia, tetany, numbness, hoarseness, and paralysis of vocal cords) occurred more frequently after thyroidectomy than after microwave ablation; however, the absolute number of events was small. The most frequently reported adverse event in the thyroidectomy group was postprocedural pain.

Based on 2 RCTs and 1 nonrandomized study, the GRADE quality of the evidence for adverse events comparing microwave ablation with thyroidectomy was Low to Very low, downgraded due to risk of bias and imprecision (Appendix 3, Table A5).

HIFU Ablation Versus Lobectomy

In the nonrandomized study by Lang et al,[199] the proportion of patients who experienced treatment-related complications was similar for the HIFU ablation and lobectomy groups.

Based on 1 nonrandomized study, the GRADE quality of the evidence for adverse events comparing HIFU ablation with lobectomy was Low, downgraded due to risk of bias (Appendix 3, Table A6).

RFA Versus Microwave Ablation

In the RCT by Chen et al,[196] the incidence of voice change was 1.3% in the RFA group and 6.6% in the microwave ablation group, but this difference was not statistically significant. There were also no statistically significant differences in transient hypertension between the RFA group (17%) and the microwave ablation group (9.2%).

Based on 1 RCT, the GRADE quality of the evidence for adverse events comparing RFA with microwave ablation was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A7).

Ablative Technologies for Cystic Thyroid Nodules

We extracted outcomes related to ablative technologies for cystic thyroid nodules from 2 selected studies[125,126] included in the systematic review by Leon-Salas et al.[77]

Nodule Volume Reduction

Ethanol Ablation Versus RFA

Table 8 summarizes the results for nodule volume reduction.

Table 8: Nodule Volume Reduction, Cystic Thyroid Nodules

Author, year	Study design	Results
Ethanol ablation vs. RFA		
Baek et al, 2015[125]	RCT	6-month follow-up (mean ± SD [range]) Volume reduction, %[a]: ethanol ablation 82.4 ± 28.6 (−35.7 to 99.2), RFA 87.5 ± 11.5 (63.1 to 99.5) Therapeutic success[b]: ethanol ablation 91.7%, RFA 100%
Sung et al, 2013[126]	RCT	6-month follow-up (mean ± SD [range]) Volume reduction, %: ethanol ablation 96.9 ± 4.1 (81.7 to 100), RFA 93.3 ± 5.4 (63.6 to 98.5) Therapeutic success[b]: ethanol ablation 100%, RFA 100%

Abbreviations: RCT, randomized controlled trial; RFA, radiofrequency ablation; SD, standard deviation.

[a] $P > .05$.

[b] Proportion of patients who showed a volume reduction of greater than 50%.

Meta-analysis of RCTs by Baek et al[125] and Sung et al[126] showed no statistically significant difference in nodule volume reduction between patients who underwent ethanol ablation and those who underwent RFA: mean difference 1.43% (95% confidence interval [CI] −5.95% to 8.81%), I^2 = 44%. Logically, there were also no differences in terms of therapeutic success, defined as the proportion of patients who showed a volume reduction of greater than 50%: relative risk 0.96 (95% CI 0.88 to 1.04), I^2 = 14%.

Based on 2 RCTs, the GRADE quality of the evidence for nodule volume reduction comparing ethanol ablation with RFA was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A8).

Symptom Improvement

Ethanol Ablation Versus RFA

Table 9 summarizes the results for symptom improvement.

Table 9: Symptom Improvement, Cystic Thyroid Nodules

Author, year	Study design	Results
Ethanol ablation vs. RFA		
Baek et al, 2015[125]	RCT	6-month follow-up (mean ± SD [range]) Symptom score[a]: ethanol ablation 0.7 ± 1.3 (0–6), RFA 0.2 ± 0.4 (0–1)
Sung et al, 2013[126]	RCT	6-month follow-up (mean ± SD [range]) Symptom score[a]: ethanol ablation 0.5 ± 0.7 (0–2), RFA 0.5 ± 0.8 (0–3)

Abbreviations: RCT, randomized controlled trial; RFA, radiofrequency ablation; SD, standard deviation.

[a] $P > .05$.

In the RCTs by Baek et al[125] and Sung et al,[126] pressure symptoms were measured using a 10 cm visual analog scale of 0 (no symptoms) to 10 (many symptoms). Meta-analysis of these 2 RCTs showed no statistically significant differences in symptom score between patients who underwent ethanol ablation versus RFA: mean difference 0.23 (95% CI −0.26 to 0.71), I^2 47%.

Based on 2 RCTs, the GRADE quality of the evidence for symptom improvement comparing ethanol ablation with RFA was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A8).

Cosmetic Appearance Improvement

Ethanol Ablation Versus RFA

Table 10 summarizes the results for cosmetic appearance improvement.

Table 10: Cosmetic Appearance Improvement, Cystic Thyroid Nodules

Author, year	Study design	Results
Ethanol ablation vs. RFA		
Baek et al, 2015[125]	RCT	6-month follow-up (mean ± SD [range]) Cosmetic score[a]: ethanol ablation 1.7 ± 1.0 (1–4), RFA 1.5 ± 0.5 (1–2)
Sung et al, 2013[126]	RCT	6-month follow-up (mean ± SD [range]) Cosmetic score[a]: ethanol ablation 1.2 ± 0.4 (1–2), RFA 1.1 ± 0.4 (1–2)

Abbreviations: RCT, randomized controlled trial; RFA, radiofrequency ablation; SD, standard deviation.
[a] $P > .05$.

In the RCTs by Baek et al[125] and Sung et al,[126] cosmetic concerns were assessed using a numeric score, with a value of 1 (nonpalpable mass), 2 (noncosmetic problem but palpable mass), 3 (cosmetic problem with swallowing only), or 4 (cosmetic problem easy to detect). Meta-analysis of these 2 RCTs showed no statistically significant differences in cosmetic score between patients who underwent ethanol ablation versus RFA: mean difference 0.12 (95% CI −0.09 to 0.34), I^2 0%.

Based on 2 RCTs, the GRADE quality of the evidence for cosmetic appearance improvement comparing ethanol ablation with RFA was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A8).

Adverse Events

Ethanol Ablation Versus RFA

Table 11 summarizes the results for adverse events.

Table 11: Adverse Events, Cystic Thyroid Nodules

Author, year	Study design	Results
Ethanol ablation vs. RFA		
Baek et al, 2015[125]	RCT	6-month follow-up[a]: ethanol ablation 1/24, RFA 0/22
Sung et al, 2013[126]	RCT	6-month follow-up[a]: ethanol ablation 0/21, RFA 0/21

Abbreviations: RCT, randomized controlled trial; RFA, radiofrequency ablation.
[a] $P > .05$.

In the RCT by Baek et al,[125] no patients in the RFA group reported any adverse events. One patient who underwent ethanol ablation complained of voice change immediately after the procedure, but this resolved without treatment at 2-month follow-up. In an RCT by Sung et al,[126] no adverse events were reported in the RFA or ethanol ablation groups. Meta-analysis of the 2 RCTs showed no

statistically significant difference in adverse events between RFA and ethanol ablation: relative risk 2.76 (95% CI 0.12 to 64.41), I^2 not reported.

Based on 2 RCTs, the GRADE quality of the evidence for adverse events comparing ethanol ablation with RFA was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A8).

Ablative Technologies for AFTNs

We extracted outcomes related to ablative technologies for AFTNs from the selected studies[127-136] included in the systematic review by Javid et al.[70]

Nodule Volume Reduction

After Versus Before RFA

Table 12 summarizes the results for nodule volume reduction.

Table 12: Nodule Volume Reduction, AFTNs

		Volume reduction rate, % (mean ± SD)				
Author, year	**Study design**	**1 mo**	**3 mo**	**6 mo**	**12 mo**	**Last follow-up**
After vs. before RFA						
Bernardi et al, 2017[129]	Prospective noncomparative study	51.06 ± 2.30	62.63 ± 2.13	69.35 ± 2.97	74.78 ± 3.01	74.78 ± 3.01
Cesareo et al, 2018[132]	Prospective noncomparative study	61 ± 10	NA	68 ± 15	75 ± 10	77 ± 11
Dobnig and Amrein, 2018[134]	Prospective noncomparative study	NA	67.4 ± 15.2	86.1 ± 13.4	NA	86.1 ± 13.4
Vu et al, 2022[136]	Prospective noncomparative study	NA	NA	NA	NA	95.65
Baek et al, 2009[127]	Retrospective noncomparative study	36.4 ± 26.1	NA	70.7 ± 22.9	NA	NA
Bernardi et al, 2018[128]	Retrospective noncomparative study	46	NA	NA	74	76
Cappelli et al, 2020[130]	Retrospective noncomparative study	39.5 ± 18.9	NA	65.0 ± 17.7	72.9 ± 18.1	72.9 ± 18.1
Cervelli et al, 2019[131]	Retrospective noncomparative study	NA	NA	NA	76.4 ± 16.9	76.4 ± 16.9
Deandrea et al, 2008[133]	Retrospective noncomparative study	33.1 ± 21.9	49.2 ± 20.1	52.6 ± 16.3	NA	52.6 ± 16.3
Sung et al, 2015[135]	Retrospective noncomparative study	45.9 ± 22.1	64.1 ± 18.4	74.5 ± 15.7	NA	81.7 ± 13.6
Pooled results	–	46.6 (95% CI 40.3–82.9) I^2 = 87.77% P < .001	62.0 (95% CI 57.6–66.4) I^2 = 69.82% P = .01	67.4 (95% CI 62.3–72.6) I^2 = 79.97% P < .001	77.2 (95% CI 79.2–81.5) I^2 = 82.13% P < .001	NA

Abbreviations: AFTN, autonomously functioning thyroid nodule; CI, confidence interval; NA, not applicable; RCT, randomized controlled trial; RFA, radiofrequency ablation; SD, standard deviation.

The pooled estimates of the volume reduction rates from 10 noncomparative studies[127-136] were 46.6%, 62.0%, 67.4%, and 77.2% at 1-, 3-, 6-, and 12-month follow-up, respectively. Nodule volume decreased progressively after RFA.

Based on 10 noncomparative studies, the GRADE quality of the evidence for nodule volume reduction in patients after versus before RFA was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A9).

Thyroid Function

After Versus Before RFA

The pooled proportion of patients with normalization of thyroid-stimulating hormone from 10 noncomparative studies[127-136] was 76.4%, meaning that 76.4% of patients who underwent RFA became euthyroid after a maximum of 12 months from treatment.

Based on 10 noncomparative studies, the GRADE quality of the evidence for normalization of thyroid-stimulating hormone in patients after versus before RFA was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A9).

Symptom Improvement

After Versus Before RFA

Table 13 summarizes the results for symptom improvement.

Table 13: Symptom Improvement, AFTNs

Author, year	Study design	Results
After vs. before RFA		
Bernardi et al, 2017[129]	Prospective noncomparative study	Symptom scale[a]: baseline 2.03 ± 0.11, last follow-up 1.07 ± 0.05
Cesareo et al, 2018[132]	Prospective noncomparative study	VAS (0–10): baseline 1.3 ± 1.7, last follow-up 0.6 ± 0.8
Vu et al, 2022[136]	Prospective noncomparative study	VAS (0–10): baseline 3.47 ± 1.91, last follow-up 0.06
Baek et al, 2009[127]	Retrospective noncomparative study	VAS (0–10): baseline 2.4 ± 1.7, last follow-up 0.6 ± 0.7
Sung et al, 2015[135]	Retrospective noncomparative study	VAS (0–10): baseline 3.3 ± 2.1, last follow-up 0.9 ± 1.0

Abbreviations: AFTN, autonomously functioning thyroid nodule; RFA, radiofrequency ablation; VAS, visual analog scale.
[a] Symptom scale: 1 = absent, 2 = mild intermittent, 3 = mild continuous, 4 = moderate.

Five noncomparative studies reported data on symptom scores. Of these, 4[127,132,135,136] used a visual analog scale with scores ranging from 0 to 10 (the lower the score, the less severe the symptoms). The remaining study[129] used a 4-point scale that depicted the different severity of symptoms, from absent to moderate. The review authors calculated a pooled reduction in symptom scores by combining results from the 4 studies that used the visual analog scale and found a statistically significant decrease in symptom score after RFA: pooled estimate 1.042 (95% CI 0.554–1.530), $P < .001$.

Based on 5 noncomparative studies, the GRADE quality of the evidence for symptom improvement in patients after versus before RFA was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A9).

Cosmetic Appearance Improvement

After Versus Before RFA

Table 14 summarizes the results for cosmetic appearance improvement.

Table 14: Cosmetic Appearance Improvement, AFTNs

Author, year	Study design	Results
After vs. before RFA		
Bernardi et al, 2017[129]	Prospective noncomparative study	4-point scale,[a] mean ± SD: baseline 3.8 ± 0.07, last follow-up 1.74 ± 0.12
Cesareo et al, 2018[132]	Prospective noncomparative study	4-point scale,[a] mean ± SD: baseline 1.2 ± 1.1, last follow-up 0.3 ± 0.5
Vu et al, 2022[136]	Prospective noncomparative study	4-point scale,[a] mean ± SD: baseline 3.59 ± 0.79, last follow-up 1.19
Baek et al, 2009[127]	Retrospective noncomparative study	4-point scale,[a] mean ± SD: baseline 3.1 ± 1.2, last follow-up 1.4 ± 1.0
Sung et al, 2015[135]	Retrospective noncomparative study	4-point scale,[a] mean ± SD: baseline 3.8 ± 0.5, last follow-up 1.9 ± 0.9

Abbreviations: AFTN, autonomously functioning thyroid nodule; RFA, radiofrequency ablation; SD, standard deviation.

[a] Cosmetic improvement 4-point scale: 1 = no palpable mass; 2 = palpable mass but no cosmetic problem; 3 = cosmetic problem on swallowing only; 4 = readily detected a cosmetic problem.

The review authors calculated a pooled reduction in cosmetic score, assessed on a 4-point scale (the lower the score, the less severe the cosmetic concerns), by combining data from 5 noncomparative studies.[127,129,132,135,136] We found a statistically significant reduction in cosmetic score after RFA: pooled estimate 2.053 (95% CI 0.889–3.217), *P* = .001.

Based on 5 noncomparative studies, the GRADE quality of the evidence for cosmetic appearance improvement in patients after versus before RFA was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A9).

Adverse Events

After Versus Before RFA

Table 15 summarizes the results for adverse events.

Table 15: Adverse Events, AFTNs

Author, year	Study design	Results
After vs. before RFA		
Bernardi et al, 2017[129]	Prospective noncomparative study	Transient voice change: n = 1
Cesareo et al, 2018[132]	Prospective noncomparative study	Complications: n = 0
Dobnig and Amrein, 2018[134]	Prospective noncomparative study	Transient voice change: n = 5 Subclinical hypothyroidism: n = 1 Wound infections: n = 2 Hematoma: n = 1
Vu et al, 2022[136]	Prospective noncomparative study	Complications: n = 0
Baek et al, 2009[127]	Retrospective noncomparative study	Subclinical hypothyroidism: n = 1
Bernardi et al, 2018[128]	Retrospective noncomparative study	Transient voice change: n = 1 Third-degree skin burn: n = 1
Cappelli et al, 2020[130]	Retrospective noncomparative study	Hematoma: n = 1
Cervelli et al, 2019[131]	Retrospective noncomparative study	Subclinical hypothyroidism: n = 2
Deandrea et al, 2008[133]	Retrospective noncomparative study	Complications: n = 0
Sung et al, 2015[135]	Retrospective noncomparative study	Complications: n = 0

Abbreviations: AFTN, autonomously functioning thyroid nodule; RFA, radiofrequency ablation.

Four[132,133,135,136] of 10 included studies reported no complications. Among the 6 studies[127-131,134] that did report complications, 7 patients experienced transient voice change, 2 sustained a hematoma, 1 developed a third-degree skin burn, 2 had wound infections, and 4 developed subclinical hypothyroidism after RFA. The pooled occurrence of subclinical hypothyroidism was 4% (95% CI 1.9–8.1%, P = .775, I^2 = 0%).

Based on 10 noncomparative studies, the GRADE quality of the evidence for adverse events in patients after RFA was Low, downgraded due to risk of bias and imprecision (Appendix 3, Table A9).

Ablative Technologies for Small, Low-Risk Papillary Thyroid Cancer

We extracted outcomes related to ablative technologies for small, low-risk papillary thyroid cancer from the systematic review by Nguyen et al.[84]

Tumour Volume Reduction

Table 16 summarizes the results for tumour volume reduction.

Table 16: Tumour Volume Reduction, Small, Low-Risk Papillary Thyroid Cancer

	Results (mean ± SD)							
Author, year	**3 mo**	**6 mo**	**12 mo**	**18 mo**	**24 mo**	**30 mo**	**36 mo**	**42 mo**
Comparative study								
Microwave ablation vs. laser ablation								
Zhou et al, 2020[154]	−58.8 ± 110.1 vs. −441.7 ± 794.7	71.5 ± 38.9 vs. 3.7 ± 86.5	98.0 ± 5.3 vs. 65.8 ± 46.8	NR	99.8 ± 1.2 vs. 96.8 ± 90.0	NR	NR	NR

Author, year	Results (mean ± SD)							
	3 mo	6 mo	12 mo	18 mo	24 mo	30 mo	36 mo	42 mo
Noncomparative studies								
RFA								
Cho et al, 2020[165]	−202.0 ± 787.0	54.0 ± 138.0	NR	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0
Ding et al, 2019[166]	51.9 ± 160.1	97.3 ± 6.3	99.3 ± 3.5	NR	NR	NR	NR	NR
Guang et al, 2017[168]	46.8 ± 9.7	62.5 ± 12.1	77.1 ± 10.6	89.2 ± 8.3	94.9 ± 5.3	NR	NR	NR
He et al, 2021[141]	22.3 ± 57.8	65.9 ± 40.1	86.1 ± 20.3	NR	96.7 ± 8.4	NR	99.8 ± 0.8	NR
He et al, 2021[170]	−170.9 ± 319.5	9.7 ± 128.4	77.9 ± 45.3	99.3 ± 3.6	99.4 ± 3.1	99.8 ± 1.5	99.8 ± 1.5	NR
Jing et al, 2024[172]	−73.5 ± 327.0	31.8 ± 191.6	80.3 ± 67.7	NR	94.6 ± 25.5	NR	99.2 ± 4.7	99.5 ± 3.1
Lim et al, 2019[175]	−953.0 ± 879.0	−348.0 ± 200.0	−16.0 ± 102.0	NR	34.0 ± 43.0	NR	99.8 ± 1.2	99.9 ± 1.0
Lim et al, 2022[157]	−14.5 ± 129.7	54.8 ± 58.9	94.7 ± 13.1	NR	NR	NR	NR	NR
Wang et al, 2024[183]	−58.3 ± 90.3	57.3 ± 36.6	98.0 ± 3.1	NR	NR	NR	NR	NR
Wu et al, 2020[186]	90.5 ± 8.2	96.1 ± 5.9	98.8 ± 3.2	99.6 ± 1.9	99.8 ± 1.0	NR	NR	NR
Yan et al, 2020[188]	−83.5 ± 178.5	34.0 ± 91.7	84.0 ± 34.9	97.8 ± 6.9	99.1 ± 4.2	NR	NR	NR
Yan et al, 2021[187]	−132.9 ± 483.0	10.2 ± 215.9	86.8 ± 34.5	93.9 ± 31.4	97.5 ± 10.1	NR	98.9 ± 7.1	98.8 ± 6.4
Yan et al, 2022[189]	−120.2 ± 452.5	22.1 ± 199.9	86.5 ± 47.3	96.5 ± 12.5	98.3 ± 7.6	NR	99.3 ± 5.5	99.4 ± 4.4
Zhang et al, 2019[192]	95.0 ± 7.0	99.0 ± 3.0	99.9 ± 0.3	100.0 ± 0.0	NR	NR	NR	NR
Zhu et al, 2021[195]	74.0 ± 29.0	90.0 ± 17.0	97.0 ± 7.0	99.0 ± 2.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0
Microwave ablation								
Dong et al, 2024[167]	−241.5 ± 513.6	36.4 ± 158.9	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0
Li et al, 2018[142]	−550.2 ± 559.7	−155.6 ± 270.6	0.6 ± 145.7	57.8 ± 82.2	NR	77.9 ± 43.1	77.9 ± 43.1	81.3 ± 36.9
Teng et al, 2018[158]	−756.0 ± 1,070.5	−62.1 ± 215.6	76.7 ± 52.5	97.8 ± 7.8	97.3 ± 7.8	98.5 ± 5.8	98.5 ± 5.6	NR
Teng et al, 2019[181]	−534.6 ± 758.9	−92.9 ± 321.8	51.1 ± 96.1	84.7 ± 45.7	93.4 ± 18.2	98.2 ± 6.9	98.6 ± 3.6	NR
Teng et al, 2020[182]	−10.7 ± 1244.3	−297.2 ± 583.7	−9.9 ± 240.4	89.6 ± 38.7	98.6 ± 5.7	99.2 ± 4.2	99.4 ± 4.0	99.4 ± 4.0
Wang et al, 2021[146]	−1,408.3 ± 1,839.1	−309.1 ± 578.6	40.6 ± 98.5	90.1 ± 18.7	99.4 ± 1.6	NR	NR	NR
Wu et al, 2021[185]	−480.0 ± 887.0	194.0 ± 611.0	22.0 ± 245.0	50.0 ± 202.0	61.0 ± 138.0	65.0 ± 136.0	86.0 ±75.0	100.0 ± 0.0
Wu et al, 2022[184]	−553.0 ± 1,371.0	−275.0 ± 985.0	−64.0 ± 788.0	−6.0 ± 532.0	13.0 ± 483.0	12.0 ± 534.0	14.0 ± 413.0	100.0 ± 0.0
Yue et al, 2014[160]	48.0 ± 286.0	91.0 ± 13.0	90.0 ± 14.0	NR	NR	NR	NR	NR
Yue et al, 2020[161]	65.8 ± 24.5	86.8 ± 13.1	98.1 ± 3.9	NR	NR	NR	NR	99.4 ± 2.2
Zhou et al, 2019[193]	34.0 ± 67.6	77.6 ± 24.7	98.2 ± 3.1	NR	NR	NR	NR	NR
Zu et al, 2021[155]	−659.2 ± 1,345.5	−166.5 ± 727.9	26.5 ± 262.8	NR	54.7 ± 38.4	NR	63.2 ± 12.5	68.8 ± 24.3
Laser ablation								
Juan et al, 2022[173]	−523.3 ± 201.2	12.1 ± 88.1	31.2 ± 45.2	50.9 ± 12.1	72.1 ± 6.0	84.8 ± 4.1	95.6 ± 2.2	99.5 ±1.0
Offi et al, 2021[177]	49.1 ± 2.1	59.8 ± 3.1	NR	NR	NR	NR	NR	NR
Zhang et al, 2018[191]	−3.3 ± 21.5	2.2 ± 7.6	44.7 ± 4.5	88.5 ± 7.6	95.3 ± 5.3	96.8 ± 5.1	99.1 ± 1.0	99.9 ± 1.0
Zhang et al, 2022[190]	80.4 ± 15.5	91.9 ± 13.0	92.1 ± 12.3	99.0 ± 3.0	99.4 ± 2.3	100.0 ± 0.0	100.0 ± 0.0	NR

Abbreviations: NR, not reported.

Microwave Ablation Versus Laser Ablation

In their comparative study, Zhou et al[154] reported a higher rate of tumour volume reduction in patients who underwent microwave ablation compared to those who underwent laser ablation at 6- and 12-month follow-up. Although both groups reached a tumour volume reduction of greater than 95% at 24-month follow-up, the standard deviation in the laser ablation group was large. No statistical significance was reported.

The GRADE quality of the evidence for tumour volume reduction for microwave ablation and laser ablation was Very low, downgraded due to risk of bias and imprecision (Appendix 3, Table A14).

After Versus Before RFA

The pooled rates for tumour volume reduction in patients who underwent RFA in 15 noncomparative studies[141,157,165,166,168,170,172,175,183,186,188,189,192,195,202] were −82.94% (95% CI −213.85% to 47.97%) at 3 months; 96.39% (95% CI 89.92% to 103.56%) at 24 months; and 99.7% (95% CI 99.47% to 99.99%) at 42 months. In most studies, tumour volume did not decrease until 6 months after RFA.

The GRADE quality of the evidence for tumour volume reduction in patients who underwent RFA was Very low, downgraded due to imprecision (Appendix 3, Table A16).

After Versus Before Microwave Ablation

The pooled rates for tumour volume reduction in patients who underwent microwave ablation in 12 noncomparative studies[142,146,155,158,160,161,167,181,182,184,185,193] were −263.98% (95% CI −375.39% to −152.58%) at 3 months; 88.58% (95% CI 76.31% to 100.8%) at 24 months; and 99.01% (95% CI 96.71% to 101.31%) at 42 months.

The GRADE quality of the evidence for tumour volume reduction in patients who underwent microwave ablation was Very low, downgraded due to imprecision (Appendix 3, Table A17).

After Versus Before Laser Ablation

The pooled rates for tumour volume reduction in patients who underwent laser ablation in 4 noncomparative studies[173,177,190,191] were −155.99% (95% CI −288.95% to −23.03%) at 3 months; 90.9% (95% CI 78.48% to 103.32%) at 24 months; and 99.69% (95% CI 98.26% to 99.99%) at 42 months.

The GRADE quality of the evidence for tumour volume reduction in patients who underwent laser ablation was Very low, downgraded due to risk of bias and imprecision (Appendix 3, Table A18).

Tumour Disappearance Rate

Table 17 summarizes the results for tumour disappearance rate.

Table 17: Tumour Disappearance Rate and Recurrence Rate, Small, Low-Risk Papillary Thyroid Cancer

Author, year	Follow-up, mo	Tumour disappearance rate, n (%)	Tumour recurrence rate, n (%)
Comparative studies			
RFA vs. surgery			
Song et al, 2021[145]	RFA: 26 Surgery: 29	RFA: 115 (100) Surgery: NR	RFA: 1 (0.9) Surgery: 2 (1.9)
Yan et al, 2021[202]	RFA: 47 Surgery: 51	RFA: 300 (90.4) Surgery: NR	RFA: 9 (2.7) Surgery: 6 (1.8)
Yan et al, 2023[149]	RFA: 74 Surgery: 72	RFA: 42 (95.5) Surgery: NR	RFA: 2 (4.5) Surgery: 2 (3.8)
Zhang et al, 2020[152]	RFA: 64 Surgery: 64	RFA: NR Surgery: NR	RFA: 1 (1.1) Surgery: 2 (2.5)
Zhang et al, 2022[151]	RFA: 30 Surgery: 30	RFA: NR Surgery: NR	RFA: 0 (0) Surgery: 1 (0.5)
Microwave ablation vs. surgery			
Guo et al, 2024[137]	MWA: 12 Surgery: 12	MWA: 52 (100) Surgery: NR	MWA: 3 (5.8) Surgery: 1 (1.4)
Li et al, 2018[142]	MWA: 42 Surgery: 42	MWA: NR Surgery: NR	MWA: 0 (0) Surgery: 0 (0)
Li et al, 2019[143]	MWA: 12 Surgery: 12	MWA: 34 (22.7) Surgery: NR	MWA: 7 (4.2) Surgery: 6 (4.2)
Wang et al, 2021[146]	MWA: 12 Surgery: 12	MWA: 55 (87.3) Surgery: NR	MWA: 0 (0) Surgery: 2 (2.4)
Wei et al, 2022[147]	MWA: 36 Surgery: 36	MWA: 249 (71.1) Surgery: NR	MWA: 14 (4.0) Surgery: 14 (4.0)
Zheng et al, 2023[138]	MWA: 13 Surgery: 13	MWA: NR Surgery: NR	MWA: 2 (2.2) Surgery: 3 (2.8)
Zu et al, 2021[155]	MWA: 94 Surgery: 94	MWA: 193 (60.3) Surgery: NR	MWA: 10 (3.1) Surgery: 13 (4.0)
Laser ablation vs. surgery			
Zhou et al, 2019[153]	LA: 36 Surgery: 28	LA: 34 (94.4) Surgery: NR	LA: 2 (5.6) Surgery: 3 (6.6)
RFA vs. microwave ablation			
Cao et al, 2021[139]	RFA: 25 MWA: 25	RFA: NR MWA: NR	RFA: 1 (2.0) MWA: 2 (1.6)
Cao et al, 2021[140]	RFA: 21 MWA: 21	RFA: NR MWA: NR	RFA: 1 (0.5) MWA: 5 (0.9)
Li et al, 2024[144]	RFA: 346 MWA: 166	RFA: NR MWA: NR	RFA: 0 (0) MWA: 0 (0)
Yan et al, 2023[203]	RFA: 77 MWA: 77	RFA: 357 (100) MWA: 114 (97.4)	RFA: 12 (3.4) MWA: 0 (0)
Microwave ablation vs. laser ablation			
Zhou et al, 2020[154]	MWA: 30 LA: 30	MWA: 32 (97.0) LA: 27 (79.4)	MWA: 0 (0) LA: 0 (0)
Noncomparative studies			
RFA			
Cho et al, 2020[165]	72	74 (100)	0 (0)

Author, year	Follow-up, mo	Tumour disappearance rate, n (%)	Tumour recurrence rate, n (%)
Ding et al, 2019[166]	9	37 (97.4)	0 (0)
Guang et al, 2017[168]	21	33 (61.1)	1 (1.8)
He et al, 2021[170]	36	44 (46.3)	1 (1.0)
Jing et al, 2024[172]	40	559 (94.4)	22 (3.7)
Kim et al, 2017[174]	48	4 (66.7)	0 (0)
Lim et al, 2019[175]	39	139 (91.5)	0 (0)
Lim et al, 2022[157]	12	8 (61.5)	0 (0)
Seo et al, 2021[179]	130	3 (60.0)	0 (0)
Song et al, 2020[180]	30	112 (100)	1 (0.9)
Wang et al, 2014[159]	12	NR	2 (10)
Wang et al, 2024[183]	12	NR	0 (0)
Wu et al, 2020[186]	26	96 (47.1)	1 (0.5)
Yan et al, 2020[188]	25	139 (65.9)	0 (0)
Yan et al, 2021[187]	42	366 (88.4)	15 (3.6)
Yan et al, 2022[189]	50	499 (91.4)	16 (2.9)
Zhang et al, 2016[162]	9	98 (100)	0 (0)
Zhang et al, 2019[192]	18	NR	0 (0)
Zhu et al, 2021[195]	60	102 (100)	2 (2.0)
Microwave ablation			
Cao et al, 2020[164]	24	17 (44.7)	0 (0)
Dong et al, 2024[167]	60	158 (100)	2 (1.3)
Han et al, 2020[169]	11	98 (100)	0 (0)
Han et al, 2023[156]	36	1,278 (100)	16 (1.3)
Teng et al, 2018[158]	42	20 (95.2)	0 (0)
Teng et al, 2019[181]	20	174 (84.5)	0 (0)
Teng et al, 2020[182]	60	40 (97.6)	0 (0)
Wu et al, 2021[185]	42	71 (67.0)	3 (2.8)
Wu et al, 2022[184]	36	47 (68.1)	5 (7.3)
Yue et al, 2014[160]	12	18 (100)	0 (0)
Yue et al, 2020[161]	17	89 (74.8)	2 (1.7)
Zheng et al, 2023[163]	26	NR	7 (1.5)
Zhou et al, 2019[193]	9	16 (76.2)	NR
Laser ablation			
Ji et al, 2019[171]	18	37 (100)	1 (2.7)
Juan et al, 2022[173]	60	31 (81.6)	1 (2.6)
Mauri et al, 2016[176]	30	NR	8 (17.4)
Peng et al, 2021[178]	65	103 (98.1)	3 (2.9)
Zhang et al, 2018[191]	26	51 (79.7)	1 (1.6)
Zhang et al, 2022[190]	18	70 (81.4)	4 (4.6)
Zhou et al, 2017[194]	11	30 (100)	0 (0)

Abbreviations: LA, laser ablation; MWA, microwave ablation; RFA, radiofrequency ablation; NR, not reported.

RFA

The pooled rate for tumour disappearance was 95.28% from 20 studies in patients who underwent RFA, which included 3 nonrandomized studies[145,149,202] comparing RFA with surgery, 1 nonrandomized study[203] comparing RFA with microwave ablation, and 16 noncomparative studies.[157,162,165,166,168,170,172,174,175,179,180,186-189,195] There was no statistically significant difference among RFA, microwave ablation, or laser ablation in terms of tumour disappearance rate.

The GRADE quality of the evidence for tumour disappearance rate after RFA was Low to Very low, downgraded due to risk of bias and imprecision (Appendix 3, Table A10, A13, and A16).

Microwave Ablation

The pooled rate for tumour disappearance was 94.45% from 18 studies in patients who underwent microwave ablation, which included 5 nonrandomized studies[137,143,146,147,155] comparing microwave ablation with surgery, 1 nonrandomized study[154] comparing microwave ablation with laser ablation, and 12 noncomparative studies.[156,158,160,161,164,167,169,181,182,184,185,193] There was no statistically significant difference between microwave ablation and laser ablation in terms of tumour disappearance rate.

The GRADE quality of the evidence for tumour disappearance rate after microwave ablation was Low to Very low, downgraded due to risk of bias and imprecision (Appendix 3, Tables A11, A14, and A17).

Laser Ablation

The pooled rate for tumour disappearance was 92.96% from 7 studies in patients who underwent laser ablation, which included 1 nonrandomized study[153] comparing laser ablation with surgery and 6 noncomparative studies.[171,173,178,190,191,194]

The GRADE quality of the evidence for tumour disappearance rate after laser ablation comparing laser ablation with surgery was Low to Very low, downgraded due to risk of bias and imprecision (Appendix 3, Tables A12 and A18).

Tumour Recurrence Rate

Table 17 (above) summarizes the results for tumour recurrence rate.

RFA

The pooled rate for tumour recurrence was 1.65% from 28 studies in patients who underwent RFA, which included 5 nonrandomized studies[145,149,151,152,202] comparing RFA with surgery, 4 nonrandomized studies[139,140,144,203] comparing RFA with microwave ablation, and 19 noncomparative studies.[157,159,162,165,166,168,170,172,174,175,179,180,183,186-189,192,195] Patients who underwent RFA had a statistically significant lower tumour recurrence rate than those who underwent laser ablation (P = .019) or surgery (P = .029).

Over a follow-up period of 18 months or less, the pooled tumour recurrence rate decreased in patients who underwent RFA compared to those who underwent microwave ablation (P = .019), laser ablation (P = .006), or surgery (P = .004). A similar statistically significant trend of lower tumour recurrence rate was observed after RFA compared with other thermal ablation techniques or surgery over a follow-up

period of 19 to 36 months (*P* = .034 for microwave ablation; *P* = .030 for laser ablation; *P* = .006 for surgery). There were no statistically significant differences in tumour recurrence rate with follow-up periods exceeding 3 years.

The GRADE quality of the evidence for tumour recurrence rate after RFA was Low to Very low, downgraded due to risk of bias and imprecision (Appendix 3, Tables A10, A13, and A16).

Microwave Ablation

The pooled rate for tumour recurrence was 1.68% from 20 studies in patients who underwent microwave ablation, which included 7 nonrandomized studies comparing microwave ablation with surgery,[137,138,142,143,146,147,155] 1 nonrandomized study[154] comparing microwave ablation with laser ablation, and 12 noncomparative studies.[156,158,160,161,163,164,167,169,181,182,184,185] Patients who underwent microwave ablation had a statistically significant lower tumour recurrence rate than those who underwent laser ablation (*P* = .002) or surgery (*P* = .003).

The GRADE quality of the evidence for tumour recurrence rate after microwave ablation was Low to Very low, downgraded due to risk of bias and imprecision (Appendix 3, Tables A11, A14, and A17).

Laser Ablation

The pooled rate for tumour recurrence was 3.26% from 8 studies in patients who underwent laser ablation, which included 1 nonrandomized study[153] comparing laser ablation with surgery and 7 noncomparative studies.[171,173,176,178,190,191,194]

The GRADE quality of the evidence for tumour recurrence rate after laser ablation was Low to Very low, downgraded due to risk of bias and imprecision (Appendix 3, Tables A12, and A18).

Surgery

In the systematic review by Nguyen et al,[84] surgery rates compared with different thermal ablation techniques were combined from 13 nonrandomized studies.[137,138,142,143,145-147,149,151-153,155,202] The pooled rate for tumour recurrence for surgery was 2.89%. Variances were not reported.

Surgical Time

Table 18 summarizes the results for surgical time.

Table 18: Surgical Time and Length of Hospital Stay, Small, Low-Risk Papillary Thyroid Cancer

Author, year	Surgical time, min (mean ± SD)	Length of hospital stay, h (mean ± SD)
Comparative studies		
RFA vs. surgery		
He et al, 2021[141]	RFA: 5.2 ± 2.1 Surgery: 109.6 ± 42.2	RFA: NR Surgery: NR
Song et al, 2021[145]	RFA: 8.3 ± 3.2 Surgery: 78.9 ± 12.2	RFA: 2.4 ± 0.2 Surgery: 235.2 ± 98.4
Yan et al, 2021[202]	RFA: 3.4 ± 2.5 Surgery: 86.0 ± 37.0	RFA: 2.4 ± 0.2 Surgery: 168.0 ± 72.0
Yan et al, 2023[149]	RFA: 3.5 ± 2.4 Surgery: 80.0 ± 35.0	RFA: 2.4 ± 0.2 Surgery: 192.0 ± 72.0
Zeng et al, 2023[150]	RFA: 24.7 ± 3.6 Surgery: 58.6 ± 5.9	RFA: 1.8 ± 0.7 Surgery: 3.8 ± 0.9
Zhang et al, 2020[152]	RFA: 8.0 ± 2.2 Surgery: 62.9 ± 15.9	RFA: 2.4 ± 0.2 Surgery: 224.4 ± 105.4
Zhang et al, 2022[151]	RFA: 26.9 ± 3.5 Surgery: 65.4 ± 9.1	RFA: 91.1 ± 30.7 Surgery: 166.6 ± 43.0
Microwave ablation vs. surgery		
Guo et al, 2024[137]	MWA: 28.9 ± 2.5 Surgery: 110.8 ± 39.5	MWA: 1.8 ± 1.7 Surgery: 6.6 ± 2.7
Li et al, 2018[142]	MWA: 10.2 ± 8.4 Surgery: 75.8 ± 11.2	MWA: 31.2 ± 12.2 Surgery: 179.3 ± 70.6
Wang et al, 2021[146]	MWA: 29.7 ± 6.5 Surgery: 69.1 ± 29.6	MWA: 28.6 ± 10.6 Surgery: 128.8 ± 31.4
Wei et al, 2022[147]	MWA: 25.0 ± 17.9 Surgery: 96.0 ± 109.4	MWA: 40.8 ± 35.7 Surgery: 72.0 ± 89.2
Xu et al, 2018[148]	MWA: 25.0 ± 4.1 Surgery: 78.8 ± 12.2	MWA: 42.5 ± 17.0 Surgery: 100.3 ± 13.2
Zheng et al, 2023[138]	MWA: 32.7 ± 5.1 Surgery: 96.6 ± 29.9	MWA: NR Surgery: NR
Zu et al, 2021[155]	MWA: 10.7 ± 8.3 Surgery: 78.5 ± 12.2	MWA: 23.5 ± 5.7 Surgery: 175.6 ± 44.8
Laser ablation vs. surgery		
Zhou et al, 2019[153]	LA: 25.9 ± 7.0 Surgery: 74.2 ± 12.5	LA: 3.6 ± 0.7 Surgery: 62.0 ± 11.4
RFA vs. microwave ablation		
Cao et al, 2021[139]	RFA: 4.0 ± 2.1 MWA: 3.5 ± 2.0	RFA: NR MWA: NR
Microwave ablation vs. laser ablation		
Zhou et al, 2020[154]	MWA: 24.0 ± 5.3 LA: 26.9 ± 5.7	MWA: 3.4 ± 0.5 LA: 3.5 ± 0.6

Abbreviations: LA, laser ablation; MWA, microwave ablation; RFA, radiofrequency ablation; NR, not reported; SD, standard deviation.

Thermal Ablations Versus Surgery

Thermal ablations required a statistically significant shorter surgical time compared to surgery: RFA, standardized mean difference (SMD) −4.81 (95% CI −6.25 to −3.38); microwave ablation, SMD −4.06 (95% CI −5.45 to −2.66); laser ablation, SMD −4.07 (95% CI −7.03 to −1.12).

Based on 7 nonrandomized studies comparing RFA and surgery,[141,145,149-152,202] 7 nonrandomized studies comparing microwave ablation and surgery,[137,138,142,146-148,155] and 1 nonrandomized study comparing laser ablation and surgery,[153] the GRADE quality of evidence for surgical time was Low, downgraded because of nonrandomized studies (Appendix 3, Tables A10, A11, and A12).

Comparison Among Thermal Ablations

There was no statistically significant difference in surgical time among different thermal ablations: laser ablation versus microwave ablation, SMD −0.02 (95% CI −2.96 to 2.93); laser ablation versus RFA, SMD 0.74 (95% CI −2.50 to 3.99); and microwave ablation versus RFA, SMD 0.76 (95% CI −1.12 to 2.63).

Based on 1 nonrandomized study comparing laser ablation with microwave ablation,[154] indirect evidence comparing laser ablation with RFA, and 1 nonrandomized study comparing microwave ablation with RFA,[139] the GRADE quality of the evidence for surgical time was Very low, downgraded due to risk of bias (Appendix 3, Tables A13, A14, and A15).

Length of Hospital Stay

Table 18 (above) summarizes the results for length of hospital stay.

Thermal Ablations Versus Surgery

Thermal ablations required a statistically significant shorter length of hospital stay compared to surgery: RFA, SMD −2.97 (95% CI −4.36 to −1.58); microwave ablation, SMD −3.29 (95% CI −4.63 to −1.95); laser ablation, SMD −4.90 (95% CI −7.46 to −2.34).

Based on 6 nonrandomized studies in RFA and surgery,[145,149-152,202] 6 nonrandomized studies comparing microwave ablation and surgery,[137,142,146-148,155] and 1 nonrandomized study comparing laser ablation and surgery,[153] the GRADE quality of the evidence for length of hospital study was Low, downgraded because of nonrandomized studies (Appendix 3, Tables A10, A11, and A12).

Comparison Among Thermal Ablations

There was no substantial difference in length of hospital stay among the different thermal ablation techniques: laser ablation versus microwave ablation, SMD −1.61 (95% CI −4.16 to 0.94); laser ablation versus RFA, SMD −1.93 (95% CI −4.84 to 0.99); and microwave ablation versus RFA, −0.32 (95% CI −2.25 to 1.61).

Based on 1 nonrandomized study comparing laser ablation and microwave ablation[154] and indirect evidence comparing RFA with microwave ablation or laser ablation, the GRADE quality of the evidence for length of hospital stay was Very low, downgraded due to risk of bias (Appendix 3, Tables A13, A14, and A15).

Postprocedural Pain

Table 19 summarizes the results for postprocedural pain.

Table 19: Postprocedural Outcomes, Small, Low-Risk Papillary Thyroid Cancer

Author, year	Postprocedural pain (mean ± SD)	Postprocedural quality of life (mean ± SD)	Recurrent laryngeal nerve palsy or voice change, n (%)	Overall complications, n (%)
Comparative studies				
RFA vs. surgery				
He et al, 2021[141]	RFA: NR Surgery: NR	RFA: NR Surgery: NR	RFA: 1 (1.1) Surgery: 7 (6.4)	RFA: 2 (2.1) Surgery: 11 (10.0)
Song et al, 2021[145]	RFA: NR Surgery: NR	RFA: 6.8 ± 0.6 Surgery: 5.3 ± 1.0	RFA: 2 (1.7) Surgery: 0 (0.0)	RFA: 2 (1.7) Surgery: 0 (0)
Yan et al, 2021[202]	RFA: NR Surgery: NR	RFA: NR Surgery: NR	RFA: 0 (0.0) Surgery: 13 (3.9)	RFA: 0 (0) Surgery: 15 (4.5)
Yan et al, 2023[149]	RFA: NR Surgery: NR	RFA: NR Surgery: NR	RFA: 0 (0.0) Surgery: 1 (1.9)	RFA: 0 (0) Surgery: 3 (5.7)
Zeng et al, 2023[150]	RFA: 1.2 ± 0.8 Surgery: 2.8 ± 0.9	RFA: NR Surgery: NR	RFA: 1 (1.2) Surgery: 3 (4.1)	RFA: 8 (9.3) Surgery: 11 (14.9)
Zhang et al, 2020[152]	RFA: 1.0 ± 0.1 Surgery: 1.4 ± 0.9	RFA: 4.0 ± 0.1 Surgery: 3.9 ± 0.3	RFA: 0 (0.0) Surgery: 2 (2.5)	RFA: 0 (0.0) Surgery: 3 (3.7)
Zhang et al, 2022[151]	RFA: NR Surgery: NR	RFA: NR Surgery: NR	RFA: 3 (1.9) Surgery: 5 (2.4)	RFA: 4 (2.5) Surgery: 7 (3.4)
Microwave ablation vs. surgery				
Guo et al, 2024[137]	MWA: 1.5 ± 1.3 Surgery: 4.8 ± 2.2	MWA: NR Surgery: NR	MWA: 5 (9.6) Surgery: 1 (1.4)	MWA: 5 (9.6) Surgery: 8 (11.3)
Li et al, 2018[142]	MWA: NR Surgery: NR	MWA: 5.8 ± 0.4 Surgery: 5.0 ± 1.0	MWA: 2 (4.3) Surgery: 8 (17.4)	MWA: 2 (4.4) Surgery: 20 (43.5)
Li et al, 2019[143]	MWA: NR Surgery: NR	MWA: NR Surgery: NR	MWA: 7 (4.2) Surgery: 7 (4.9)	MWA: 7 (4.2) Surgery: 17 (11.9)
Wang et al, 2021[146]	MWA: 0.0 Surgery: 3.4 ± 1.7	MWA: NR Surgery: NR	MWA: 0 (0.0) Surgery: 4 (4.8)	MWA: 24 (38.1) Surgery: 82 (98.8)
Wei et al, 2022[147]	MWA: NR Surgery: NR	MWA: NR Surgery: NR	MWA: 19 (2.4) Surgery: 22 (6.3)	MWA: 22 (6.3) Surgery: 26 (7.4)
Xu et al, 2018[148]	MWA: NR Surgery: NR	MWA: NR Surgery: NR	MWA: 1 (2.4) Surgery: 2 (4.3)	MWA: 2 (4.9) Surgery: 7 (15.2)
Zheng et al, 2023[138]	MWA: 1.4 ± 0.9 Surgery: 3.2 ± 2.0	MWA: 3.8 ± 0.3 Surgery: 3.8 ± 0.3	MWA: 3 (3.3) Surgery: 2 (1.9)	MWA: 3 (3.3) Surgery: 4 (3.8)
Zu et al, 2021[155]	MWA: NR Surgery: NR	MWA: 6.3 ± 1.1 Surgery: 5.4 ± 1.0	MWA: 13 (1.4) Surgery: 12 (3.7)	MWA: 14 (4.4) Surgery: 46 (14.2)
Laser ablation vs. surgery				
Zhou et al, 2019[153]	LA: NR Surgery: NR	LA: NR Surgery: NR	LA: 0 (0.0) Surgery: 2 (4.4)	LA: 1 (2.8) Surgery: 3 (6.7)
RFA vs. microwave ablation				
Cao et al, 2021[139]	RFA: NR MWA: NR	RFA: NR MWA: NR	RFA: 1 (2.0) MWA: 7 (5.7)	RFA: 2 (4.1) MWA: 7 (5.7)
Cao et al, 2021[140]	RFA: NR MWA: NR	RFA: NR MWA: NR	RFA: 2 (1.1) MWA: 12 (2.2)	RFA: 5 (2.7) MWA: 14 (2.6)

Author, year	Postprocedural pain (mean ± SD)	Postprocedural quality of life (mean ± SD)	Recurrent laryngeal nerve palsy or voice change, n (%)	Overall complications, n (%)
Li et al, 2024[144]	RFA: NR MWA: NR	RFA: NR MWA: NR	RFA: 7 (2.0) MWA: 0 (0.0)	RFA: 7 (2.0) MWA: 0 (0.0)
Yan et al, 2023[203]	RFA: NR MWA: NR	RFA: NR MWA: NR	RFA: 1 (0.3) MWA: 7 (5.9)	RFA: 1 (0.3) MWA: 7 (5.9)
Microwave ablation vs. laser ablation				
Zhou et al, 2020[154]	MWA: NR LA: NR	MWA: NR LA: NR	MWA: 1 (3.0) LA: 0 (0.0)	MWA: 3 (9.1) LA: 1 (2.9)

Abbreviations: LA, laser ablation; MWA, microwave ablation; NR, not reported; RFA, radiofrequency ablation; SD, standard deviation.

Thermal Ablations Versus Surgery

Patients who underwent thermal ablations had substantially less postprocedural pain than those who underwent surgery: RFA, SMD −1.28 (95% CI −2.38 to −0.18); microwave ablation, SMD −1.82 (95% CI −2.73 to −0.92).

Based on 2 nonrandomized studies comparing RFA and surgery[150,152] and 3 nonrandomized studies comparing microwave ablation with surgery,[137,138,146] the GRADE quality of the evidence for postprocedural pain was Low, due to nonrandomized studies (Appendix 3, Tables A10 and A11).

Microwave Ablation Versus RFA

There was no substantial difference in postprocedural pain between microwave ablation and RFA: SMD, −0.54 (95% CI −1.97 to 0.88).

Based on indirect evidence, the GRADE quality of the evidence for postprocedural pain was Very low, downgraded due to risk of bias (Appendix 3, Table A13).

Postprocedural Quality of Life

Table 19 (above) summarizes the results for postprocedural quality of life.

Thermal Ablations Versus Surgery

Patients who underwent thermal ablations had substantially better postprocedural quality of life than those who underwent surgery: RFA, SMD 1.21 (95% CI 0.33 to 2.09); microwave ablation, SMD 0.60 (95% CI 0.06 to 1.14).

Based on 2 nonrandomized studies comparing RFA and surgery,[145,152] and 3 nonrandomized studies comparing microwave ablation and surgery,[138,142,155] the GRADE quality of the evidence for postprocedural quality of life was Low, due to nonrandomized studies (Appendix 3, Tables A10 and A11).

Microwave Ablation Versus RFA

There was no substantial difference in postprocedural quality of life between microwave ablation and RFA: SMD −0.61 (95% CI −1.74 to 0.52).

Based on indirect evidence, the GRADE quality of the evidence for postprocedural quality of life was Very low, downgraded due to risk of bias (Appendix 3, Table A13).

Recurrent Laryngeal Nerve Palsy or Voice Change

Table 19 (above) summarizes the results for recurrent laryngeal nerve palsy or voice change.

Thermal Ablations Versus Surgery

The rate of recurrent laryngeal nerve palsy or voice change was lower in patients who underwent RFA than those who underwent surgery (OR 0.34 [95% CI 0.16–0.74]), and this difference was statistically significant. There was no statistically significant difference in recurrent laryngeal nerve palsy or voice change when comparing microwave ablation or laser ablation with surgery.

Based on 7 nonrandomized studies comparing RFA and surgery,[141,145,149-152,202] 8 nonrandomized studies comparing microwave ablation and surgery,[137,138,142,143,146-148,155] and 1 nonrandomized study comparing laser ablation and surgery,[153] the GRADE quality of the evidence for recurrent laryngeal nerve palsy or voice change was Low, due to nonrandomized studies (Appendix 3, Tables A10, A11, and A12).

Comparison Among Thermal Ablations

The rate of recurrent laryngeal nerve palsy or voice change was lower in patients who underwent RFA compared to those who underwent microwave ablation (OR 0.39 [95% CI 0.17–0.87]), and this difference was statistically significant. There was no statistically significant difference when comparing microwave ablation and laser ablation.

Based on 4 nonrandomized studies comparing RFA and microwave ablation[139,140,144,203] and 1 nonrandomized study comparing microwave ablation and laser ablation,[154] the GRADE quality of the evidence for recurrent laryngeal nerve palsy or voice change was Very low, downgraded due to risk of bias (Appendix 3, Tables A13 and A14).

Overall Complications

Table 19 (above) summarizes the results for overall complications.

Thermal Ablations Versus Surgery

Compared with patients who underwent surgery, those who underwent RFA (OR 0.14 [95% CI 0.05 to 0.37]) or microwave ablation (OR 0.26 [95% CI 0.12 to 0.60]) had statistically significant lower overall complication rates. There was no significant difference between laser ablation and surgery (OR 0.18 [95% CI 0.02 to 1.85]).

Based on 7 nonrandomized studies comparing RFA and surgery,[141,145,149-152,202] 8 nonrandomized studies comparing microwave ablation and surgery[137,138,142,143,146-148,155] and 1 nonrandomized study comparing laser ablation and surgery,[153] the GRADE quality of the evidence for overall complications was Low, due to nonrandomized studies (Appendix 3, Tables A10, A11, and A12).

Comparison Among Thermal Ablations

There was no statistically significant difference in overall complication rates among different thermal ablations: laser ablation versus microwave ablation, OR 0.68 (95% CI 0.07 to 7.00); laser ablation versus RFA, OR 1.28 (95% CI 0.11 to 15.26); and microwave ablation versus RFA, OR 1.89 (95% CI 0.67 to 5.36).

Based on 1 nonrandomized study comparing laser ablation and microwave ablation,[156] indirect evidence from comparisons between laser ablation and RFA, and 4 nonrandomized studies comparing microwave ablation with RFA,[141,142,146,204] the GRADE quality of the evidence for overall complications was Very low, downgraded due to risk of bias and imprecision (Appendix 3, Tables A13, A14, and A15).

Ongoing Studies

We are aware of 6 ongoing studies (2 RCTs and 4 prospective cohort studies) on ClinicalTrials.gov and 7 systematic reviews on PROSPERO that have potential relevance to this review (Appendix 6, Tables A23 and A24).

Discussion

In this clinical evidence review on ablative technologies for thyroid nodules, we based our evidence synthesis on data reported in the published reviews. For symptomatic benign thyroid nodules, we leveraged the systematic review published by Nicolopoulos et al (Austrian Institute of Health Technology Assessment).[85] That review specified a priori that it would report evidence of higher quality (i.e., randomized controlled trials and propensity-matched cohort studies), which increased the validity of the conclusions. For cystic thyroid nodules, the systematic review we chose included only 2 randomized controlled trials that were relevant to this health technology assessment, highlighting the scarcity of high-quality evidence in this population.[77] For AFTNs, we found no systematic reviews of comparative studies; instead, we selected a review of noncomparative studies that was low in risk of bias.[70] For papillary thyroid cancer, we selected a network meta-analysis that included 61 publications: only 2 were prospective comparative studies, and the rest of the evidence came from retrospective and/or noncomparative studies.[84] These study designs were limited by risk of selection, recall, and reporting bias, as well as confounding, which meant that their evidence was of low quality.

Despite their heterogeneity in study design and conduct – as well as in patient populations – most of the included studies reported that ablative technologies were as effective as surgery, but generally safer. The effectiveness and safety of the different thermal ablation techniques appeared to be similar, but the evidence was uncertain. Nanosecond pulsed-field ablation is evolving: its nonthermal nature has the potential to reduce the risk of complications and improve healing, and a first in-human clinical feasibility study has been recently published.[204] In principle, thermal ablations cause tissue coagulative necrosis with extreme temperatures, but the various ablative technologies are differentiated by their methods of generating heat. Some systematic reviews and primary studies considered thermal ablation as an overall class for comparison with other treatment options, but this approach did not delineate the specific efficacy of and indications for each type of thermal ablation. The literature is inconclusive about whether different thermal ablative technologies are similar enough to draw single conclusions about them as a class. The 2020 European Thyroid Association Clinical Practice Guideline outlined the indications for each thermal ablative technology as first- or second-line treatment, or based on patient or nodule characteristics.[4] We have reported the outcomes for each ablative technology separately,

which is of particular relevance to this health technology assessment because RFA is the only thermal ablative technology licensed by Health Canada and available for clinical use in Ontario at present.

Most included studies on symptomatic benign thyroid nodules and papillary thyroid cancer were conducted in China; the 2 included studies on cystic thyroid nodules were from South Korea. Although this may limit the generalizability of the results to the Canadian setting, findings may be applicable to a certain extent, considering that immigrants in Ontario from the Philippines, South Korea, and China are at particularly elevated risk of thyroid cancer compared with non-immigrants.[36]

We did not find any data on return to work; however, thyroid diseases have been shown to have an impact on working capacity and income, including risk of unemployment and long-term sick leave.[205] Such effects lead to additional inequities for those who cannot afford the cost of RFA; they must undergo surgery instead, which requires several weeks off work for recovery. In addition, some important patient-reported outcomes – such as the presence of neck scar, lifelong thyroid hormone replacement, and anxiety about cancer progression with delayed surgery – may influence people's preferences for treatment options and may not have been captured in the studies included in this review.

Although RFA is a viable alternative to surgery in symptomatic benign thyroid nodules and small, low-risk papillary thyroid cancer, its indication compared to active surveillance is less defined. We did not find any direct evidence comparing RFA and active surveillance that reported clinical outcomes. Considerations should balance the potential for tumour regrowth with RFA (which may necessitate repeated interventions) and the risk of worsening symptoms and progressive growth with active surveillance.[206] A proportion of people with thyroid nodules or thyroid cancer may avoid surgery or RFA when there is marginal potential therapeutic gain over active surveillance. A recently published Ontario-based prospective cohort study demonstrated that active surveillance is a durable long-term treatment option for small, low-risk papillary thyroid cancer.[207] Patients of older age may be less likely to cross over to surgery after choosing active surveillance.

Ablative technologies are minimally invasive, but they are not risk-free, particularly compared with active surveillance. Adverse events from ablative interventions may be less frequent or less severe than from surgery, but ablative interventions may present a different set of risks. Thermal injury to the recurrent laryngeal nerve causing voice changes or hoarseness has been reported, as well as pain related to applied heat.[55]

A number of international clinical practice guidelines have recommended ultrasound-guided ablative technologies as a treatment option for symptomatic benign thyroid nodules and small, low-risk papillary thyroid cancer, although the evidence these guidelines are based on is of low quality. The literature contains heterogeneities in demographics, nodule and tumour characteristics, treatment conditions, and reported outcomes, as well as the inherent limitations of retrospective and noncomparative study designs. There are also challenges associated with conducting research in these populations, such as difficulty masking treatment and the fact that it is unethical or impractical to perform a sham procedure.

Ablative technologies offer a minimally invasive and reasonably safe option in the spectrum of treatments for people with symptomatic benign thyroid nodules or small, low-risk papillary thyroid cancer. However, active surveillance (i.e., no intervention) for small, low-risk papillary thyroid cancer should also be recognized as a reasonable option, and to date there is no RCT or research that directly

compares thermal ablation and active surveillance. People's anxiety about active surveillance for thyroid cancer may drive them toward a low-risk nonsurgical ablative intervention.

Conclusions

Effectiveness of Ablative Technologies

Symptomatic Benign Thyroid Nodules

- Compared with surgery, RFA may be as effective in reducing nodule volume, improving symptoms, improving cosmetic appearance, and avoiding nodule regrowth. It may also result in better quality of life (GRADEs: Low).
- Compared with microwave ablation, RFA may be as effective in reducing nodule volume, improving symptoms, and improving cosmetic appearance (GRADEs: Low).
- Compared with surgery, microwave ablation may be as effective in reducing nodule volume, but the evidence is very uncertain (GRADE: Very low). It may be as effective in improving symptoms and cosmetic appearance, and it may result in better quality of life (GRADEs: Low).
- Compared with surgery, HIFU ablation may be as effective in reducing nodule volume and improving symptoms, but the evidence is very uncertain (GRADEs: Very low).

Cystic Thyroid Nodules

- Compared with ethanol ablation, RFA may be as effective in reducing nodule volume, improving symptoms, and improving cosmetic appearance (GRADEs: Low).

AFTNs

- Compared with before the intervention, RFA may reduce nodule volume, normalize thyroid-stimulating hormone levels, improve symptoms, and improve cosmetic appearance (GRADEs: Low).

Small, Low-Risk Papillary Thyroid Cancer

- Compared with surgery, RFA may be as effective in terms of tumour disappearance but have a lower tumour recurrence rate. It may require less surgical time and a shorter length of hospital stay. It may be associated with less postprocedural pain and better postprocedural quality of life (GRADEs: Low).
- Compared with microwave ablation, RFA may be similar in terms of tumour disappearance rate, tumour recurrence rate, surgical time, postprocedural pain, and postprocedural quality of life, and it may require a shorter length of hospital stay. However, the evidence is very uncertain (GRADEs: Very low).
- Compared with laser ablation, RFA may require a similar surgical time but may have lower tumour recurrence rate and require a shorter length of hospital stay. However, the evidence is very uncertain (GRADEs: Very low).

- Compared with before the procedure, RFA may reduce tumour volume and be associated with a higher tumour disappearance rate and lower tumour reappearance rate. However, the evidence is very uncertain (GRADEs: Very low).
- Compared with surgery, microwave ablation may be as effective for tumour disappearance, but the evidence is very uncertain (Grade: Very low). It may have a lower tumour recurrence rate, require less surgical time, require a shorter length of hospital stay, and be associated with less postprocedural pain and a better postprocedural quality of life (GRADEs: Low).
- Compared with laser ablation, microwave ablation may be associated with more reduced tumour volume and lower tumour recurrence rate, but may have a similar tumour disappearance rate, surgical time, and length of hospital stay. However, the evidence is very uncertain (GRADEs: Very low).
- Compared with before the procedure, microwave ablation may be associated with a higher tumour disappearance rate (GRADE: Low). It may also be associated with reduced tumour volume and a lower tumour reappearance rate, but the evidence is very uncertain (GRADEs: Very low).
- Compared with surgery, laser ablation may be as effective in terms of tumour disappearance and tumour recurrence, and it may require less surgical time and a shorter length of hospital stay (GRADEs: Low).
- Compared with before the procedure, laser ablation may reduce tumour volume and be associated with a higher tumour disappearance rate and a lower tumour reappearance rate, but the evidence is very uncertain (GRADEs: Very low).

Safety of Ablative Technologies

- Thermal ablative technologies (including RFA, microwave ablation, HIFU ablation, and laser ablation) may not result in hypothyroidism and may lead to fewer adverse events than surgery, but they are not risk-free. The safety profiles among various thermal ablative technologies are comparable (GRADEs: Low to Very low).
- Compared with surgery, RFA may result in a lower rate of recurrent laryngeal nerve palsy or voice changes (GRADE: Low).
- Chemical ablation is a safe procedure associated with minimal adverse events (GRADE: Low).

Economic Evidence

Research Question

What is the cost-effectiveness of ablative technologies compared with surgery, active surveillance, or other ablative technologies for the treatment of symptomatic benign thyroid nodules, cystic thyroid nodules, autonomously functioning thyroid nodules (AFTNs), or small, low-risk papillary thyroid cancer in adults?

Methods

Economic Literature Search

We performed an economic literature search on February 25, 2025, to retrieve studies published from database inception until the search date. To retrieve relevant studies, we developed a search using the clinical search strategy with an economic and costing filter applied.

We created database auto-alerts in MEDLINE and Embase and monitored them until April 1, 2025. We also performed a targeted grey literature search following a standard list of websites developed internally, which includes the International HTA Database and the Tufts Cost-Effectiveness Analysis Registry. See Clinical Literature Search, above, for further details on methods used. See Appendix 2 for our literature search strategies, including all search terms.

Eligibility Criteria

Studies

Inclusion Criteria

- English-language full-text publications
- Cost-benefit analyses, cost-effectiveness analyses, or cost–utility analyses

Exclusion Criteria

- Cost–consequence analyses or cost-minimization analyses
- Systematic reviews
- Narrative reviews, editorials, case reports, commentaries, and abstracts

Population

Inclusion Criteria

- Adults with symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer (tumours < 2 cm maximum diameter)

Exclusion Criteria

- Children (< 18 years of age)
- Pregnant people

Interventions

Inclusion Criteria

- Thermal ablation, including radiofrequency ablation (RFA), microwave ablation, laser ablation, and high-intensity focused ultrasound ablation
- Chemical ablation, including ethanol
- Nanosecond pulsed-field ablation

Exclusion Criteria

- Nonablative technologies

Comparators

Inclusion Criteria

- Surgery
- Active surveillance
- Other ablative technologies (e.g., RFA versus microwave ablation)

Exclusion Criteria

- One versus multiple treatments with the same ablative technology (e.g., 1 vs. 2 RFA sessions)

Outcome Measures

- Costs
- Health outcomes (e.g., quality-adjusted life-years)
- Incremental costs
- Incremental effectiveness
- Incremental cost-effectiveness ratios

Literature Screening

A single reviewer conducted an initial screening of titles and abstracts using Covidence[29] and then obtained the full texts of studies that appeared eligible for review according to the inclusion criteria. The same reviewer then examined the full-text articles and selected studies eligible for inclusion.

Data Extraction

We extracted relevant data on study characteristics and outcomes to collect information about the following:

- Source (e.g., citation information, study type)
- Methods (e.g., study design, analytic technique, perspective, time horizon, population, intervention[s], comparator[s])
- Outcomes (e.g., health outcomes, costs, incremental cost-effectiveness ratios)

Study Applicability and Limitations

We determined the usefulness of each identified study for decision-making by applying a modified quality appraisal checklist for economic evaluations originally developed by the National Institute for Health and Care Excellence (NICE) in the United Kingdom.[208] The NICE checklist has 2 sections: the first is for assessing study applicability, and the second is for assessing study limitations. We modified the wording of the questions of the first section to make it specific to Ontario. Using this checklist, we assessed the applicability of each study to the research question (directly, partially, or not applicable). Next, we assessed the limitations (minor, potentially serious, or very serious) of the studies that we found to be applicable.

Results

Economic Literature Search

The economic literature search yielded 295 citations, including grey literature results and after removing duplicates, published from database inception to February 25, 2025. We identified no additional eligible studies from other sources, including database alerts (monitored until April 1, 2025). In total, we identified 4 studies that met our inclusion criteria. Figure 3 presents the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the economic literature search.

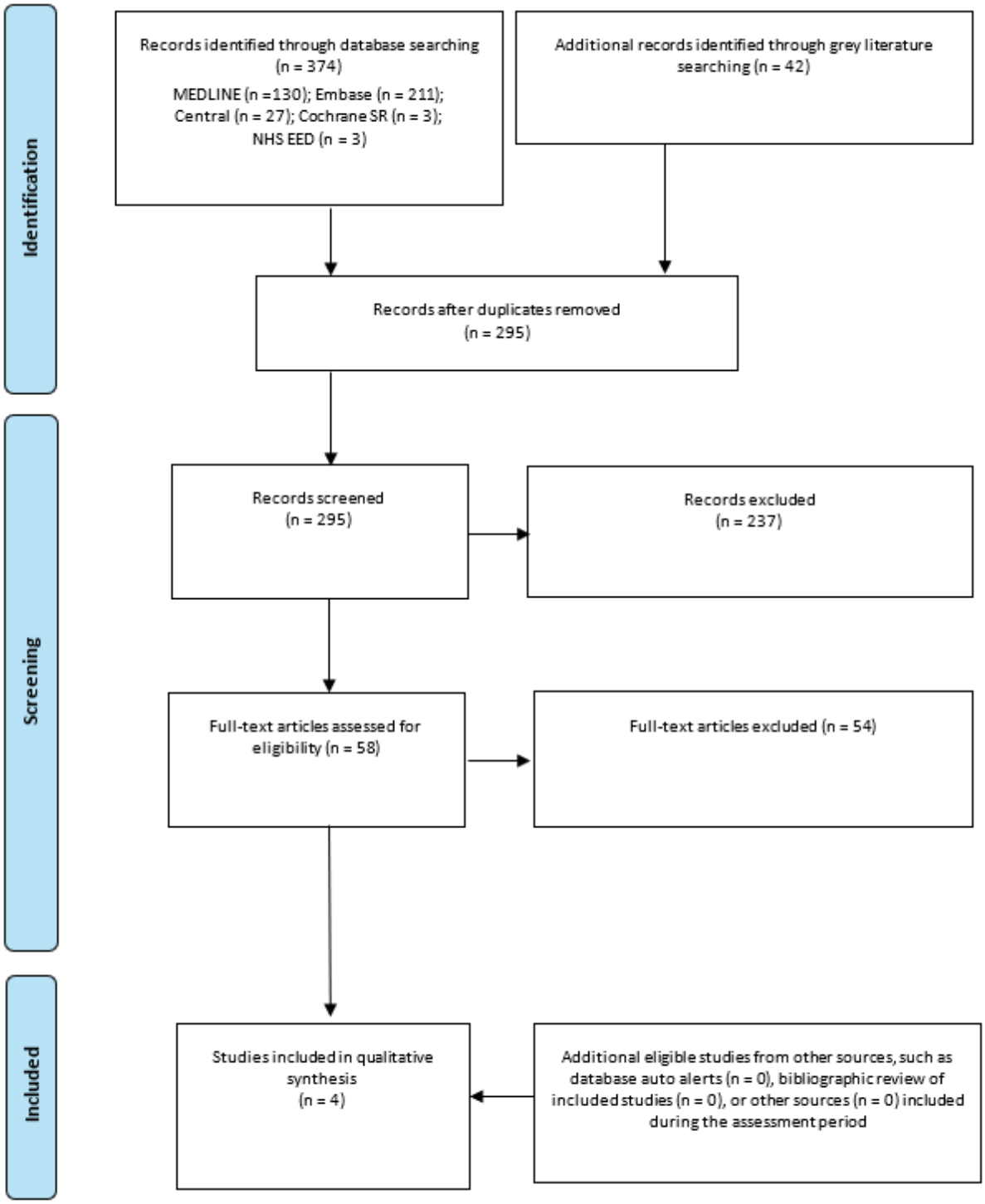

Figure 3: PRISMA Flow Diagram – Economic Systematic Review

PRISMA flow diagram for the economic systematic review. The economic literature search yielded 295 citations, including grey literature results and excluding duplicates, published between database inception and February 25, 2025. We screened 295 abstracts and excluded 237. We assessed the full text of 58 articles and excluded a further 54. In the end, we included 4 articles in the qualitative synthesis.
Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.
Source: Adapted from Page et al.[40]

Overview of Included Economic Studies

We conducted an economic evidence review to identify any relevant economic evaluations assessing the cost-effectiveness of minimally invasive ultrasound-guided ablative technologies compared with standard care for the treatment of adults with symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer (Table 20). Our economic evidence review identified 4 economic studies[123,209-211] that were partially applicable to the research question. All studies evaluated RFA compared with at least 1 alternative strategy for adults with symptomatic benign thyroid nodules,[123,211] AFTNs,[209] or small, low-risk papillary thyroid cancer.[210]

Table 20: Characteristics of Studies Included in the Economic Literature Review

	Analysis				Study population (reference case)			Results		
Author, year, country, intervention, comparator	**Technique**	**Design**	**Perspective**	**Time horizon (discount rate)**	**Age, mean, y**	**Sex**	**Nodule type**	**Health outcomes**	**Costs**	**Cost-effectiveness**
Carlisle et al, 2025,[209] United States I: RFA C: PT, RAI	CUA	Markov model	NR	2 y (3%)	40	F	ATFN[a]	QALYs RFA: 1.78 PT: 1.82 RAI: 1.89 Mean difference, QALYs: RFA vs. PT: −0.04 RFA vs. RAI: −0.11	USD, year NR RFA: $10,087 PT: $9,452 RAI: $2,000 Mean cost difference: RFA vs. PT: $635 RFA vs. RAI: $8,087	RAI was dominant (i.e., lower cost and higher cumulative utility than both PT and RFA). PT was the second less costly option and generated greater utility than RFA PSA showed that at WTP values of $50,000 and $100,000 per QALY, the probabilities of RFA being cost-effective compared with PT were 38% and 40%, respectively. RAI remained the optimal strategy across all WTP values
Carlisle et al, 2024,[210] United States I: RFA C: Active surveillance	CEA	Markov model	Payer (insurance)	10 y (3%)	45	NR	PTMC[b]	NNT to prevent 1 10-year progression, mean (IQR) RFA vs. active surveillance: 18.1 (14.3–30.5)	USD, year NR RFA: $11,684 Active surveillance: $6,366 Mean cost difference, RFA vs. active surveillance: $5,318	The NNT for RFA to prevent 1 outcome of 10-year progression relative to active surveillance was 18.1 (IQR 14.3–30.5), and the cost per progression avoided was $106,500. PSA showed that the probabilities that the NNT would be > 10, > 20, and > 40 for RFA to prevent a single 10-year progression were 94%, 50%, and 16%, respectively

Author, year, country, intervention, comparator	Analysis				Study population (reference case)			Results		
	Technique	Design	Perspective	Time horizon (discount rate)	Age, mean, y	Sex	Nodule type	Health outcomes	Costs	Cost-effectiveness
Kuo et al, 2023,[211] United States I: RFA C: PT	CUA	Patient-level micro-simulation Markov model	Payer	Lifetime (3%)	45	F	Symptomatic benign thyroid nodule[c]	QALYs RFA: 21.31 PT: 21.13 Mean difference, QALYS, RFA vs. PT: 0.18	USD, 2021 RFA: $16,563 PT: $19,262 Mean cost difference, RFA vs. PT: –$2,699	RFA was dominant (i.e., more effective and less costly). At a WTP value of $100,000/QALY, RFA was cost-effective 64% of the time RFA remained cost-effective 63% to 80% of the time when the WTP value varied from $0 to $200,000/QALY RFA was no longer cost-effective if its cost exceeded $12,330 or $17,950 under WTP values of $50,000 and $100,000, respectively

Author, year, country, intervention, comparator	Analysis				Study population (reference case)			Results		
	Technique	Design	Perspective	Time horizon (discount rate)	Age, mean, y	Sex	Nodule type	Health outcomes	Costs	Cost-effectiveness
Yue et al, 2016,[123] China I: RFA C: PT	CUA	Economic evaluation alongside propensity-matched cohort study	Societal	6 mo (NA)	RFA: F 52,[d] M 48.3[e] PT: F 51.5,[d] M 41.9[e]	RFA: M 33.3% PT: M 36.1%	Symptomatic benign thyroid nodule[c]	QALYs RFA: 0.425 PT: 0.415 Mean difference, QALYs, RFA vs. PT: 0.01	CNY, year NR (results also presented in USD using the conversion 1 CNY = $0.1505 USD) Mean direct cost RFA: 18,209 CNY ($2,740 USD) PT: 12,439 CNY ($1,872 USD) Mean total (direct + indirect) cost RFA: 18,660 CNY ($2,808 USD) PT: 13,185 CNY ($1,984 USD) Mean direct cost difference, RFA vs. PT: 5,770 CNY ($868 USD) Mean total (direct + indirect) cost difference, RFA vs. PT: 5,475 CNY ($824 USD)	RFA was more effective and more costly than PT, generating an ICER of $82,400/QALY (calculated) At a WTP value of $50,000/QALY, the probability that RFA would be cost-effective was 12.9% and 15.5% when direct and total (direct and indirect) costs were considered, respectively

Abbreviations: AFTN, autonomously functioning thyroid nodule; AS, active surveillance; C, comparator; CEA, cost-effectiveness analysis; CNY, Chinese yuan; CUA, cost–utility analysis; I, intervention; IQR, interquartile range; NA, not applicable; NNT, number needed to treat; NR, not reported; QALY, quality-adjusted life-year; PSA, probabilistic sensitivity analysis; PT, partial thyroidectomy; PTMC, papillary thyroid microcarcinoma; RAI, radioactive iodine; RFA, radiofrequency ablation.

[a] Presenting with symptoms or biochemical evidence of hyperthyroidism due to 1 dominant AFTN.

[b] PTMC are a subset of papillary thyroid cancer that are less than 1 cm in size.

[c] Solitary benign non-AFTN.

[d] Mean age of women after propensity-score matching.

[e] Mean age of men after propensity-score matching.

Symptomatic Benign Thyroid Nodules

Two studies[123,211] evaluated the cost-effectiveness of RFA compared with partial thyroidectomy for adults with symptomatic benign thyroid nodules.

Kuo et al[211] conducted a patient-level microsimulation (i.e., state-transition) model from the perspective of a third-party payer in the United States over a lifetime time horizon. Future costs and health outcomes were discounted at a rate of 3%. The reference case was a 45-year-old woman with a solitary 30 cm^3 benign thyroid nodule (~4.5 cm in maximum dimension). In the RFA arm of the model, treatment success was defined as a reduction in nodule volume of greater than 50%. Nodule regrowth was defined as a 50% increase in nodule volume within 5 years of the index procedure. The model assumed that people who did not achieve success at 6 months (22%) and those who experienced nodule regrowth (25%) underwent a second RFA session. Health utilities for the different health states were calculated from published literature.

The total cost of the RFA treatment strategy included the cost of each RFA session ($5,000 USD); the costs of follow-up ultrasounds at 1, 3, 6, and 12 months in the first year after the procedure; and the costs of subsequent annual ultrasounds. In comparison, partial thyroidectomy was associated with a 1-time cost ($10,477 USD). It was unclear whether patients who underwent partial thyroidectomy incurred additional follow-up costs. The authors found RFA to be the dominant strategy (i.e., more effective and less costly) at $16,563 USD and 21.31 QALYs, compared with partial thyroidectomy at $19,262 USD and 21.13 QALYs per patient over their lifetime. Results from the probabilistic analyses found that at willingness-to-pay (WTP) thresholds of $50,000 and $100,000 per QALY, RFA had 63% and 64% probabilities of being cost-effective, respectively.

The second study, Yue et al,[123] was a cost–utility analysis, conducted alongside a retrospective propensity-matched cohort study. The study adopted a societal perspective over a 6-month time horizon and compared RFA with partial thyroidectomy. The study included 108 matched patient pairs.

The RFA strategy was associated with a device cost of 13,600 CNY ($2,047 USD), a procedure cost of 22,000 CNY ($3,311 USD), and the cost of a hospital stay (mean duration 2.6 days). Indirect costs (i.e., productivity losses) were calculated using a standard human capital approach. The authors found RFA to be more effective (with an incremental gain of 0.01 in QALYs) and more costly (with an incremental cost of 5,475 CNY [$824 USD]) than partial thyroidectomy. This resulted in an ICER of $82,400 USD per QALY. At a WTP value of $50,000 USD per QALY, RFA had a 15.5% probability of being cost-effective. This probability increased to 36.6% and 88.4% when the device cost for RFA was reduced by 10% and 30%, respectively.

Cystic Thyroid Nodules

We did not identify any relevant studies that evaluated the cost-effectiveness of minimally invasive, ultrasound-guided ablation compared with standard care for adults with cystic thyroid nodules.

AFTNs

Carlisle et al[209] conducted a Markov model–based cost–utility analysis that evaluated RFA compared with partial thyroidectomy and radioactive iodine therapy over a 2-year time horizon. Its reference case was a 40-year-old woman presenting with hyperthyroidism due to AFTNs. Treatment success was defined as achieving a euthyroid state. In the RFA arm, patients could become euthyroid or experience

persistent hyperthyroidism. If hyperthyroidism persisted, patients would undergo partial thyroidectomy. Patients who underwent partial thyroidectomy could become euthyroid or develop hypothyroidism. If hypothyroidism developed, patients were placed on lifelong thyroid hormone replacement therapy. In the radioactive iodine therapy arm, patients could become euthyroid, experience persistent hyperthyroidism, or develop hypothyroidism. Patients with persistent hyperthyroidism would undergo a second radioactive iodine treatment. If their hyperthyroidism persisted following a second treatment, they would undergo partial thyroidectomy. Similar to the study by Kuo et al,[211] RFA cost $5,000 USD per session.

Carlisle et al[209] found radioactive iodine to be more effective (1.89 QALYs) than RFA (1.78 QALYs) and partial thyroidectomy (1.82 QALYs). Radioactive iodine was also less costly ($2,000 USD) compared to RFA ($10,087 USD) and partial thyroidectomy ($9,452 USD). Of the 3 strategies, RFA generated the lowest cumulative utility and highest costs over 2 years. In probabilistic analyses, the probabilities of RFA being more cost-effective than partial thyroidectomy were 38% and 40% at WTP thresholds of $50,000 and $100,000 per QALY, respectively.

Small, Low-Risk Papillary Thyroid Cancer

Carlisle et al[210] conducted a Markov-based cost-effectiveness analysis of RFA compared with active surveillance in adults with papillary thyroid microcarcinoma (PTMC), a subset of small, low-risk papillary thyroid cancers that are less than 1 cm in size. The time horizon was 10 years, and the analysis adopted a societal perspective in the United States. The reference case was a 45-year-old patient with PTMC who had declined surgical treatment. The primary health outcome was the number needed to treat (NNT) for RFA to prevent 1 case of 10-year cancer progression compared to active surveillance. In each cycle, patients in the RFA arm who were in the progression-free health state (i.e., stable disease) were at risk of experiencing disease progression. Patients who experienced disease progression would undergo partial or total thyroidectomy, placing them at risk of permanent recurrent laryngeal nerve injury or hypothyroidism, for which they would require lifelong thyroid hormone replacement therapy. As with the other United States studies,[209,211] the direct cost of RFA was $5,000 USD per session.

Carlisle et al[210] found that the NNT for RFA to prevent a single 10-year progression relative to active surveillance was 18.1 (interquartile range 14.3–30.5) and that the average 10-year costs for RFA and active surveillance were $11,684 USD and $6,366 USD, respectively. The cost per progression avoided was $106,500 USD. In probabilistic analyses, the probabilities that the NNT would be greater than 10, 20, and 40 for RFA to prevent a single 10-year progression were 94%, 50%, and 16%, respectively.

Applicability and Limitations of the Included Studies

Appendix 7 (Tables A25 and A26) provides the results of the quality appraisal checklist for economic evaluations applied to the included studies. All 4 studies were partially applicable to our research question,[123,209-211] and we assessed the limitations of these studies. Two studies had potentially serious limitations[123,209] and the other 2 had minor limitations.[210,211]

Discussion

Our economic evidence review found studies that evaluated the cost-effectiveness of RFA compared with alternative treatment strategies in 3 of our 4 adult populations of interest: those with symptomatic benign nodules, AFTNs, and small, low-risk papillary thyroid cancer. We did not identify any studies that met our inclusion criteria for adults with cystic thyroid nodules. We also did not find any

relevant studies that evaluated the cost-effectiveness of other minimally invasive ultrasound-guided ablation technologies (i.e., chemical ablation, nanosecond pulse-field ablation, or other thermal ablation technologies, such as laser ablation, microwave ablation, or high-intensity focused ultrasound ablation) for the treatment of thyroid nodules.

Symptomatic Benign Thyroid Nodules

For adults with symptomatic benign thyroid nodules, Kuo et al[211] found that RFA was dominant (i.e., more effective and less costly) compared with thyroidectomy. Yue et al[123] found that RFA was more effective but more costly than partial thyroidectomy. In both studies, results were most sensitive to the utility scores associated with post-treatment health states and the direct costs of RFA and partial thyroidectomy.[123,211] There were limitations associated with these parameters across both studies.

For instance, due to a limited availability of studies on preference-based utilities for post-treatment states in thyroid conditions, Kuo et al[211] derived estimated data for health-related quality of life across multiple studies, including studies[123] that may not have been representative of the general population in the United States. This approach introduced uncertainty into the utility parameters used in the model. Yue et al[123] obtained data for health-related quality of life by administering the EQ-5D-3L questionnaire at baseline and 6 months post-treatment for both treatment groups without assessing changes in their quality of life due to thyroid-specific events that may have developed into long-term complications (e.g., hypothyroidism or recurrent laryngeal nerve injury). Therefore, their method of obtaining utilities may not have been sensitive enough (and the study's time horizon long enough) to comprehensively capture important differences in health-related quality of life between groups.

Kuo et al[211] determined the cost of RFA to be $5,000 USD per session, but referenced no source for this value, so it is unclear if this unit cost is generalizable to an Ontario setting. Similarly, the cost parameters included in Yue et al[123] may not represent true resource use and costs in Ontario, because they reflect the health care system in China. Most notably, RFA was costed as an inpatient procedure with an average hospital stay of 2.6 days.[123] In contrast, RFA is currently performed only in outpatient settings in Ontario.

AFTNs

For adults with AFTNs, Carlisle et al[209] found that RFA was the least optimal strategy compared with radioactive iodine and partial thyroidectomy. The results showed that mean QALYs over a 2-year period were similar across all strategies. In contrast, the mean total costs per patient varied substantially. This difference in cost between strategies can be explained by the clinical pathway assumed by the model. In the radioactive iodine arm, patients who experienced persistent hyperthyroidism following treatment were expected to undergo a second radioactive iodine treatment. In comparison, patients with persistent hyperthyroidism after RFA treatment were treated with conventional surgery. Therefore, the RFA strategy incurred not only the cost of the ablation procedure itself but also the cost of partial thyroidectomy and associated surgical complications for patients who did not achieve a euthyroid state after a single initial RFA session. This treatment pathway may not reflect current clinical practice for managing AFTNs with RFA in Ontario. As well, radioactive iodine is associated with important contraindications and may not be suitable for all patients.[212] Last, as with the study by Kuo et al,[211] RFA was assigned a unit cost of $5,000 USD per session without referencing a source for this value.

Small, Low-Risk Papillary Thyroid Cancer

For adults with PMTC (a subset of papillary thyroid cancer), RFA was found to prevent more cases of tumour progression at an incremental cost of $106,500 USD per progression avoided compared to active surveillance.[210] In this study by Carlisle et al, treatment effectiveness was based on being progression-free, without adjustments in health-related quality of life for patients in this health state. Given that patients who are progression-free generally experience greater health-related quality of life compared with those who experience disease progression, the absence of QALYs as an outcome may have underestimated the overall effectiveness of RFA. As well, as with the other United States–based studies,[209,211] the estimated cost of RFA was assumed to be $5,000 USD per session, citing the study by Kuo et al[211] as reference.

Equity Considerations

None of the studies identified equity issues in their assessment processes or incorporated equity-related factors into their analyses.

Strengths and Limitations

Our economic evidence review was a comprehensive review of the literature, because we retrieved studies published from database inception to February 25, 2025. We also performed a grey literature search and reviewed the reference lists of the included studies for any additional studies not identified by our search strategy. As such, it is unlikely that we missed any relevant studies. We also critically appraised the applicability of the studies to our research question and the study limitations using a modified quality appraisal checklist for economic evaluations developed by NICE.[208]

Model structures (reflecting the clinical management pathways for people receiving RFA) varied depending on the study population (i.e., symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer).[123,209-211] The definition of treatment success (e.g., achieving reduction in nodule size, euthyroid state, or progression-free survival) also differed across studies. Therefore, the cost-effectiveness of RFA is likely unique to each study population.

To evaluate the cost-effectiveness of RFA for the treatment of adults with symptomatic benign thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer in Ontario using published literature, it was important to ensure that key cost parameters in the included studies were representative of treatment costs in Ontario. However, the costs reported in the included studies[123,209-211] were unlikely to be generalizable to the Ontario context given that the direct costs of RFA were obtained from a health care system that is substantially different from Ontario's[123] or that were arbitrarily assigned.[209-211] As well, the clinical management pathways modelled in these studies differed from current practice in Ontario. Only half of the included studies evaluated the cost-effectiveness of RFA against all current treatment options in Ontario.[123,211] Similarly, radioactive iodine was used as a comparator to RFA in the study by Carlisle et al,[209] but it is not a first-line treatment strategy for adults with AFTNs in Ontario and is not considered part of usual care. Therefore, a cost-effectiveness analysis of RFA for the treatment of AFTNs in the Ontario setting should include only conventional surgery as the relevant comparator.

Conclusions

We identified 4 economic studies relevant to our research question that evaluated the cost-effectiveness of RFA compared with alternative treatment strategies for 3 of our populations of

interest: adults with symptomatic benign thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer.[123,209-211] For symptomatic benign thyroid nodules, RFA was the dominant strategy (i.e., more effective and less costly) compared with partial thyroidectomy in 1 study[211] and was more effective but more costly in a second study.[123] For AFTNs, RFA was less effective and more costly compared with partial thyroidectomy and radioactive iodine, the latter of which is not routinely used as a first-line treatment in Ontario for this population. For small, low-risk papillary thyroid cancer, RFA was more effective and more costly compared with active surveillance. Across all studies, clinical management pathways and the direct cost of RFA may not have been representative of the Ontario setting.[123,209-211] Furthermore, 2 of the 4 studies did not evaluate RFA against all relevant comparators in their cost-effectiveness analysis.[209,210]

Primary Economic Evaluation

The published economic evaluations identified in the economic literature review addressed the interventions of interest, but none took a Canadian perspective. Furthermore, some evaluations did not include all of the relevant comparators to reflect standard care in Ontario. Owing to these limitations, we conducted a primary economic evaluation to obtain clinical parameters, estimates of resource use, and costs from sources that are generalizable to the Ontario setting.

In this primary economic evaluation, we focused on evaluating minimally invasive, ultrasound-guided radiofrequency ablation (RFA) for 3 populations of interest: symptomatic benign thyroid nodules, autonomously functioning thyroid nodules (AFTNs), and small, low-risk papillary thyroid cancer.

We did not conduct a primary economic evaluation of minimally invasive, ultrasound-guided ethanol ablation for adults with cystic thyroid nodules based on the following considerations:

- Ethanol ablation requires minimal health care resource use and no specialized equipment, and it is a relatively low-cost procedure.
  - The ethanol used in this procedure is not subject to Health Canada regulatory approval and is accessible at a low cost.
  - Ethanol ablation is a brief procedure that typically lasts between 15 and 30 minutes.
- The indication for ethanol ablation is very narrow (Antoine Eskander, MD, telephone communication, March 26, 2025).
  - Ethanol ablation is most effective in purely cystic (entirely fluid-filled) or predominantly cystic thyroid nodules.[18]
  - The number of people with symptomatic cystic thyroid nodules is small. We estimated that the crude prevalence of cystic thyroid nodules that cause compressive symptoms is approximately 0.08% of the adult general population in Canada. We estimated this prevalence using published literature.[7,213] See Appendix 8, Table A27, for further details.
- Given the minimal health care resource use, low cost, and ease of access to necessary supplies for ethanol ablation, as well its very restricted indication, there are few barriers to access in Ontario.

For these reasons, we assumed that the overall cost of ethanol ablation to treat adults with cystic thyroid nodules and the potential impact for the Ministry of Health budget would likely be very small.

Research Questions

1) What is the cost-effectiveness of RFA compared with thyroidectomy for the treatment of symptomatic benign thyroid nodules in adults from the perspective of the Ontario Ministry of Health?
2) What is the cost-effectiveness of RFA compared with thyroidectomy for the treatment of AFTNs in adults from the perspective of the Ontario Ministry of Health?
3) What is the cost-effectiveness of RFA compared with thyroidectomy and active surveillance for the treatment of small, low-risk papillary thyroid cancer in adults from the perspective of the Ontario Ministry of Health?

Methods

The information presented in this report follows the reporting standards set out by the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement.[214] The content of this report is based on a previously developed economic project plan.

Type of Analysis

For each research question, we conducted a cost–utility analysis as recommended by Canada's Drug Agency (CDA) guidelines for economic evaluations.[215] The primary effectiveness outcome was quality-adjusted life-years (QALYs), which quantify both survival and health-related quality of life. A generic outcome measure such as the QALY allows decision-makers to make comparisons across different conditions and interventions. As well, considering people's health-related quality of life captures meaningful differences in effectiveness between interventions as a result of the following:

- The different interventions were not expected to substantially affect long-term survival in our populations of interest. The prognosis for both symptomatic benign thyroid nodules (including AFTNs) and small, low-risk papillary thyroid cancer is highly favourable.[216] The 5-year net survival for thyroid cancer is 98.4% for all thyroid cancers and 99.9% for localized thyroid cancer, such as small, low-risk papillary thyroid cancer.[217] Disease progression (i.e., progressing from benign to malignant) is also unlikely in people with symptomatic benign thyroid nodules and AFTNs.[218]
- Despite this positive prognosis, people living with symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer have reported negative effects for their psychosocial and physical well-being that diminishes their quality of life.[85] Such negative effects include compressive symptoms and cosmetic concerns, endocrine symptoms, and anxiety about the future potential for tumour growth and spread.[85]

Population of Interest

Our populations of interest were adults presenting with symptomatic benign thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer.

We defined symptomatic benign thyroid nodules and AFTNs as those causing persistent and substantial issues that warranted treatment, including difficulty breathing or swallowing, changes in voice, considerable cosmetic concerns, and endocrine symptoms.

We further defined symptomatic benign thyroid nodules as nontoxic ("cold") nodules that are solid or predominantly solid and are large enough (typically > 4 cm in maximum diameter) to cause local pressure on the surrounding structures. This may lead to compressive symptoms, cosmetic concerns, or neck discomfort and pain.[85,219] People with symptomatic benign thyroid nodules may have single or multiple nodules located unilaterally (i.e., the right or the left lobe) or bilaterally (i.e., both lobes).[220]

AFTNs are a subclassification of benign thyroid nodules and are defined as toxic adenomas ("hot nodules") that cause overt hyperthyroidism. AFTNs are largely solitary nodules.[221,222] A population-based study found that in a stable, iodine-sufficient area of Sweden, the incidence of solitary toxic adenomas with overt hyperthyroidism was 1.0 per 100,000 person-years.[223]

For small, low-risk papillary thyroid cancer, people were eligible for RFA therapy if they presented as low-risk with localized papillary thyroid cancer that measured 2 cm or less in maximum diameter, and who either declined or could not undergo surgery.[10,20,224,225]

Subgroup Analysis

Because of limited data, we did not conduct an equity-focused subgroup analysis. In Ontario, more research may be warranted to better understand potential disparities in access to RFA across different population groups.

Perspective

We conducted this analysis from the perspective of the Ontario Ministry of Health.

Interventions and Comparators

We compared the cost-effectiveness of RFA with thyroidectomy for adults with symptomatic benign thyroid nodules and ATFNs. We compared the cost-effectiveness of RFA with 2 standard care options – thyroidectomy and active surveillance – for adults with small, low-risk papillary thyroid cancer. Table 21 summarizes the interventions evaluated in the economic model.

Table 21: Disease Interventions and Comparators Evaluated in the Primary Economic Model

Intervention	Comparator	Population	Outcome
RFA	Partial thyroidectomy	Adults with symptomatic benign thyroid nodules	Incremental QALYs Incremental costs ICERs ($/QALY)
RFA	Partial thyroidectomy	Adults with AFTNs	Incremental QALYs Incremental costs ICERs ($/QALY)
RFA	Partial thyroidectomy[a] Active surveillance	Adults with small, low-risk papillary thyroid cancer	Incremental QALYs Incremental costs ICERs ($/QALY)

Abbreviations: AFTN, autonomously functioning thyroid nodule; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] A partial thyroidectomy may be followed by a complete thyroidectomy if pathology assessment of the initial lobectomy shows risk factors, such as angioinvasion or local invasion.[226,227]

RFA

In Canada, RFA is the only ultrasound-guided ablative technology currently used for the treatment of symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer. To the best of our knowledge, other ablative technologies are unlikely to become available soon in Canada for the treatment of thyroid nodules. This is primarily because of insufficient evidence (i.e., for laser ablation) or comparatively higher costs (i.e., for microwave ablation and high-intensity focused ultrasound ablation). For these reasons, our primary economic evaluation focused on RFA.

Thyroidectomy

The current standard care in Ontario for our populations of interest is thyroidectomy (i.e., surgical removal of the thyroid gland). The 2 main types of thyroidectomy are as follows:

- Partial thyroidectomy (also "lobectomy"), which involves complete removal of 1 lobe of the thyroid gland (i.e., right or left) plus the pyramidal lobe, with or without removal of the isthmus
- Total thyroidectomy, which involves complete removal of the entire thyroid gland, including both lobes, the pyramidal lobe, and the isthmus[228]

In some cases (e.g., tumour recurrence), people who have had a partial thyroidectomy may need subsequent surgery to remove the remaining thyroid gland. This is referred to as a *completion* or *revision* thyroidectomy.

Symptomatic Benign Thyroid Nodules

Most symptomatic benign thyroid nodules are treated with partial thyroidectomy, because they are commonly confined to a single lobe (right or left) of the thyroid gland.[85] Total thyroidectomy may be indicated for symptomatic benign thyroid nodules found in both lobes (e.g., multinodular goiter).[85] In our reference case, we assumed that standard care for all adults with symptomatic benign thyroid nodules was partial thyroidectomy (see Main Assumptions, below, for further details).

There are sometimes concerns that thyroidectomy may be an overtreatment, because it often results in the removal of more than just the nodule and may lead to surgical complications, including neck scarring, injury of the recurrent laryngeal nerve, and development of hypothyroidism.[224,229]

AFTNs

In Ontario, standard care for AFTNs is largely partial thyroidectomy (Antoine Eskander, MD, written communication, April 2024) because AFTNs are generally solitary nodules located in unilateral lobes.[222]

Small, Low-Risk Papillary Thyroid Cancer

For small, low-risk papillary thyroid cancer, standard care in Ontario includes 2 possible options: partial thyroidectomy (a definitive treatment) and active surveillance.[230] This aligns with recommendations in the 2025 American Thyroid Association guidelines.[17]

Active Surveillance

Small, low-risk papillary thyroid cancer is typically asymptomatic and detected incidentally.[231] Active surveillance of the affected nodules (or "watchful waiting") is appropriate, especially for people who would prefer to avoid surgery, are at high surgical risk, or have a relatively short life expectancy.[232,233] However, a portion of small, low-risk papillary thyroid cancers may present with more aggressive features that go undetected under active surveillance.[226,232,233] Furthermore, ongoing active surveillance does not address patient anxiety, which may affect quality of life even in the absence of tumour progression.[232]

Time Horizon and Discounting

We used a lifetime horizon in our reference case analysis with a cycle length of 1 year. This time horizon was appropriate to account for differences in long-term costs (e.g., follow-up, additional treatments) and health outcomes (e.g., symptom relief, hypothyroidism) between treatment strategies. In accordance with the CDA guidelines,[215] we applied an annual discount rate of 1.5% to both costs and QALYs incurred after the first year. All costs are expressed in 2025 Canadian dollars.

Model Structure/Structure of the Analysis

We developed 3 separate Markov models to simulate the relevant costs and health outcomes for each of our populations of interest to assess the cost-effectiveness of minimally invasive ultrasound-guided RFA compared to relevant standard care. The RFA and thyroidectomy arms of these 3 models shared the same structure, but patients incurred different costs and health outcomes depending on their condition. All models had a cycle length of 1 year.

Symptomatic Benign Thyroid Nodules and AFTNs

Figure 4 presents the schematic of the model structure for 2 of the models: adults with symptomatic benign thyroid nodules and adults with AFTNs.

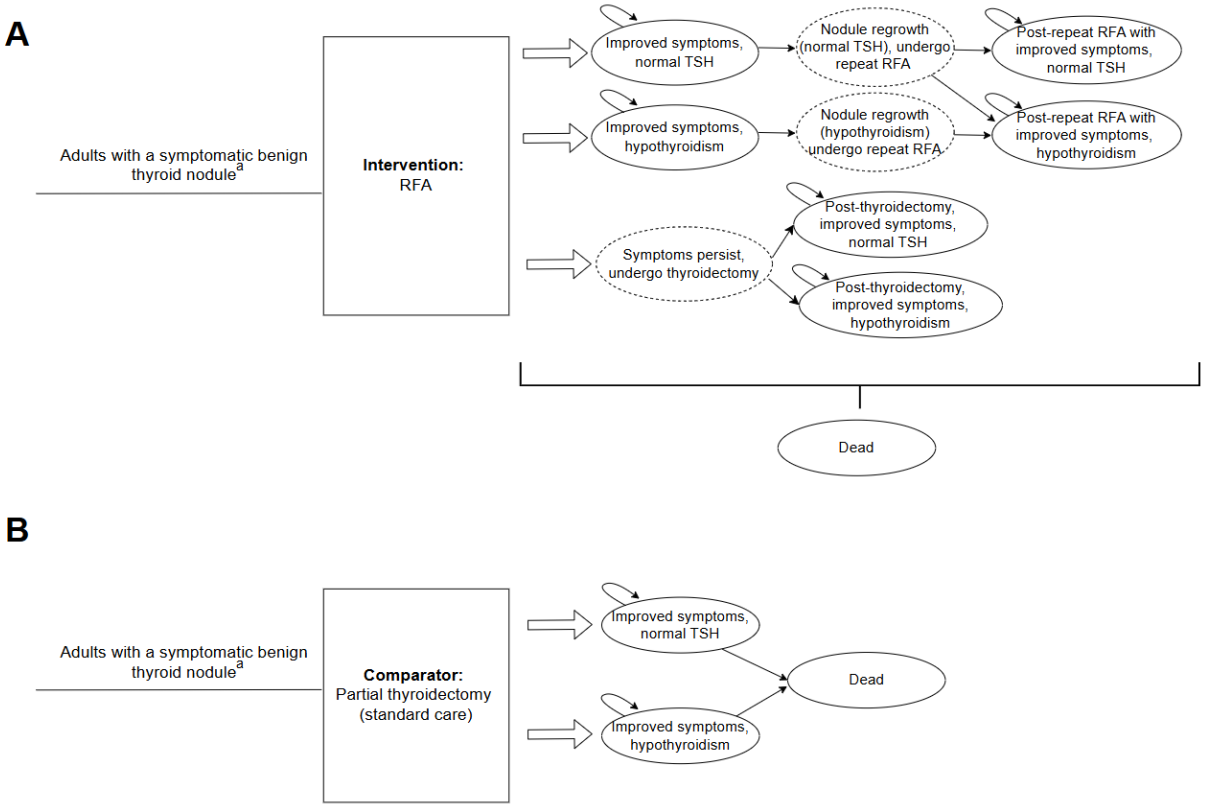

Figure 4: Model Structure for Symptomatic Benign Thyroid Nodules and AFTNs

Figure 4 depicts the model schematic for symptomatic benign thyroid nodules and AFTNs. Rectangles represent decision nodes (about which intervention patients use). Ovals represent health states: those with a solid outline indicate a typical health state, and those with a dotted outline indicate a temporary health state. Arrows represent all possible transitions that occur with each model cycle.

Abbreviations: AFTN, autonomously functioning thyroid nodule; RFA, radiofrequency ablation; TSH, thyroid-stimulating hormone.

[a] Depending on the model, the population of interest may be adults with a symptomatic benign thyroid nodule or adults with an AFTN.

RFA

In the RFA strategy, adults with symptomatic benign thyroid nodules or AFTNs would: achieve treatment success and improved symptoms while maintaining normal thyroid function (i.e., maintain normal TSH levels); achieve treatment success and improved symptoms but develop post-treatment hypothyroidism as a long-term complication; or not achieve treatment success and continue to experience persisting symptoms. People were also at risk of transient injury to the recurrent laryngeal nerve, a potential short-term, procedure-related complication following RFA or partial thyroidectomy. Those who experienced transient recurrent laryngeal nerve injury experienced reduced health-related quality of life in the first cycle only, because this commonly resolves on its own.[234] People who developed post-

treatment hypothyroidism required thyroid hormone supplementation (i.e., levothyroxine) and experienced reduced health-related quality of life for the remainder of their expected lifespan.

In subsequent cycles, people who achieved symptom relief following RFA could continue to experience improvement (with or without hypothyroidism) or develop nodule regrowth. Those who experienced nodule regrowth would undergo a repeat RFA session, which was expected to restore symptom relief. They could also incur an additional 1-time utility decrement due to procedure-related recurrent laryngeal nerve injury. People who developed hypothyroidism after the initial RFA session would continue levothyroxine treatment, and those who initially maintained normal TSH levels would remain at risk of developing post-treatment hypothyroidism.

Those who failed to achieve treatment success with RFA in the first cycle would proceed to partial thyroidectomy, which would provide symptom relief with or without the development of hypothyroidism for the remainder of the model. In any given cycle, people would have a probability of death.

Partial Thyroidectomy

In the partial thyroidectomy strategy, people would enter the model in the improved symptoms health state, with normal TSH levels or with post-treatment hypothyroidism. As in the RFA arm, people would be at risk of transient recurrent laryngeal nerve injury following partial thyroidectomy, which is associated with a temporary reduction in health-related quality of life during the first cycle only. In subsequent cycles, people would continue to experience symptom relief, with or without hypothyroidism. In this strategy there was no risk of nodule regrowth, because the procedure removes the entire nodule along with the affected lobe. In any given cycle, people would have a probability of death.

Small, Low-Risk Papillary Thyroid Cancer

Figure 5 presents the schematic of the model structure for adults with small, low-risk papillary thyroid cancer.

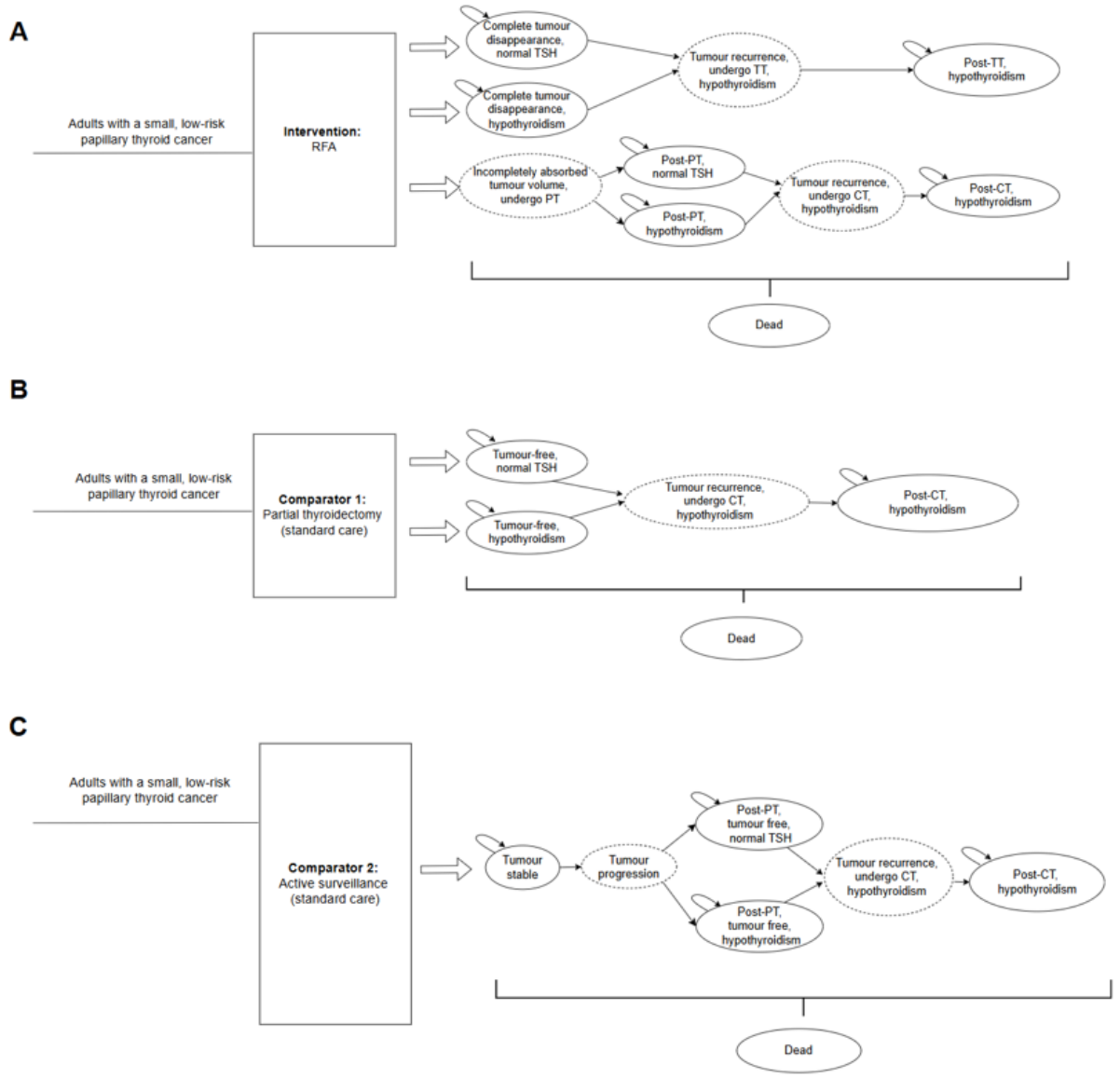

Figure 5: Model Structure for Small, Low-Risk Papillary Thyroid Cancer

Figure 5 depicts the model schematic for small, low-risk papillary thyroid cancer. Rectangles represent decision nodes (about which intervention patients use). Ovals represent health states: those with a solid outline indicate a typical health state, and those with dotted outline indicate a temporary health state. Arrows represent all possible transitions that occur with each model cycle.

Abbreviations: CT, completion thyroidectomy; PT, partial thyroidectomy; RFA, radiofrequency ablation; TSH, thyroid-stimulating hormone; TT, total thyroidectomy.

RFA

Adults with small, low-risk papillary thyroid cancer undergoing RFA would: achieve complete tumour disappearance while maintaining normal thyroid function; achieve complete tumour disappearance but develop lifelong hypothyroidism as a long-term complication; or not achieve treatment success and have remaining incompletely absorbed tumour volume. As in the RFA arm for the other 2 models, people would also be at risk of transient injury to the recurrent laryngeal nerve.

In subsequent cycles, people who achieved complete tumour disappearance following RFA could continue to remain progression-free (with or without hypothyroidism) or experience tumour recurrence. Those who experienced tumour recurrence would undergo total thyroidectomy, which is curative but exposes people to higher risk of transient injury to the recurrent laryngeal nerve and results in definite post-treatment hypothyroidism. Following total thyroidectomy, all people would be tumour-free.

People with tumours that were incompletely absorbed by RFA in the first cycle would proceed with partial thyroidectomy to have their tumour surgically removed, after which they would transition through the same model structure as the partial thyroidectomy strategy for the remainder of the model. In any given cycle, people would have a probability of death.

Partial Thyroidectomy

In the partial thyroidectomy strategy, people would enter the model tumour-free, with or without post-treatment hypothyroidism, and would be at risk of transient injury to the recurrent laryngeal nerve in the first cycle. In subsequent cycles, people would remain progression-free or have a tumour recurrence. Those who experienced tumour recurrence would undergo completion thyroidectomy (also called *revision* thyroidectomy), from which they would again be exposed to a higher risk of transient injury to the recurrent laryngeal nerve and develop post-treatment hypothyroidism. Following completion thyroidectomy, all people would be tumour-free. In any given cycle, people would have a probability of death.

Active Surveillance

With active surveillance, people would enter the model in a stable tumour health state. In subsequent cycles, they would either remain in a stable tumour state with no change, or they would experience tumour progression. Those who experienced tumour progression would undergo partial thyroidectomy and transition through the same model structure as the partial thyroidectomy strategy for the remainder of the model. In any given cycle, people would have a probability of death.

Main Assumptions

Our models' main assumptions were as follows:

Symptomatic Benign Thyroid Nodules

- People entering the model presented with a single, symptomatic thyroid nodule that was solid or predominantly solid in composition; wanted an intervention to resolve symptoms; and had nodules that were confirmed to be benign based on the Bethesda System for Reporting Thyroid

Cytopathology[235] for thyroid fine-needle aspiration cytology before their procedure (RFA or partial thyroidectomy). We made these simplifying assumptions from the following considerations:

  - Based on the 2023 American Thyroid Association statement[18] on the adoption of ablation techniques for symptomatic benign thyroid nodules, RFA was specified as most appropriate for people who experience compressive symptoms and/or cosmetic complaints that are attributed to a single or dominant nodule.
  - There is a very small risk that a nodule with a benign result from fine-needle aspiration cytology is malignant. This risk is reported as less than 3% and may often not affect or require any changes to patient management.[235] Therefore, we did not account for this error rate in our reference case, but we did account for it in a scenario analysis (see scenario 5 of our model for adults with symptomatic benign thyroid nodules).

- The mortality rate for people with symptomatic benign thyroid nodules was equal to that of the general population.
- For RFA:
  - The technical efficacy of RFA (referred to as "treatment success") was defined as a decrease of greater than 50% in the nodule's initial volume at 1 year postprocedure. This was expressed as a volume reduction ratio of greater than 50%.[85,103] Most studies used this threshold to define treatment success, because a decrease in nodule volume is associated with improvement in symptoms.[85]
  - 2.3% of patients undergoing RFA would require a second ablation session in the first cycle of the model.[120]
  - Nodule regrowth following treatment success with the initial RFA was defined as meeting 1 or more of the following criteria: an increase of greater than 50% over the smallest recorded volume; an increase of greater than 20% in nodule volume from the volume at 1 year after RFA; and nodule volume larger than the initial nodule volume.[236]
  - All patients with nodule regrowth would receive RFA treatment again, and we further assumed that this would achieve treatment success. We made these assumptions because of a scarcity of long-term data on treatment outcomes for nodule regrowth following RFA.
  - All people were at risk of a 1-time nodule regrowth in the first 10 years following the initial RFA treatment, after which we assumed the risk would be zero. We made this assumption because of a lack of published literature on lifelong nodule regrowth among ablated thyroid nodules. As such, the frequency of nodule regrowth over a person's lifetime is currently unknown.[237]
- For partial thyroidectomy:
  - All people were treated with a partial thyroidectomy.
  - We assumed that the risk of perioperative mortality associated with partial thyroidectomy was zero, because it is a generally safe procedure with a low rate of perioperative mortality.[238]

Autonomously Functioning Thyroid Nodules

- People entering the model presented with a solitary toxic adenoma that was causing overt hyperthyroidism and they wanted intervention to resolve symptoms.

- The mortality rate for people with AFTNs was equal to that of the general population.
- For RFA:
  - Treatment success was defined as when normalization of thyroid-stimulating hormone (TSH) was achieved (i.e., when the patient became euthyroid).[239]
  - Nodule regrowth following treatment success with the initial RFA was defined in the same way as for symptomatic benign thyroid nodules, above.
  - We made the same assumptions about nodule regrowth as we did for symptomatic benign thyroid nodules, because the included populations in primary clinical studies and systematic reviews on thermoablation technologies often include patients with either "cold" or "hot" nodules without reporting outcomes further by subclass.[85]
- For partial thyroidectomy:
  - All people were treated with a partial thyroidectomy.
  - We assumed that the risk of perioperative mortality associated with partial thyroidectomy was zero.

Small, Low-Risk Papillary Thyroid Cancer

- All people entering the model presented with a single primary small, low-risk papillary thyroid cancer.
- The mortality rate for people with small, low-risk papillary thyroid cancer was equal to that of the general population. We made this simplifying assumption because small, low-risk papillary thyroid cancer has an excellent prognosis, and excess mortality is very low.[218]
- Tumour recurrence following treatment in this population is defined as local tumour progression at the lymph nodes or the contralateral lobe.[84] We made this assumption because small, low-risk papillary thyroid cancer is considered to be indolent; the occurrence of distant metastases is extremely rare.[240,241]
  - All people were at risk of a 1-time tumour recurrence following RFA treatment or partial thyroidectomy within the first 3 years. We did not account for tumour recurrence after this time period, because there is no statistically significant difference in tumour recurrence rates among patients who received RFA or partial thyroidectomy with a follow-up time exceeding 3 years[84] (see Clinical Evidence for further details).
  - For simplicity, we assumed a constant rate of tumour recurrence within the first 3 years following treatment.
- For RFA:
  - Treatment success for ablation therapy in this population was defined as the complete disappearance of tumour tissue.[84]
  - We assumed that all people undergoing RFA required only 1 ablation session, because low-risk papillary thyroid cancers are smaller than symptomatic benign thyroid nodules and AFTNs.
  - We assumed conservatively that tumour recurrence following the initial RFA session would be treated with total thyroidectomy in our reference case.

- For partial thyroidectomy:
  - All people were treated initially with partial thyroidectomy. This assumption was aligned with the 2025 American Thyroid Association guidelines for differentiated thyroid cancer, which recommend partial thyroidectomy as the initial surgical procedure for low-risk thyroid cancers of 2 cm or less in maximum diameter.[17] People may subsequently undergo a completion thyroidectomy in the event of tumour recurrence.
  - We assumed that the risk of perioperative mortality associated with all thyroidectomies (i.e., partial, total, or completion) was zero, because they are generally safe procedures with a low rate of perioperative mortality.[242]
- For active surveillance:
  - Tumour progression was defined as a tumour size increase of 3 mm or more in 1 dimension or as development of lymph node metastases.[233,243]
  - People were at risk of tumour progression only in the first 10 years of the model. After this, we assumed that the risk of tumour progression was zero. We made this assumption because the longest observational trial of active surveillance in adults with papillary thyroid cancer to date has a 10-year follow-up period.[244] The available data did not support reliable extrapolation of tumour progression outcomes in this population beyond 10 years.
- We made the following additional assumptions for people receiving total or completion thyroidectomy following tumour recurrence:
  - We did not account for risk of tumour recurrence following a total or completion thyroidectomy. The overall risk of tumour recurrence is very low (1.3%) following total or completion thyroidectomy for small, low-risk papillary thyroid cancer.[245] As well, treatment options for tumour recurrence following total or completion thyroidectomy may vary greatly (from active surveillance to neck dissection or targeted therapy) depending on the location, extent, and other clinical factors of the tumour.
  - We assumed the same complication rates for total and completion thyroidectomy, because the surgical risks and side effects for both are similar.[17]

Clinical Outcomes and Utility Parameters

We determined the starting age for each cohort using the average age of participants reported in key clinical sources. We estimated the annual probability of all-cause mortality for all cohorts based on survival estimates for Ontario from Statistics Canada life tables for 2023.[246] Where possible, we obtained clinical parameter inputs from the systematic reviews included in the clinical evidence review.

Symptomatic Benign Thyroid Nodules and AFTNs

For adults with symptomatic benign thyroid nodules, we obtained the comparative efficacy of RFA compared with partial thyroidectomy and the starting age of the cohort from Bo et al,[120] a retrospective, propensity-score-matched nonrandomized study included in the 2024 systematic review by Nicolopoulos et al (Austrian Institute of Health Technology Assessment)[85] that was identified in the clinical evidence review. Bo et al[120] evaluated treatment outcomes for those who underwent thermal ablation (i.e., RFA or microwave ablation), partial thyroidectomy, and endoscopic thyroidectomy. For

our model, we based the starting age of adults with symptomatic benign thyroid nodules on the average age of participants in the thermal ablation group in that study, which was 50.9 ± 14.0 years (range: 21 to 74 years).

Data from Bo et al[120] were not extracted for the clinical evidence review because outcomes were not reported separately for each ablative technology. However, we did extract data for the economic evaluation because the authors reported volume reduction ratio and technical efficacy (i.e., treatment success) for thermal ablation. Given that safety profiles and tumour reduction efficacy are comparable for RFA and microwave ablation (see Clinical Evidence), we assumed that the reported outcomes for thermal ablation would be representative of each technology separately. From Bo et al,[120] we estimated that the technical efficacy rate for RFA was 92.2%, based on observed counts of those who experienced technical success with RFA and those who did not (119/129); 2.3% of patients (3/129) received a second ablation session. No technical efficacy rate was reported for the partial thyroidectomy group, because the entire affected thyroid lobe was removed.

For adults with AFTNs, we obtained the comparative efficacy of RFA and partial thyroidectomy, as well as the starting age for this cohort, from the systematic review by Javid et al,[70] which was included in the clinical evidence review. The authors estimated that 76.4% of the pooled proportion of patients were euthyroid following RFA. We based the starting age of adults with AFTNs for our model on the average age of participants across all included studies in the systematic review, which was 57.31 years of age.

Given that the safety outcomes for RFA and partial thyroidectomy are similar for the treatment of symptomatic benign thyroid nodules and AFTNs, we applied the following clinical parameters to both models. For procedure-related complications, Bo et al[120] reported that post-treatment hypothyroidism was lower in patients who had undergone thermal ablation (0.8%) compared to those who had undergone surgery (25.4%), and this difference was statistically significant ($P < .001$). This finding was consistent with the outcomes reported for thyroid function in the clinical evidence review for both treatment groups (see Clinical Evidence for further details).

The second most common procedure-related complication of partial thyroidectomy is injury to the recurrent laryngeal nerve. Injury to this nerve may be temporary or permanent, but most people with this postoperative complication recover on their own under observation. We obtained the occurrence of transient injury to the recurrent laryngeal nerve following surgery from Beka et al.[247] This large, retrospective study from Sweden analyzed procedure-related complications from partial thyroidectomies performed to relieve compressive symptoms for symptomatic benign thyroid nodules or to investigate a cancer suspicion (i.e., exclude malignancy). The authors reported that postprocedure transient unilateral injury to the recurrent laryngeal nerve occurred in 2.8% of the compression group. We obtained the occurrence of transient injury to the recurrent laryngeal nerve following RFA from a network meta-analysis conducted by Chorti et al.[53] This review, which compared short-term outcomes of thermal ablation techniques and surgical interventions for the treatment of symptomatic benign thyroid nodules, found that RFA had a reduced risk of transient injury to the recurrent laryngeal nerve compared with thyroidectomy (risk ratio 0.05 [95% CI 0.00–0.40]).

Finally, we obtained the probability of nodule regrowth following RFA from Park et al,[236] who examined the long-term outcomes of RFA for the treatment of benign thyroid nodules in a large, retrospective study. They reported that the 10-year cumulative incidence of nodule regrowth among ablated thyroid nodules was 21%. To obtain the annual probability of nodule regrowth, we digitized the Kaplan–Meier

curve from the source publication and estimated the annual probability of nodule regrowth at each yearly interval (see Appendix 8, Table A28, for further details).

Table 22 summarizes the clinical parameter inputs for symptomatic benign thyroid nodules and ATFNs.

Table 22: Clinical Parameter Inputs Used in the Economic Model, Symptomatic Benign Thyroid Nodules and ATFNs

Model parameter	Mean (95% CI)	Distribution (parameter 1, parameter 2)[a]	Reference
Partial thyroidectomy			
Probability of transient injury to the RLN	0.028 (0.023–0.034)[b]	Beta (97, 3,373)[b]	Beka et al, 2023[247]
Probability of post-treatment hypothyroidism	0.254 (0.214–0.29)[c]	Beta (30, 88)	Bo et al, 2022[120]
RFA			
Treatment success rate[d] at 1 year, symptomatic benign thyroid nodules	0.922 (0.90–0.95)[c,e]	Beta (119, 10)	Bo et al, 2022[120]
Treatment success rate[f] at 1 year, AFTNs	0.764 (0.58–0.884)	Beta (22, 7)	Javid et al, 2024[70]
Probability of requiring an additional ablation session	0.023 (0.005–0.055)[g]	Beta (3, 126)	Bo et al, 2022[120]
Treatment effect on risk of transient injury to the RLN	RR 0.050 (0.00–0.40)[h]	Lognormal (−2.996, 5.64)	Chorti et al, 2023[53]
Probability of post-treatment hypothyroidism	0.008 (0.0002–0.031)[g]	Beta (1, 117)	Bo et al, 2022[120]
10-year cumulative probability of nodule regrowth[i]	0.21 (NA)	Fixed	Park et al 2024[236]

Abbreviations: AFTN, autonomously functioning thyroid nodule; CI, confidence interval; NA, not applicable; RFA, radiofrequency ablation; RLN, recurrent laryngeal nerve; RR, risk ratio; TSH, thyroid-stimulating hormone.

[a] For beta distribution, parameter 1 = alpha, parameter 2 = beta; for lognormal distribution, parameter 1 = alpha, parameter 2 = beta.

[b] We estimated a beta distribution in a probabilistic analysis for this variable, and we calculated the shape parameters for this distribution using the mean and an assumed standard error of 10% of the mean. We also estimated the 95% CI around the mean using the beta quantile function to compute the 2.5th and 97.5th percentiles of the beta distribution.

[c] We estimated the 95% CI by estimating the standard error using the formula $SE = \sqrt{\frac{p(1-p)}{n}}$, where *SE* is the standard error, *p* is the population proportion, and *n* is the total number of the sample population.

[d] The treatment success rate (also referred to as the "technical efficacy rate") of ablation for symptomatic benign thyroid nodules is defined as a reduction in the nodule's initial volume of greater than 50% at 1 year postprocedure, expressed as a volume reduction ratio of greater than 50%.

[e] The expected value of the point estimate based on the observed counts in the primary source material of those who experienced technical success with RFA and those who did not.[120] The source material reported that the technical success rate was 92.2% (119/129).

[f] The treatment success rate of ablation for AFTNs is defined as when normalization of TSH is achieved (i.e., the patient becomes euthyroid).

[g] We estimated the 95% CI around the mean using the beta quantile function to compute the 2.5th and 97.5th percentiles of the beta distribution.

[h] For the purpose of estimating a lognormal distribution in a probabilistic analysis for this variable, we used a proxy lower-bound 95% CI value of 10^{-10} and then calculated the shape parameters for this distribution using the mean of logs and standard deviation of logs.

[i] We estimated the annual cumulative probability of nodule regrowth over 10 years after RFA by digitizing the Kaplan–Meier curve from the source publication[236] and estimating the annual probability of nodule regrowth among ablated nodules at each yearly interval (see Appendix 8, Table A28, for further details).

Small, Low-Risk Papillary Thyroid Cancer

For adults with small, low-risk papillary thyroid cancer, we obtained the comparative efficacy and safety of RFA and partial thyroidectomy, as well as the starting age of the cohort, from the systematic review by Nguyen et al,[84] which is included in the clinical evidence review. The authors estimated that 95.28% of the overall pooled proportion of patients achieved complete tumour disappearance after treatment with RFA. This pooled rate included studies with follow-up periods ranging from 18 months or less to greater than 36 months. The pooled proportion of patients achieving complete tumour disappearance decreased to 84.97% when only studies with a follow-up period of 18 months or less were included.[84]

We explored this lower rate of treatment success in a scenario analysis (see scenario 1 of the model for small, low-risk papillary thyroid cancer). We based the starting age of adults with small, low-risk papillary thyroid cancer for our model on the average age of participants across the comparative studies included in the systematic review, which was 44.5 years of age.

When comparing postoperative complications, Nguyen et al[84] found that overall, patients in the RFA group had a substantially lower rate of transient injury to the recurrent laryngeal nerve compared with patients in the partial thyroidectomy group (OR 0.34, 95% CI 0.16–0.74). This review also found that the incidence of post-treatment hypothyroidism following RFA was zero. Finally, the cumulative probability of tumour recurrence was lower for RFA compared with partial thyroidectomy (1.65% vs. 2.89%, respectively; *P* = .03), and this finding was statistically significant. There were no statistically significant differences in recurrence rates observed at follow-up exceeding 3 years.

We obtained information about postoperative complications following partial and total thyroidectomy in adults with small, low-risk papillary thyroid cancer from Hsiao et al,[245] a systematic review and meta-analysis that evaluated complication rates from these 2 surgical procedures in patients with papillary thyroid microcarcinoma. This review found that patients who underwent partial thyroidectomy had a substantially lower risk of transient injury to the recurrent laryngeal nerve compared to those who underwent total thyroidectomy (2.0% vs. 4.2%). We assumed the same complication rates for total and completion thyroidectomy, because the surgical risks and side effects for both are similar.[17]

We obtained the annual probability of tumour progression under active surveillance from Ito et al,[248] a retrospective study that evaluated tumour progression in adults diagnosed with papillary thyroid microcarcinoma over 10 years. This long-term study found that the 10-year cumulative probability of tumour progression in this population was 6.8%. We estimated the annual probability of tumour progression at each yearly interval using the same methods as described previously for estimating the probability of nodule regrowth following RFA for symptomatic benign thyroid nodules (see Appendix 8, Table A29, for further details).

Table 23 summarizes the clinical parameter inputs for small, low-risk papillary thyroid cancer.

Table 23: Clinical Parameter Inputs Used in the Economic Model, Small, Low-Risk Papillary Thyroid Cancer

Model parameter	Mean (95% CI)	Distribution (parameter 1, parameter 2)[a]	Reference
Partial thyroidectomy			
Probability of transient injury to the RLN	0.02 (0.175–0.33)[b]	Beta (28, 1,388)	Hsiao et al, 2022[245]
Probability of post-treatment hypothyroidism	0.254 (0.214–0.29)[b]	Beta (30, 88)	Bo et al, 2022[120]
3-year cumulative probability of tumour recurrence	0.0289 (NA)	Beta (56, 1,885)	Nguyen et al, 2025[84]
Total or completion thyroidectomy			
Probability of transient injury to the RLN	0.04 (0.038–0.05)[b]	Beta (101, 2,310)	Hsiao et al, 2022[245]
Probability of post-treatment hypothyroidism	1.0 (NA)	Fixed	ATA, 2020[249]
RFA			
Treatment success rate at 1 year[c]	0.953 (0.843–0.987)	Beta (31.47, 1.56)	Nguyen et al, 2025[84]
Treatment effect on risk of transient injury to the RLN	OR 0.34 (0.16–0.74)	Lognormal (−1.07, 1.16)	Nguyen et al, 2025[84]
Probability of post-treatment hypothyroidism	0.0 (NA)	Fixed	Nguyen et al, 2025[84]
3-year cumulative probability of tumour recurrence	0.0165 (NA)	Fixed	Nguyen et al, 2025[84]
Active surveillance			
10-year cumulative probability of tumour progression[d]	0.068 (NA)	Fixed	Ito et al, 2014[248]

Abbreviations: ATA, American Thyroid Association; CI, confidence interval; NA, not applicable; OR, odds ratio; RFA, radiofrequency ablation; RLN, recurrent laryngeal nerve.

[a] For beta distribution, parameter 1 = alpha, parameter 2 = beta; for lognormal distribution, parameter 1 = alpha, parameter 2 = beta.

[b] We estimated the 95% CI by estimating the standard error using the formula $SE = \sqrt{\frac{p(1-p)}{n}}$, where *SE* is the standard error, *p* is the population proportion, and *n* is the total number of the sample population.

[c] The treatment success rate (also referred to as the "technical efficacy rate") of ablation for small, low-risk papillary thyroid cancer is defined as complete tumour disappearance.

[d] We estimated the annual cumulative probability of tumour progression under active surveillance over 10 years by digitizing the Kaplan–Meier curve from the source publication[248] and estimating the annual probability of tumour progression at each yearly interval (see Appendix 8, Table A29, for further details).

Health State Utilities

A health state utility represents a person's preference for a certain health state or outcome. Utilities are often measured on a scale ranging from 0 (death) to 1 (full health). For our analysis, we estimated the utility (or utility decrement) values associated with health states (e.g., being symptom-free) or adverse events (i.e., having a transient injury to the recurrent laryngeal nerve) from published literature.

We estimated the baseline utility for symptomatic benign thyroid nodules based on information from Kuo et al.[211] We obtained the baseline utility for AFTN from Tengs and Wallace,[250] a comprehensive review of 1,000 health-related quality of life weights for different health states. Patients with regrown nodules resumed the baseline utility for a symptomatic benign thyroid nodule or AFTN for 1 cycle.

We obtained the baseline utility for adults with untreated papillary thyroid cancer, as well as the utility of tumour recurrence following treatment, from Hedman et al,[251] a study on health-related quality of life in a Swedish population of patients with differentiated thyroid carcinoma. In our model, patients with a stable tumour under active surveillance assumed the baseline utility for untreated papillary thyroid cancer. Patients under active surveillance who experienced tumour progression assumed the same utility as patients who experienced tumour recurrence following treatment.

We obtained disutility values for receiving RFA and partial thyroidectomy from Kuo et al,[211] who estimated the health state utilities of patients following RFA or surgery by subtracting the disutility score associated with undergoing either procedure from the utility assuming perfect health (utility score = 1). For adults with symptomatic benign thyroid nodules or AFTNs, we modified this approach using the age- and sex-specific utility for the general population of Canada aged 50 to 54 years (utility = 0.849).[252] For adults with small, low-risk papillary thyroid cancer, we modified this approach using the age- and sex-specific utility for the general population of Canada aged 40 to 44 years (utility = 0.887).[252] We obtained the health state utilities of patients following total or completion thyroidectomy from McIntyre et al,[253] a UK quality-of-life study in patients with differentiated thyroid cancer who underwent total thyroidectomy.

We obtained utility decrements associated with untreated hypothyroidism and with achieving euthyroid status with levothyroxine therapy from Houten et al,[254] a systematic review of health state utility values for thyroid cancer. In our models, those who developed post-treatment hypothyroidism were assigned a disutility that reflected untreated hypothyroidism during the first 2 months after the procedure, followed by a reduced disutility corresponding to achieving euthyroid status on levothyroxine therapy for the remaining 8 months of the cycle. In subsequent cycles, we assumed that patients had the disutility associated with being euthyroid on levothyroxine therapy.

We obtained the utility decrement associated with transient unilateral injury to the recurrent laryngeal nerve from Kebebew et al,[255] who used a time trade-off approach to survey patients undergoing surgery for low-risk differentiated thyroid cancer. We estimated a comorbid health state of experiencing both hypothyroidism and transient recurrent laryngeal nerve injury using the multiplicative approach.[256]

Table 24 summarizes the health state utilities used in the economic models.

Table 24: Utilities Used in the Economic Models

Health state or event	Mean (95% CI)	Duration	Distribution (parameter 1, parameter 2)[a]	Reference
Utility				
Baseline utility, symptomatic benign thyroid nodules	0.815 (0.631–0.944)[b]	1 year	Beta (17.69, 4.01)[b]	Estimate based on Kuo et al, 2023,[211] and Guertin et al, 2018[252]
Baseline utility, AFTNs	0.741 (0.583–0.871)[b]	1 year	Beta (25.20, 8.83)[b]	Tengs and Wallace, 2000[250]
Baseline utility, small, low-risk papillary thyroid cancer	0.803 (0.787–0.819)[b]	1 year	Beta (1,969, 483)[b]	Hedman et al, 2018[251]
Symptom-free[c] after RFA: symptomatic benign thyroid nodules and AFTNs	0.822 (0.635–0.950)[b]	1 year	Beta (16.98, 3.68)[b]	Estimate based on Kuo et al, 2023,[211] and Guertin et al, 2018[252]
Symptom-free[c] after partial thyroidectomy: symptomatic benign thyroid nodules and AFTNs	0.819 (0.633–0.948)[b]	1 year	Beta (17.28, 3.82)[b]	Estimate based on Kuo et al, 2023,[211] and Guertin et al, 2018[252]
Tumour-free after RFA: small, low-risk papillary thyroid cancer	0.86 (0.654–0.979)[b]	1 year	Beta (13.14, 2.14)[b]	Estimate based on Kuo et al, 2023,[211] and Guertin et al, 2018[252]
Tumour-free after partial thyroidectomy: small, low-risk papillary thyroid cancer	0.857 (0.653–0.977)[b]	1 year	Beta (13.44, 2.24)[b]	Estimate based on Kuo et al, 2023,[211] and Guertin et al, 2018[252]
Tumour-free after total/completion thyroidectomy: small, low-risk papillary thyroid cancer	0.776 (0.120–1.00)[d]	1 year	Beta (1.22, 0.35)[d]	McIntyre et al, 2018[253]
Tumour progression/recurrence: small, low-risk papillary thyroid cancer	0.745 (0.586–0.876)[b]	1 year	Beta (24.76, 8.47)[b]	Hedman et al, 2018[251]
Utility decrement[e]				
Hypothyroidism (untreated)[f]	0.042 (0.035–0.051)	1 year	Lognormal (−3.17, 0.01)[g]	Houten et al, 2000[254]
Hypothyroidism (treated, euthyroid on levothyroxine therapy)	0.085 (0.070–0.103)	1 year	Lognormal (−2.47, 0.01)[g]	Houten et al, 2000[254]
Transient unilateral injury to the RLN	0.192 (0.158–0.233)	1 year	Lognormal (−1.65, 0.01)[g]	Kebebew et al, 2000[255]

Abbreviations: AFTN, autonomously functioning thyroid nodule; CI, confidence interval; RFA, radiofrequency ablation; RLN, recurrent laryngeal nerve.

[a] For beta distribution, parameter 1 = alpha, parameter 2 = beta; for gamma distribution, parameter 1 = alpha, parameter 2 = theta.

[b] We estimated a beta distribution in a probabilistic analysis for this variable, and we calculated the shape parameters for this distribution using the mean and an assumed standard error of 10% of the mean. We also estimated the 95% CI around the mean using the beta quantile function to compute the 2.5th and 97.5th percentiles of the beta distribution.

[c] *Symptom-free* refers to freedom from compressive or cosmetic concerns, and/or endocrine symptoms of benign thyroid nodules or AFTNs.

[d] We estimated a beta distribution in a probabilistic analysis for this variable, and we calculated the shape parameters for this distribution using the mean of 0.776 and standard deviation of 0.26 reported in the source material. We also estimated the 95% CI around the mean using the beta quantile function to compute the 2.5th and 97.5th percentiles of the beta distribution.

[e] Utility decrements are a measure of the decrease in a person's quality of life attributed to the negative effects of an adverse event or condition. They are the same concept as a disutility. We have presented utility decrement values as a positive value and multiplied them by –1 to express the value as a disutility.

[f] The disutility value associated with untreated hypothyroidism. When a person first develops post-treatment hypothyroidism, we estimated that the disutility value associated with hypothyroidism accounts for untreated hypothyroidism, annualized to the first 2 months of that cycle. The remaining 10 months in this cycle were reflected by the annualized disutility associated with treated hypothyroidism, in which the patient achieves euthyroid status on levothyroxine therapy.

[g] We estimated a lognormal distribution in a probabilistic analysis for this variable, and we calculated the shape parameters for this distribution using the mean and an assumed standard error of 10% of the mean.

Cost Parameters

We obtained cost parameters from health administrative databases via IntelliHealth Ontario, the Ontario Health Insurance Plan (OHIP) Schedule of Benefits for Physician Services,[257] the Schedule of Benefits for Laboratory Services,[258] and consultations with Southmedic Inc. (Barrie, Ontario), the distributor of the Viva Combo RF Generator. All costs are reported in 2025 Canadian dollars. Table 25 summarizes the costs used in the economic models.

Table 25: Costs Used in the Economic Models

Variable	Unit cost, $	Distribution (parameter 1, parameter 2)[a]	Duration or quantity	Total cost, $	Reference
Partial thyroidectomy					
Procedure					
Physician billing (code: S789)[b]	$1,110.21	Fixed	Per surgery	$1,110.21	SoB for Physician Services[257]
Average cost of hospital care	$4,762.00	NA	NA	$4,762.00	Calculated
Proportion performed as an outpatient procedure	0.46	Beta (54, 63)[c]	NA	NA	IntelliHealth Ontario (DAD and NACRS)
Average cost of inpatient hospital care	$5,169.66	Gamma (100, 0.019)[d]	Per surgery	$5,169.66	IntelliHealth Ontario (DAD)
Average cost of outpatient hospital care	$4,283.43	Gamma (99.9, 0.023)[d]	Per surgery	$4,283.43	IntelliHealth Ontario (NACRS)
Postprocedure					
Follow-up year 1, symptomatic benign thyroid nodules and AFTNs	$61.11	NA	Per year	$61.11	See Appendix 8, Table A30, for details
Annual follow-up, small, low-risk papillary thyroid cancer[e]	$45.81 to $143.89	NA	Per year	$45.81 to $143.89	See Appendix 8, Table A30, for details
Total and completion thyroidectomy					
Procedure					
Physician billing, TT (code: S788)[b]	$1,374.24	Fixed	1	$1,374.24	SoB for Physician Services[257]
Physician billing, CT (code: S793)[b]	$1,246.94	Fixed	1	$1,246.94	SoB for Physician Services[257]
Average cost of hospital care associated with TT and CT	$7,017.11	Gamma (100, 0.014)[d]	Per surgery	$7,017.11	IntelliHealth Ontario (DAD)
Postprocedure					
Annual follow-up, small, low-risk papillary thyroid cancer[f]	$45.89 to $108.39	NA	Per year	$45.89 to $108.39	See Appendix 8, Table A30, for details
RFA					
Preprocedure					
FNA, symptomatic benign thyroid nodules	$38.00	Fixed	1	$38.00	SoB for Physician Services[257]
Procedure					
Capital cost of specialized RFA equipment per RFA session[g]	$40.50	NA	Per session	$40.50	Calculated

Variable	Unit cost, $	Distribution (parameter 1, parameter 2)[a]	Duration or quantity	Total cost, $	Reference
VIVA combo RF system	$40,500	Fixed	Per hospital	$40,500	Southmedic, email communication, March 31, 2025
Projected lifespan of RF system	10 years	Fixed	NA	NA	Assumption
Projected number of RFA sessions per year	100	Fixed	Per year	NA	Assumption
Monopolar RFA electrodes	$1,500.00	Fixed	Per session	$1,500.00	Southmedic, email communication, March 31, 2025
Capital cost of standard ultrasound machine per RFA session[g]	$126.90	NA	Per session	$126.90	Calculated
Standard ultrasound machine[h]	$63,448.00	Gamma (100, 0.0016)[d]	Per machine	$63,448.00	Adams et al, 2021[259]
Annual maintenance[h]	$6,344.80	Gamma (100, 0.016)[d]	Per year	$6,344.80	Adams et al, 2021[259]
Projected lifespan of ultrasound machine	10 years	Fixed	NA	NA	Assumption
Projected number of uses per year for RFA	100	Fixed	Per year	NA	Assumption
Consumables	$100.00	Gamma (100, 1)[d]	Per session	$100.00	Assumption
Physician billing (proxy code: J069)[i]	$515.70	Fixed	Per session	$515.70	SoB for Physician Services[257]
Nursing support	$141.21	Gamma	Per session	$141.21	Local hospital agreements with ONA[260-262]
Postprocedure					
Annual follow-up, years 1 to 5, symptomatic benign thyroid nodules	$105.11 to $399.11	NA	Per year	$105.11 to $399.11	See Appendix 8, Table A30, for details
Annual follow-up, years 1 to 5, AFTNs	$119.33 to $413.33	NA	Per year	$119.33 to $413.33	See Appendix 8, Table A30, for details
Annual follow-up, small, low-risk papillary thyroid cancer	$116.89 to $410.89	NA	Per year	$116.89 to $410.89	See Appendix 8, Table A30, for details
Active surveillance					
Annual follow-up, small, low-risk papillary thyroid cancer	$116.89 to $233.78	NA	Per year	$116.89 to $233.78	See Appendix 8, Table A30, for details
Patient management for post-treatment hypothryoidism					
Drug costs paid for by ODB programs	$26.05	NA	Per year	NA	Calculated
Total cost of levothyroxine[j]	$73.14	Fixed	Per year	$73.14	Caclulated
Proportion of Ontario population covered by ODB programs[k]	0.356	Beta (0.64, 116)[c]	NA	NA	Calculated from Ministry of Health[263] and Ministry of Finance[264]
Thyroid function tests (code: J105)	$7.11	Fixed	Per year	$7.11	SoB for Laboratory Services[258]

Abbreviations: CT, completion thyroidectomy; DAD, Discharge Abstract Database; FNA, fine needle aspiration; NACRS, National Ambulatory Care Reporting System; ODB, Ontario Drug Benefit; ONA, Ontario Nurses' Association; PT, partial thyroidectomy; RFA, radiofrequency ablation; SoB, Schedule of Benefits; TT, total thyroidectomy.

[a] For beta distribution, parameter 1 = alpha, parameter 2 = beta; for gamma distribution, parameter 1 = alpha, parameter 2 = lambda.

[b] This cost includes surgical assistant and anesthesiologist fees. We estimated the total procedure cost for partial thyroidectomy based on an average procedure time of 75 to 90 minutes. We estimated the total procedure costs for total and completion thyroidectomy based on average procedure time of 105 to 120 minutes.

[c] We estimated a beta distribution in a probabilistic analysis for this variable, and we calculated the shape parameters for this distribution using the mean and an assumed standard error of 10% of the mean.

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[d] We estimated a gamma distribution in a probabilistic analysis for this variable, and we calculated the shape and scale parameters for this distribution using the mean and an assumed standard error of 10% of the mean.

[e] The follow-up strategy after partial thyroidectomy for adults with papillary thyroid cancer consists of 2 physician visits, bloodwork testing for thyroid function and thyroglobulin measurements, and thyroid ultrasound in year 1; 1 physician visit and bloodwork testing for thyroid function and thyroglobulin measurements in year 2; 1 annual physician visit, annual bloodwork testing for thyroid function, and 1 ultrasound over years 3 to 5; and 1 annual physician visit, annual bloodwork for thyroid function, and 1 ultrasound every 5 years for the rest of a person's life.[265]

[f] The follow-up strategy after total or completion thyroidectomy for adults with papillary thyroid cancer consists of 2 physician visits, bloodwork testing for thyroid function, and thyroglobulin measurements in year 1; 1 physician visit, bloodwork testing for thyroid function and thyroglobulin measurements, and 1 thyroid ultrasound in year 2; 1 annual physician visit, bloodwork testing for thyroid function and thyroglobulin measurements, and 1 thyroid ultrasound over years 3 to 5; and 1 annual physician visit and annual bloodwork testing for thyroid function and thyroglobulin measurements for the rest of a person's life.[265]

[g] We calculated the capital cost of the VIVA combo RF system per RFA session using the following formula: cost of acquiring the VIVA combo RF system over 10 years ÷ (projected number of RFA sessions performed at a high-volume centre per year × 10 years) = $40,500 ÷ (100 × 10) = $40.50. We calculated the capital cost of a standard ultrasound machine per RFA session using the following formula: (cost of acquiring a standard ultrasound machine + annual cost of maintenance over 10 years) ÷ (projected number of ultrasound uses for RFA sessions performed at a high-volume centre per year × 10 years) = ($63,448 + $6,344.80 × 10) ÷ (100 × 10).

[h] We adjusted costs for inflation to 2025 Canadian dollars.

[i] For the purpose of our analysis, we used this billing code as a proxy to estimate the cost of physician services for RFA. If publicly funded, this service may be included in an existing insured service or may require its own fee code. Changes to the schedule of benefits are jointly negotiated between the Ministry of Health and the Ontario Medical Association.

[j] Based on common dose recommendations for an adult at 1.6 µg per kilogram per day[266] and an average adult weight of 70 kg. Specifically, we estimated the cost of levothyroxine based on a 0.125 mg daily tablet of Synthroid (DIN: 02172119), accounting for markup and total dispensing fees.[263]

[k] Calculated using the number of people covered by ODB programs in fiscal year 2018/19 (n = 5,200,000)[263] and the total population of Ontario in 2019 (14,600,000).[264]

Preprocedure Costs

The preprocedure workup for RFA and partial thyroidectomy – which includes fine-needle aspiration, blood work for thyroid function testing (i.e., TSH and free T3), and thyroid ultrasound – is similar for both procedures, except for the following:

- Before RFA, adults with symptomatic benign thyroid nodules receive 2 separate fine-needle aspirations to confirm benign cytology.[219] Adults with AFTNs or small, low-risk papillary thyroid cancer undergo only 1 fine-needle aspiration before RFA.
- Before partial thyroidectomy, only 1 fine-needle aspiration is required for all populations.

In the RFA arm, we included the cost of a second, confirmatory fine-needle aspiration for adults with symptomatic benign thyroid nodules only. The cost of performing a fine-needle aspiration is $38.00, according to the Schedule of Benefits for Physician Services (billing code: Z771).[257]

Procedure Costs

Partial Thyroidectomy

In Ontario, partial thyroidectomies are billed as either hemithyroidectomy (i.e., without removal of the isthmus) or subtotal thyroidectomy (i.e., with removal of the isthmus), depending on physician judgment. For simplicity, we used the billing fee for subtotal thyroidectomy (code: S789)[257] and assumed an average procedure duration of 75 to 90 minutes to estimate the total cost of surgeon, surgical assistant, and anaesthesiologist fees for this procedure, which was $1,110.21.

Partial thyroidectomies may be performed as inpatient or outpatient procedures. The costs of the procedure in either setting include the costs of hospital care, which we estimated using data from the

Discharge Abstract Database for inpatient procedures and the National Ambulatory Care Reporting System for outpatient procedures. We estimated the total average cost of hospital care associated with partial thyroidectomy based on the weighted average of inpatient and outpatient hospital care costs. We arrived at a total average hospital care cost associated with partial thyroidectomy for symptomatic benign thyroid nodules and AFTNs of $4,762 per procedure. See Appendix 9 for further details about the methods.

Total and Completion Thyroidectomy

We used the billing fees for total (code: S788) and completion (code: S793) thyroidectomy[257] and assumed an average procedure duration of 105 to 120 minutes to estimate the total costs of surgeon, surgical assistant, and anaesthesiologist fees for these procedures, which were $1,374.24 and $1,246.94, respectively.

In Ontario, total and completion thyroidectomies are performed as inpatient procedures. We estimated the costs of hospital care associated with these procedures using data from the Discharge Abstract Database for inpatient procedures. Using the same methodology as described above to estimate the cost of hospital care for partial thyroidectomy, we estimated that the average cost of hospital care associated with total and completion thyroidectomies was $7,017.11 per procedure. See Appendix 9 for further details about the methods.

RFA

The main components of RFA include acquisition of the VIVA combo RF system ($40,500 per system; Southmedic, email communication, March 31, 2025); 1-time use monopolar RFA electrodes ($1,500 per session; Southmedic, email communication, March 31, 2025); acquisition and annual maintenance of a standard ultrasound machine (estimated at $63,448, with annual maintenance costs of $6,344.80)[259]; consumables (e.g., syringe, needle, drapes, bandages; $100 per session; assumption); physician services for performing the ablation procedure; and nursing support.

To calculate the cost per RFA session for the capital cost of the specialized RFA equipment and standard ultrasound machine, we made the following assumptions:

- The projected lifespans of the VIVA combo RF system and the standard ultrasound machine were 10 years.
- The projected number of annual RFA sessions in a high-volume hospital was 100 sessions per year. If publicly funded, we expected RFA to be delivered in centres with an adequate volume of eligible patients. In our analysis, we defined high-volume hospitals for RFA as those with a case load of 100 or greater per year.
- We assumed that a centre performing RFA for thyroid nodules would acquire a single VIVA combo RF system and a new standard ultrasound machine.

Based on these assumptions, we estimated that the costs per RFA session would be $40.50 for the VIVA combo RF system and $126.90 for the standard ultrasound machine.

At present, the OHIP Schedule of Benefits for Physician Services[257] does not have a dedicated fee code for ultrasound-guided thermal ablation for thyroid nodules. To estimate the physician costs for this procedure, we used the billable procedure for percutaneous focal thermal ablation of solid tumours using computed tomography or ultrasound guidance (billing code: J069) as a proxy. The estimated cost for physician services for RFA was $515.70. If publicly funded, this procedure may be included in an existing insured service or may require its own fee code. Changes to the schedule of services are negotiated jointly between the Ministry of Health and the Ontario Medical Association.

Finally, we estimated the cost of nursing support ($141.21 per session) based on 3 hours' hourly wage for a midcareer registered nurse, as listed in local agreements between teaching hospitals in the Greater Toronto Area and the Ontario Nurses' Association.[260-262]

Overall, we estimated the total average cost for RFA to be $2,424.31 per session.

Postprocedure Costs

We estimated the following postprocedure costs based on common practice in Ontario and on guideline recommendations. In practice, there may be variations in follow-up care.

Partial Thyroidectomy

Adults with symptomatic benign thyroid nodules and AFTNs are typically monitored for 1 year after partial thyroidectomy. This follow-up includes 2 physician visits at 1 week and 1 month postsurgery to assess recovery and discuss pathology results. Follow-up also includes bloodwork to evaluate thyroid function around 6 weeks postsurgery (Karen Devon, MD, telephone consultation, August 21, 2025; Antoine Eskander, MD, telephone consultation, August 28, 2025). Each physician visit is billed at $27 (billing code: A244),[257] and the total estimated cost of the bloodwork is $7.11.[258]

Adults with small, low-risk papillary thyroid cancer are monitored for the remainder of their lives. The recommended annual follow-up after partial thyroidectomy may include a physician visit, bloodwork to evaluate thyroid function and thyroglobulin, and/or thyroid ultrasound. The thyroglobulin bloodwork (billing code: L609)[258] and thyroid ultrasound (billing code: J105)[257] cost $11.78 and $71.00, respectively. The frequency of follow-up elements varies by year and is based on the follow-up guidelines for people with thyroid cancer in Canada who are at low risk of recurrence.[265]

Total and Completion Thyroidectomy

The recommended annual follow-up after total and completion thyroidectomy for adults with small, low-risk papillary thyroid cancer includes elements similar to those described for partial thyroidectomy. The frequency of follow-up also varies by year and is also based on guidelines for people with thyroid cancer in Canada who are at low risk of recurrence.[265]

RFA

For adults with symptomatic benign thyroid nodules and AFTNs, postprocedural follow-up care for those who receive RFA includes more frequent visits during the first year to monitor symptom relief and reduction in nodule volume, followed by annual visits for up to 5 years postprocedure (Karen Devon, MD, telephone consultation, August 21, 2025; Antoine Eskander, MD, telephone consultation, August 28, 2025). For adults with symptomatic benign thyroid nodules, postprocedure follow-up during the first

year consists of a physician visit and thyroid ultrasound every 3 months, as well as 1 annual thyroid function blood test. From years 2 through 5, follow-up consists of 1 annual physician visit, thyroid ultrasound, and thyroid function blood testing. For adults with AFTNs, postprocedure follow-up during the first year includes 1 physician visit, thyroid ultrasound every 3 months, and bloodwork for thyroid function testing every 4 months. From years 2 through 5, follow-up consists of 1 physician visit and thyroid ultrasound every year, and thyroid function testing every 4 months.

For adults with small, low-risk papillary thyroid cancer, postoperative follow-up care consists of a physician visit and thyroid ultrasound every 3 months and annual bloodwork for thyroid function testing and thyroglobulin measurement. At present, long-term follow-up strategies after RFA in this population have not been standardized in Canada; we assumed that long-term follow-up after RFA would mirror that of active surveillance for the rest of a person's life.

Active Surveillance

Under active surveillance, adults with small, low-risk papillary thyroid cancer are monitored for the rest of their lives or until tumour progression, after which they may choose to undergo treatment. For this population, active surveillance typically involves annual thyroid ultrasound, bloodwork for thyroid function testing and thyroglobulin measurement, and physician visits for physical examination and discussion of treatment options every 6 months for 2 years, followed by annual monitoring thereafter.[267]

Patient Management of Post-treatment Hypothyroidism

Post-treatment hypothyroidism is managed by lifelong thyroid hormone replacement therapy, typically with levothyroxine.[266] The dosing of levothyroxine is weight-based and may require adjustment over a person's lifetime. Therefore, the total costs for the management of hypothyroidism include annual bloodwork for thyroid function testing and daily thyroid hormone supplementation with levothyroxine.

To estimate the cost of thyroid hormone supplementation, we applied weight-based dosing for an average adult. The standard dose of levothyroxine for treating hypothyroidism in adults is 1.6 µg per kilogram per day.[266] Based on an average adult weight of 70 kg, this corresponds to a daily dose of approximately 0.125 mg of levothyroxine. Incorporating annual dispensing fees and the applicable markup associated with levothyroxine,[268] the estimated annual cost of treatment for hypothyroidism is $73.14. Accounting for the proportion of the Ontario population covered under the Ontario Drug Benefit Program (at approximately 35.6%),[263] the Ministry of Health can be expected to pay $26.05 annually for each person who requires post-treatment thyroid hormone supplementation.

Internal Validation

The secondary health economist conducted formal internal validation. This process included testing the mathematical logic of the model, checking for errors, and ensuring the accuracy of parameter inputs and equations.

Analysis

Our reference case and sensitivity analyses adhered to CDA guidelines[215] when appropriate. The reference case represents the analysis with the most likely set of input parameters and model assumptions.

We calculated the reference case of this analysis by running 5,000 simulations (probabilistic analysis) that simultaneously captured the uncertainty in all parameters that were expected to vary. We set distributions for variables within the model. We calculated mean costs with credible intervals and mean QALYs with credible intervals for each intervention assessed. We also calculated the mean incremental costs with credible intervals, incremental QALYs with credible intervals, and ICERs for the following:

- RFA versus partial thyroidectomy for adults with symptomatic benign thyroid nodules
- RFA versus partial thyroidectomy for adults with AFTNs
- RFA versus partial thyroidectomy and active surveillance for adults with small, low-risk papillary thyroid cancer

Models for Symptomatic Benign Thyroid Nodules and AFTNs

The results of the probabilistic analyses are presented in a scatter plot on a cost-effectiveness plane and in a cost-effectiveness acceptability curve. Although not used as definitive willingness-to-pay (WTP) thresholds, including graphical indications of the location of the results relative to guideposts of $50,000 per QALY and $100,000 per QALY facilitates interpretation of the findings and comparison with historical decisions. We also present uncertainty quantitatively as the probability that an intervention is cost-effective at previously mentioned WTP guideposts. This uncertainty is also presented qualitatively, in 1 of 5 categories defined by the Ontario Decision Framework[269]: highly likely to be cost-effective (80%–100% probability of being cost-effective), moderately likely to be cost-effective (60%–79% probability), uncertain if cost-effective (40%–59% probability), moderately likely to not be cost-effective (20%–39% probability), or highly likely not to be cost-effective (0%–19% probability).

Model for Small, Low-Risk Papillary Thyroid Cancer

Following the CDA guidelines,[215] we reported sequential incremental cost-effectiveness ratios (ICERs) and an ICER produced from a common comparator (i.e., active surveillance). We ordered treatments by average total cost, from lowest to highest. For sequential ICERs, after excluding treatments that were either dominated or subject to extended dominance, we calculated the ICER for a less costly comparator compared with the next more costly comparator. In addition to estimating the ICER for each comparison, we also used net monetary benefit (NMB) to evaluate the cost-effectiveness of the 3 included treatments (see Glossary, Incremental net benefit).

The results of the probabilistic analysis are also presented on a cost-effectiveness acceptability curve. We present uncertainty quantitatively as the probability that a treatment is cost-effective at WTP values of $0 to $100,000 per QALY. For each simulation, the treatment with the maximum NMB at the given WTP was considered the most cost-effective of the 3 treatments we compared.[269] The probability of being cost-effective for each treatment was equal to the proportion of the 5,000 simulations for which this treatment had the highest NMB.

Scenario Analyses

Symptomatic Benign Thyroid Nodules and AFTNs

For our models for adults with symptomatic benign thyroid nodules and AFTNs, we conducted scenario analyses by varying parameter inputs and applying alternative assumptions (Table 26). Except for scenario 5, all scenarios were conducted for both populations.

- Scenario 1: Assumed that a higher proportion of patients undergoing RFA would require 1 additional ablation session (2 times that of the reference case, at 4.6%)
- Scenario 2: Assumed that 2.3% of patients undergoing RFA would require 2 additional ablation sessions
- Scenario 3: Assumed that the total cost for RFA per session would be higher by 25% ($3,030.38 per session versus $2,424.31 per session in the reference case). The total cost of RFA per session included RFA specialized equipment, 1-time use electrodes, a standard ultrasound machine, nursing support, consumables, and physician services for conducting the procedure
- Scenario 4: Assumed a time horizon of 10 years (versus a lifetime time horizon in the reference case) to capture differences in costs and benefits between treatment strategies up to the 10-year cumulative probability of nodule regrowth following RFA
- Scenario 5: Accounted for a false-negative rate of 3% in fine-needle aspiration cytology[235] for thyroid nodules by assuming a lower treatment success rate (at 89.2%) at 1 year after RFA in people with symptomatic benign thyroid nodules. This assumption considered that RFA has been found to result in incomplete ablation of malignant nodules that were misdiagnosed as benign.[270] Patients with malignant nodules misdiagnosed as benign from fine-needle aspiration would transition to the "Symptoms persist" health state, along with patients with true benign nodules who failed to achieve treatment success and continued to experience persisting symptoms. All patients in this health state would undergo partial thyroidectomy (this scenario applied only to the model for adults with symptomatic benign thyroid nodules; AFTNs are almost always benign)
- Scenario 6: Assumed that all partial thyroidectomies for symptomatic benign thyroid nodules and AFTNs were performed as inpatient procedures in Ontario
- Scenario 7: Assumed that all partial thyroidectomies for symptomatic benign thyroid nodules and AFTNs were performed as outpatient procedures in Ontario
- Scenario 8: Applied a 0% discount rate to both costs and QALYs. We conducted this scenario as recommended by the CDA guidelines
- Scenario 9: Applied a 3% discount rate to both costs and QALYs. We conducted this scenario as recommended by the CDA guidelines. This scenario also allowed us to compare our results with those of the studies included in our economic evidence review,[209,211] because those studies also used this discount rate

Table 26: Variables Varied in Scenario Analyses, Symptomatic Benign Thyroid Nodules and AFTNs

Scenario	Parameter	Reference case	Source	Scenario analysis	Source
Scenario 1: Assumed that a higher proportion of patients undergoing RFA would require 1 additional ablation session	Proportion of patients requiring a second ablation session	0.023	Bo et al, 2022[120]	0.046	Assumption
Scenario 2: Assumed that a higher proportion of patients undergoing RFA would require 2 additional ablation sessions	Proportion of patients requiring a third ablation session	0	NA	0.023	Assumption
Scenario 3: Assumed higher total costs for RFA (by 25%)	Total cost of RFA per session[a]	$2,424.31	Calculated	$3,030.38	Assumption
Scenario 4: Assumed a time horizon of 10 years	Time horizon	Lifetime	Assumption	10 years	Assumption
Scenario 5: Accounted for a false-negative rate of 3% in FNA cytology for symptomatic benign thyroid nodules[b,c]	Treatment success rate at 1 year	0.932	Bo et al, 2022[120]	0.902	Assumption based on 3% false-negative rate for FNA cytology[235]
Scenario 6: Assumed that all partial thyroidectomies were performed as inpatient procedures in Ontario	Proportion of the patient population undergoing partial thyroidectomy as an outpatient procedure	0.461	IntelliHealth Ontario (DAD and NACRS)	0	Assumption
Scenario 7: Assumed that all partial thyroidectomies were performed as outpatient procedures in Ontario	Proportion of the patient population undergoing partial thyroidectomy as an outpatient procedure	0.461	IntelliHealth Ontario (DAD and NACRS)	1	Assumption
Scenario 8: Applied a 0% discount rate to both costs and QALYs	Discount rate	0.015	CDA guidelines[215] for reference case	0	Recommended scenario analysis in CDA guidelines[215]
Scenario 9: Applied a 3% discount rate to both costs and QALYs	Discount rate	0.015	CDA guidelines[215] for reference case	0.03	Recommended scenario analysis in CDA guidelines[215]

Abbreviations: AFTN, autonomously functioning thyroid nodule; CDA, Canada's Drug Agency; DAD, Discharge Abstract Database; FNA, fine-needle aspiration; NA, not applicable; NACRS, National Ambulatory Care Reporting System; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] Total RFA cost per session includes the cost of RFA specialized equipment per session, standard ultrasound use per session, 1-time RFA electrodes, nursing support, physician services for conducting the procedure, and the cost of consumables.

[b] The false-negative rate for FNA cytology of thyroid nodules was accounted for by a lower treatment success rate for RFA in this scenario. This is because RFA has been found to result in incomplete ablation of malignant nodules that were misdiagnosed as benign.[270] In 1 retrospective Korean study, the median volume reduction ratio at 12 months was lower for malignant nodules than for benign nodules (51.4% [range: 0–57.8] versus 83.8% [range: 47.9–89.6]; $P = 0.01$).[270] All nodules were previously confirmed as benign by 2 FNAs before undergoing RFA, as per American Thyroid Association guidelines.[219]

[c] This scenario applies to the model for adults with symptomatic benign thyroid nodules only, because AFTNs are almost always benign.

Small, Low-Risk Papillary Thyroid Cancer

For our model for adults with small, low-risk papillary thyroid cancer, we conducted scenario analyses by varying parameter inputs and applying alternative assumptions (Table 27).

- Scenario 1: Assumed a lower rate of treatment success following RFA in adults with small, low-risk papillary thyroid cancer by assuming that the proportion of patients with complete tumour disappearance following RFA was 85.97% (versus 95.28% in the reference case)
- Scenario 2: Assumed that the total cost for RFA per session would be higher by 25% (at $3,030.38 per session versus $2,424.31 per session in the reference case)
- Scenario 3: Assumed a time horizon of 3 years (versus a lifetime time horizon in the reference case) to capture differences in costs and benefits between treatment strategies up to the 3-year cumulative probability of tumour recurrence following RFA and partial thyroidectomy
- Scenario 4: Assumed a time horizon of 10 years (versus a lifetime time horizon in the reference case) to capture differences in costs and benefits between treatment strategies up to the 10-year cumulative probability of tumour progression under active surveillance
- Scenario 5: Assumed that all partial thyroidectomies for small, low-risk papillary thyroid cancer were performed as inpatient procedures in Ontario
- Scenario 6: Assumed that all partial thyroidectomies for small, low-risk papillary thyroid cancer were performed as outpatient procedures in Ontario
- Scenario 7: Applied a 0% discount rate to both costs and QALYs. We conducted this scenario as recommended by CDA guidelines
- Scenario 8: Applied a 3% discount rate to both costs and QALYs. We conducted this scenario as recommended by CDA guidelines. This scenario also allowed us to compare our results with those of the studies included in our economic evidence review,[209,211] because they also used this discount rate

Table 27: Variables Varied in Scenario Analyses, Small, Low-Risk Papillary Thyroid Cancer

Scenario	Parameter	Reference case	Source	Scenario analysis	Source
Scenario 1: Assumed a lower rate of treatment success following RFA for small, low-risk papillary thyroid cancer	Proportion of patients with complete tumour disappearance within 1 year after RFA	0.9528	Nguyen et al, 2025[84]	0.8597	Nguyen et al, 2025[84]
Scenario 2: Assumed higher total costs for RFA (by 25%)	Total cost of RFA per session[a]	$2,424.31	Calculated	$3,030.38	Assumption
Scenario 3: Assumed a time horizon of 3 years	Time horizon	Lifetime	Assumption	3 years	Assumption
Scenario 4: Assumed a time horizon of 10 years	Time horizon	Lifetime	Assumption	10 years	Assumption
Scenario 5: Assumed that all partial thyroidectomies were performed as inpatient procedures in Ontario	Proportion of the patient population undergoing partial thyroidectomy as an outpatient procedure	0.461	IntelliHealth Ontario (DAD and NACRS)	0	Assumption
Scenario 6: Assumed that all partial thyroidectomies were performed as outpatient procedures in Ontario	Proportion of the patient population undergoing partial thyroidectomy as an outpatient procedure	0.461	IntelliHealth Ontario (DAD and NACRS)	1	Assumption
Scenario 7: Applied a 0% discount rate to both costs and QALYs	Discount rate	0.015	CDA guidelines[215] for reference case	0	Recommended scenario analysis in CDA guidelines[215]
Scenario 8: Applied a 3% discount rate to both costs and QALYs	Discount rate	0.015	CDA guidelines[215] for reference case	0.03	Recommended scenario analysis in CDA guidelines[215]

Abbreviations: CDA, Canada's Drug Agency; DAD, Discharge Abstract Database; NACRS, National Ambulatory Care Reporting System; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] Total RFA cost per session includes the cost of RFA specialized equipment per session, standard ultrasound use per session, 1-time RFA electrodes, nursing support, physician services for conducting the procedure, and the cost of consumables.

Results

Reference Case

Symptomatic Benign Thyroid Nodules

For adults with symptomatic benign thyroid nodules, the mean total costs for RFA and partial thyroidectomy were $4,258 and $6,148, respectively. The mean total effect was 21.45 QALYs for RFA and 20.89 QALYs for partial thyroidectomy. RFA resulted in a small average increase of 0.55 QALYs versus partial thyroidectomy over the duration of the model. Table 28 summarizes the reference case analysis results for symptomatic benign thyroid nodules.

Table 28: Reference Case Analysis Results, Symptomatic Benign Thyroid Nodules

Strategy	Average total costs, $ (95% CrI)	Incremental cost, $ (95% CrI)[a,b,c]	Average total QALYs (95% CrI)	Incremental QALYs (95% CrI)[c,d]	ICER[c]
RFA	4,258 (4,049 to 4,528)	−1,890 (−2,584 to −1,255)	21.45 (17.00 to 24.55)	0.55 (−5.01 to 6.13)	Dominant[e]
Partial thyroidectomy	6,148 (5,508 to 6,851)	–	20.89 (15.94 to 24.26)	–	–

Abbreviations: CrI, credible interval; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] Incremental cost = average cost (strategy B) − average cost (strategy A).

[b] Negative costs indicate savings.

[c] Results may appear inexact due to rounding.

[d] Incremental effect = average effect (strategy B) − average effect (strategy A).

[e] RFA was less costly and more effective than partial thyroidectomy.

The results of our probabilistic analysis in a scatter plot showed that although RFA generated lower total costs than partial thyroidectomy in all simulations, it was more effective only 58.76% of the time. When we plotted the results of our probabilistic analysis in a cost-effectiveness acceptability curve, we found that RFA remained the optimal strategy compared with partial thyroidectomy, irrespective of WTP values. Figures 6 and 7 visualize the results of our probabilistic analysis in a scatter plot and on a cost-effectiveness acceptability curve, respectively.

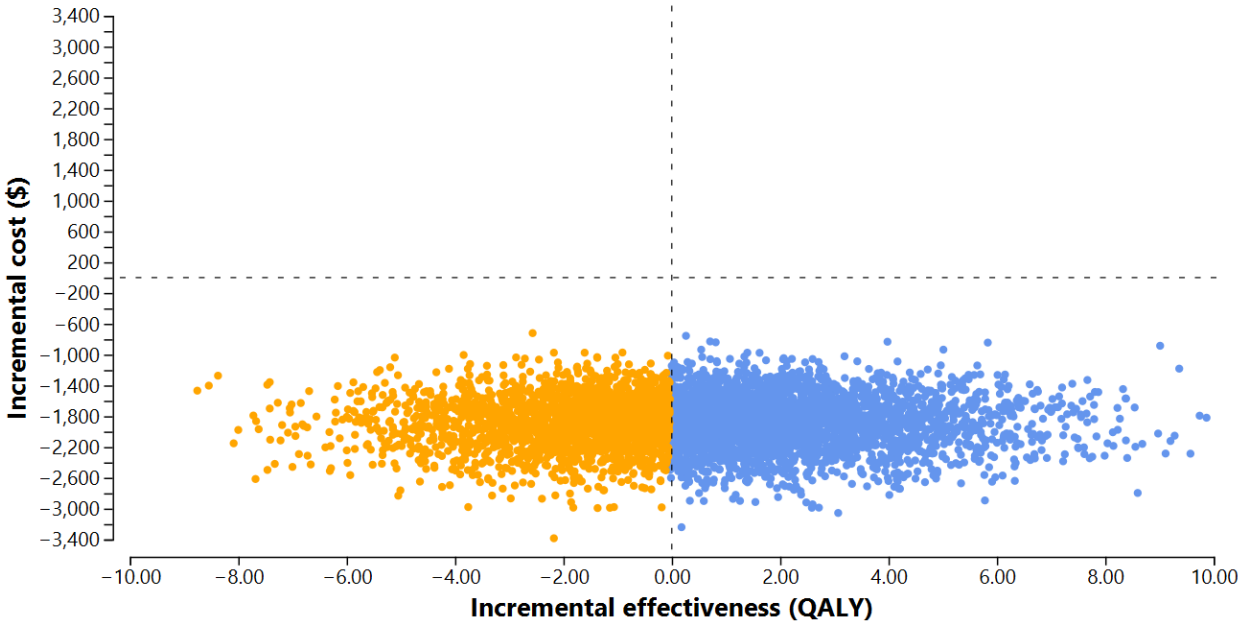

Figure 6: Scatter Plot of Probabilistic Results, Symptomatic Benign Thyroid Nodules

This figure visualizes the results of the probabilistic analysis in a scatter plot on a cost-effectiveness plane for symptomatic benign thyroid nodules. Each point represents the outcome of 1 simulation derived from a unique set of parameter values generated from their probability distributions.

Abbreviation: QALY, quality-adjusted life-year.

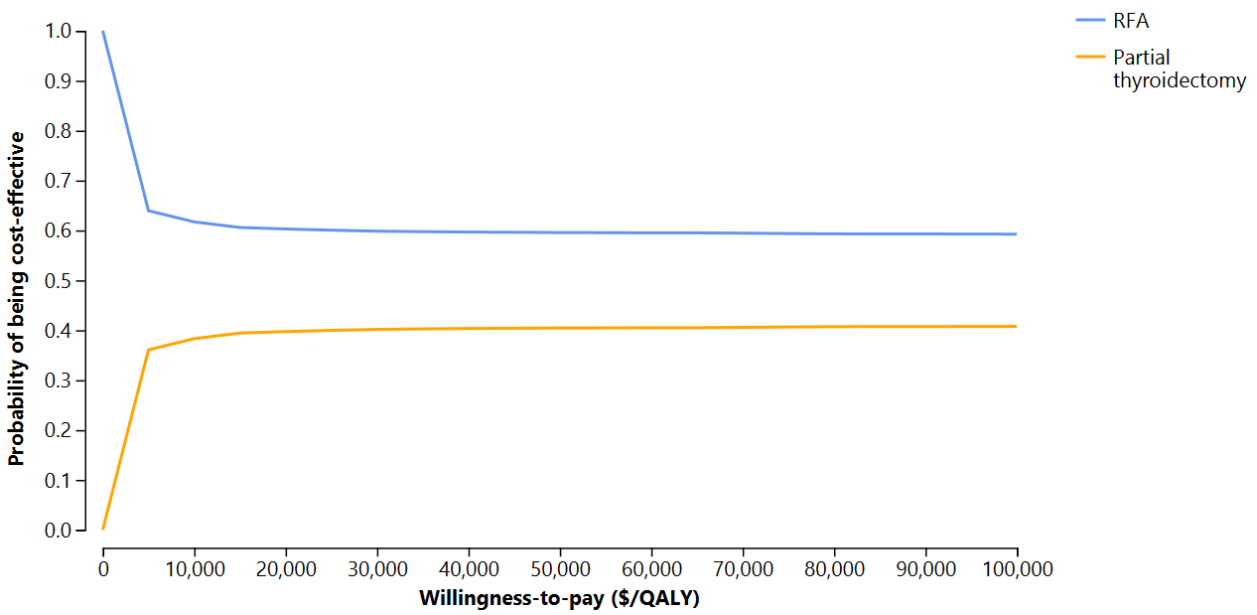

Figure 7: Cost-Effectiveness Acceptability Curve, Symptomatic Benign Thyroid Nodules

This figure visualizes the probability of RFA and partial thyroidectomy being cost-effective over a range of WTP values for symptomatic benign thyroid nodules. WTP values are plotted on the horizonal axis, and the probabilities of RFA and partial thyroidectomy being cost-effective at corresponding WTP values are plotted on the vertical axis.

Abbreviation: QALY, quality-adjusted life-year; RFA, radiofrequency ablation; WTP, willingness to pay.

Autonomously Functioning Thyroid Nodules

For adults with AFTNs, the mean total costs for RFA and partial thyroidectomy were $5,019 and $6,118, respectively. The mean total effect was 18.58 QALYs for RFA and 18.12 QALYs for partial thyroidectomy. Similar to the results for symptomatic benign thyroid nodules, RFA generated a small increase in average QALYs (0.46 QALYs) versus partial thyroidectomy for adults with AFTNs over the duration of the model. Table 29 summarizes the reference case analysis results for AFTNs.

Table 29: Reference Case Analysis Results, AFTNs

Strategy	Average total costs, $ (95% CrI)	Incremental cost, $ (95% CrI)[a,b,c]	Average total QALYs (95% CrI)	Incremental QALYs (95% CrI)[c,d]	ICER[c]
RFA	5,019 (4,392 to 5,838)	−1,099 (−1,968 to −211)	18.58 (15.19 to 21.07)	0.46 (–3.63 to 4.67)	Dominant[e]
Partial thyroidectomy	6,118 (5,462 to 6,807)	–	18.12 (13.84 to 21.08)	–	–

Abbreviations: AFTN, autonomously functioning thyroid nodule; CrI, credible interval; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] Incremental cost = average cost (strategy B) − average cost (strategy A).

[b] Negative costs indicate savings.

[c] Results may appear inexact due to rounding.

[d] Incremental effect = average effect (strategy B) − average effect (strategy A).

[e] RFA was less costly and more effective than partial thyroidectomy.

Similar to our results for symptomatic benign thyroid nodules, the results of our probabilistic analysis in a scatter plot showed that RFA generated lower total costs than partial thyroidectomy in almost all simulations and was more effective 59.6% of the time. When we plotted the results of our B probabilistic analysis on a cost-effectiveness acceptability curve, we found that RFA also remained the optimal strategy compared with partial thyroidectomy, irrespective of WTP values. Figures 8 and 9 visualize the results of our probabilistic analysis in a scatter plot and on a cost-effectiveness acceptability curve, respectively.

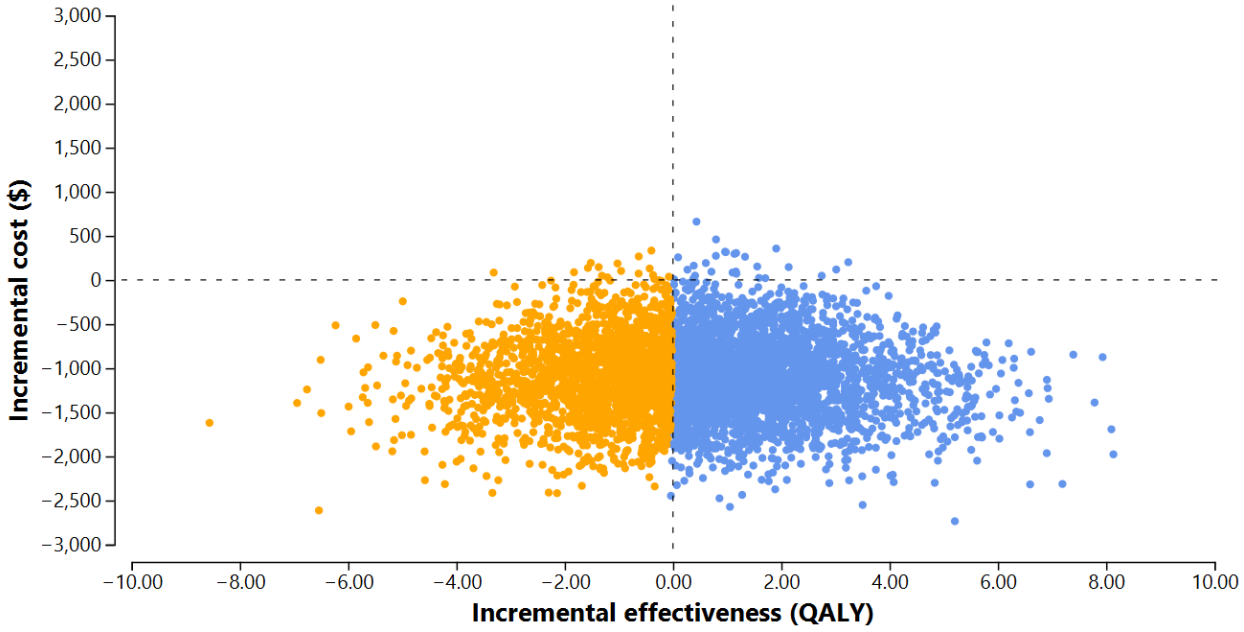

Figure 8: Scatter Plot of Probabilistic Results, AFTNs

This figure visualizes the results of the probabilistic analysis in a scatter plot on a cost-effectiveness plane for AFTNs. Each point represents the outcome of 1 simulation derived from a unique set of parameter values generated from their probability distributions.
Abbreviations: AFTN, autonomously functioning thyroid nodule; QALY, quality-adjusted life-year.

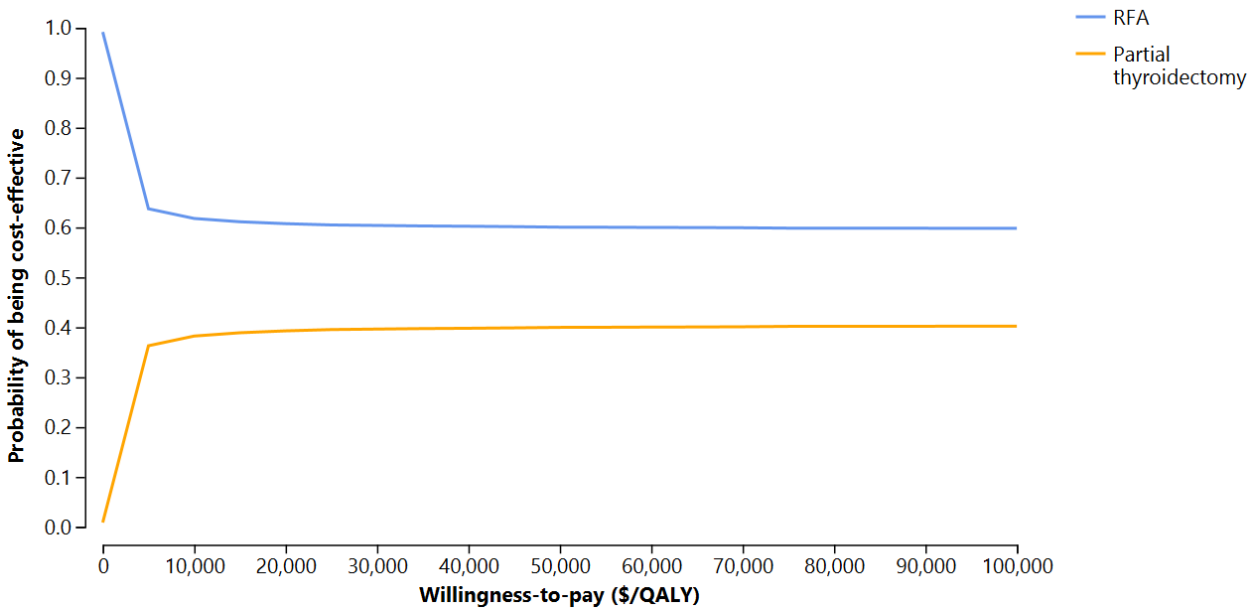

Figure 9: Cost-Effectiveness Acceptability Curve, AFTNs

This figure visualizes the probability of RFA and partial thyroidectomy being cost-effective over a range of WTP values for AFTNs. WTP values are plotted on the horizonal axis, and the probabilities of RFA and partial thyroidectomy being cost-effective at corresponding WTP values are plotted on the vertical axis.

Abbreviations: AFTN, autonomously functioning thyroid nodule; QALY, quality-adjusted life-year; RFA, radiofrequency ablation; WTP, willingness to pay.

Small, Low-Risk Papillary Thyroid Cancer

For adults with small, low-risk papillary thyroid cancer, the mean total costs were $6,465 for RFA, $9,267 for partial thyroidectomy, and $3,884 for active surveillance. The mean total effects were 25.48 QALYs for RFA, 24.64 QALYs for partial thyroidectomy, and 23.84 QALYs for active surveillance. Overall, partial thyroidectomy was dominated by RFA (i.e., it was more costly and less effective). Compared with active surveillance, RFA resulted in an ICER of $1,574 per QALY. Table 30 summarizes the reference case analysis results for small, low-risk papillary thyroid cancer. Please see Appendix 8, Table A31, for an expanded table that includes incremental cost and effect.

Table 30: Reference Case Analysis Results, Small, Low-Risk Papillary Thyroid Cancer

Strategy[a]	Average total costs (95% CrI), $	Average total effects (95% CrI), QALYs	ICER, $/QALY	
			Versus active surveillance	Sequential ICER
Active surveillance	3,884 (3,854 to 3,915)	23.84 (23.32 to 24.32)	–	–
RFA	6,465 (6,295 to 6,807)	25.48 (19.81 to 28.73)	1,574	1,574
Partial thyroidectomy	9,267 (8,645 to 9,922)	24.64 (18.75 to 28.22)	6,729	Dominated[b] by RFA

Abbreviations: CrI, credible interval; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] Treatment strategies are ordered by average total cost, from lowest to highest.

[b] *Dominated* indicates that partial thyroidectomy was more costly and less effective than RFA.

The results of the probabilistic analysis found that at a WTP value of $50,000 per QALY, the probabilities of RFA, partial thyroidectomy, and active surveillance being cost-effective were 57.4%, 35%, and 7.6%, respectively. At a WTP value of $100,000 per QALY, the probabilities of RFA, partial thyroidectomy, and active surveillance being cost-effective remained relatively unchanged at 57.4%, 35.16%, and 7.44%, respectively. Figure 10 visualizes the results of our probabilistic analysis on a cost-effectiveness curve.

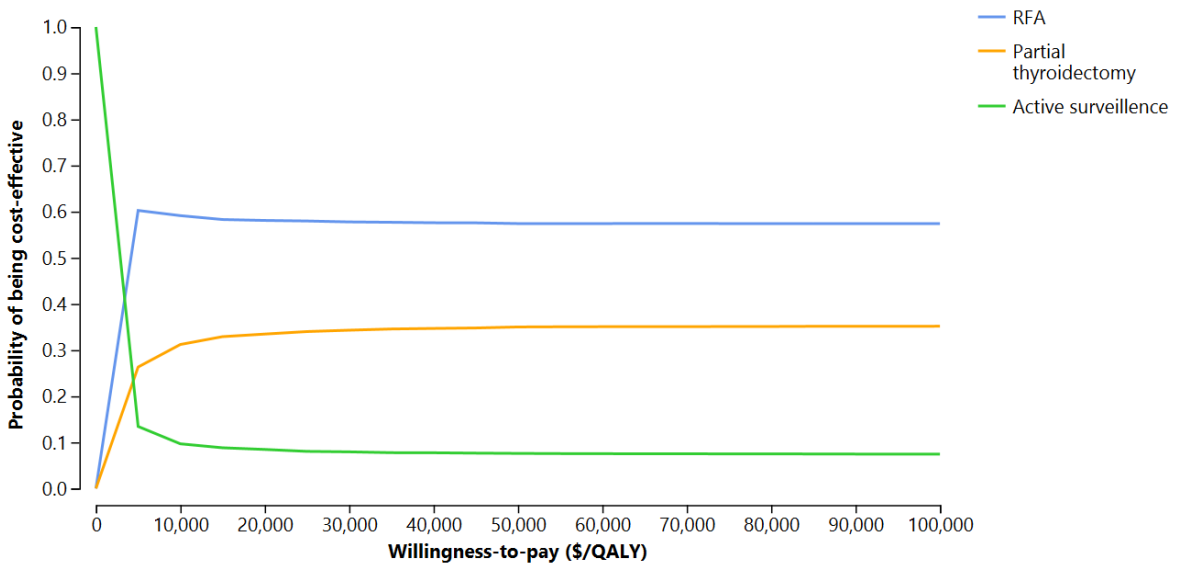

Figure 10: Cost-Effectiveness Acceptability Curve, Small, Low-Risk Papillary Thyroid Cancer

This figure visualizes the probability of RFA, partial thyroidectomy, and active surveillance being cost-effective over a range of WTP values for small, low-risk papillary thyroid cancer. WTP values are plotted on the horizonal axis, and the probabilities of RFA, partial thyroidectomy, and active surveillance being cost-effective at corresponding WTP values are plotted on the vertical axis.
Abbreviation: QALY, quality-adjusted life-year; RFA, radiofrequency ablation; WTP, willingness to pay.

Scenario Analysis

For adults with symptomatic benign thyroid nodules and AFTNs, RFA was the dominant strategy (i.e., more effective and less costly) compared with partial thyroidectomy across all scenarios.

For adults with symptomatic benign thyroid nodules, the scenarios that affected reference case results most were when we assumed the following (Table 31):

- A higher (25% increase) overall RFA cost per session (scenario 3), which resulted in smaller cost savings for RFA
- A higher hospital care cost associated with partial thyroidectomy (scenario 6), which resulted in greater cost savings for RFA
- A lower hospital care cost associated with partial thyroidectomy (scenario 7), which resulted in smaller cost savings for RFA

For all remaining scenarios, the reference case results remained relatively unchanged.

Table 31: Scenario Analysis Results, Symptomatic Benign Thyroid Nodules

Strategy	Average total costs, $	Incremental cost, $[a,b,c]	Average total effects, QALYs	Incremental effect, QALYs[c,d]	ICER ($/QALY)[c]
Reference case	RFA: 4,258 PT: 6,148	–1,890	RFA: 21.45 PT: 20.89	0.55	Dominant[e]
Scenario 1: Assumed that a higher proportion of patients undergoing RFA would require 1 additional ablation session	RFA: 4,308 PT: 6,148	–1,840	RFA: 21.45 PT: 20.89	0.55	Dominant[e]
Scenario 2: Assumed that a higher proportion of patients undergoing RFA would require 2 additional ablation sessions	RFA: 4,365 PT: 6,148	–1,783	RFA: 21.45 PT: 20.89	0.55	Dominant[e]
Scenario 3: Assumed higher total costs for RFA (by 25%)	RFA: 4,975 PT: 6,148	–1,174	RFA: 21.45 PT: 20.89	0.55	Dominant[e]
Scenario 4: Assumed a time horizon of 10 years	RFA: 4,236 PT: 6,019	–1,783	RFA: 8.90 PT: 8.67	0.23	Dominant[e]
Scenario 5: Accounted for a false-negative rate of 3% in FNA cytology for symptomatic benign thyroid nodules	RFA: 4,407 PT: 6,148	–1,742	RFA: 21.43 PT: 20.89	0.54	Dominant[e]
Scenario 6: Assumed that all partial thyroidectomies were performed as inpatient procedures in Ontario	RFA: 4,290 PT: 6,558	–2,268	RFA: 21.45 PT: 20.89	0.55	Dominant[e]
Scenario 7: Assumed that all partial thyroidectomies were performed as outpatient procedures in Ontario	RFA: 4,221 PT: 5,668	–1,446	RFA: 21.45 PT: 20.89	0.55	Dominant[e]
Scenario 8: Applied a 0% discount rate to both costs and QALYs	RFA: 4,327 PT: 6,212	–1,886	RFA: 27.67 PT: 26.96	0.71	Dominant[e]
Scenario 9: Applied a 3% discount rate to both costs and QALYs	RFA: 4,198 PT: 6,104	–1,906	RFA: 17.17 PT: 16.72	0.44	Dominant[e]

Abbreviations: FNA, fine-needle aspiration; ICER, incremental cost-effectiveness ratio; PT, partial thyroidectomy; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] Incremental cost = average cost (strategy B) − average cost (strategy A).

[b] Negative costs indicate savings.

[c] Results may appear inexact due to rounding.

[d] Incremental effect = average effect (strategy B) − average effect (strategy A).

[e] RFA was less costly and more effective than partial thyroidectomy.

Except for scenario 5 (which we explored only for adults with symptomatic benign thyroid nodules), we observed similar trends in all scenarios for adults with AFTNs (Table 32).

Table 32: Scenario Analysis Results, AFTNs

Strategy[a]	Average total costs, $	Incremental cost, $[b,c,d]	Average total effects, QALYs	Incremental effect, QALYs[d,e]	ICER ($/QALY)[d]
Reference case	RFA: 5,019 PT: 6,118	–1,099	RFA: 18.58 PT: 18.12	0.46	Dominant[f]
Scenario 1: Assumed that a higher proportion of patients undergoing RFA would require 1 additional ablation session	RFA: 5,062 PT: 6,118	–1,056	RFA: 18.58 PT: 18.12	0.46	Dominant[f]
Scenario 2: Assumed that a higher proportion of patients undergoing RFA would require 2 additional ablation sessions	RFA: 5,105 PT: 6,118	–1,013	RFA: 18.58 PT: 18.12	0.46	Dominant[f]
Scenario 3: Assumed higher total costs for RFA (by 25%)	RFA: 5,715 PT: 6,118	–403	RFA: 18.58 PT: 18.12	0.46	Dominant[f]
Scenario 4: Assumed a time horizon of 10 years	RFA: 4,985 PT: 6,016	–1,031	RFA: 8.74 PT: 8.52	0.21	Dominant[f]
Scenario 6: Assumed that all partial thyroidectomies were performed as inpatient procedures in Ontario	RFA: 5,116 PT: 6,525	–1,410	RFA: 18.58 PT: 18.12	0.46	Dominant[f]
Scenario 7: Assumed that all partial thyroidectomies were performed as outpatient procedures in Ontario	RFA: 4,907 PT: 5,640	–733	RFA: 18.58 PT: 18.12	0.46	Dominant[f]
Scenario 8: Applied a 0% discount rate to both costs and QALYs	RFA: 5,084 PT: 6,165	–1,081	RFA: 23.14 PT: 22.56	0.57	Dominant[f]
Scenario 9: Applied a 3% discount rate to both costs and QALYs	RFA: 4,963 PT: 6,084	–1,121	RFA: 15.31 PT: 14.93	0.38	Dominant[f]

Abbreviations: AFTN, autonomously functioning thyroid nodule; ICER, incremental cost-effectiveness ratio; PT, partial thyroidectomy; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] Scenario 5 is not reported here; it applied only to benign symptomatic thyroid nodules.

[b] Incremental cost = average cost (strategy B) − average cost (strategy A).

[c] Negative costs indicate savings.

[d] Results may appear inexact due to rounding.

[e] Incremental effect = average effect (strategy B) − average effect (strategy A).

[f] RFA was less costly and more effective than partial thyroidectomy.

For adults with small, low-risk papillary thyroid cancer, RFA remained the optimal strategy across all scenarios. RFA dominated (i.e., was less costly and more effective than) partial thyroidectomy across all scenarios (Table 33). Compared with active surveillance, scenarios that most impacted the cost-effectiveness of RFA in our reference case were when we captured differences between costs and health outcomes over a shorter time horizon (scenarios 3 and 4), which resulted in higher ICERs. For all other scenarios, the impact on the cost-effectiveness of RFA compared with active surveillance in the reference case was relatively small.

Table 33: Scenario Analysis Results, Small, Low-Risk Papillary Thyroid Cancer

Strategy	Average total costs, $	Average total effects, QALYs	ICER, $/QALY [a]	
			Versus active surveillance	Sequential ICER
Reference case	RFA: 6,465 PT: 9,267 AS: 3,884	RFA: 25.48 PT: 24.64 AS: 23.84	RFA vs. AS: 1,574 PT vs. AS: 6,729	RFA vs. AS: 1,574 PT vs. RFA: Dominated[b] by RFA
Scenario 1: Assumed a lower rate of treatment success following RFA for small, low-risk papillary thyroid cancer	RFA: 6,796 PT: 9,267 AS: 3,884	RFA: 25.46 PT: 24.64 AS: 23.84	RFA vs. AS: 1,798 PT vs. AS: 6,729	RFA vs. AS: 1,798 PT vs. RFA: Dominated[b] by RFA
Scenario 2: Assumed higher total costs for RFA (by 25%)	RFA: 7,071 PT: 9,267 AS: 3,884	RFA: 25.48 PT: 24.64 AS: 23.84	RFA vs. AS: 1,943 PT vs. AS: 6,729	RFA vs. AS: 1,943 PT vs. RFA: Dominated[b] by RFA
Scenario 3: Assumed a time horizon of 3 years	RFA: 3,556 PT: 6,157 AS: 688	RFA: 3.36 PT: 3.25 AS: 3.13	RFA vs. AS: 12,470 PT vs. AS: 45,575	RFA vs. AS: 12,470 PT vs. RFA: Dominated[b] by RFA
Scenario 4: Assumed a time horizon of 10 years	RFA: 4,260 PT: 6,868 AS: 1,676	RFA: 8.70 PT: 8.42 AS: 8.13	RFA vs. AS: 4,533 PT vs. AS: 17,903	RFA vs. AS: 4,533 PT vs. RFA: Dominated[b] by RFA
Scenario 5: Assumed that all partial thyroidectomies were performed as inpatient procedures in Ontario	RFA: 6,483 PT: 9,649 AS: 3,902	RFA: 25.48 PT: 24.64 AS: 23.84	RFA vs. AS: 1,574 PT vs. AS: 7,184	RFA vs. AS: 1,574 PT vs. RFA: Dominated[b] by RFA
Scenario 6: Assumed that all partial thyroidectomies were performed as outpatient procedures in Ontario	RFA: 6,444 PT: 8,818 AS: 3,862	RFA: 25.48 PT: 24.64 AS: 23.84	RFA vs. AS: 1,574 PT vs. AS: 6,195	RFA vs. AS: : 1,574 PT vs. RFA: Dominated[b] by RFA
Scenario 7: Applied a 0% discount rate to both costs and QALYs	RFA: 7,613 PT: 10,510 AS: 5,057	RFA: 34.18 PT: 33.06 AS: 31.98	RFA vs. AS: 1,162 PT vs. AS: 5,049	RFA vs. AS: 1,162 PT vs. RFA: Dominated[b] by RFA
Scenario 8: Applied a 3% discount rate to both costs and QALYs	RFA: 5,713 PT: 8,455 AS: 3,110	RFA: 19.79 PT: 19.14 AS: 18.51	RFA vs. AS: 2,034 PT vs. AS: 8,484	RFA vs. AS: 2,034 PT vs. RFA: Dominated[b] by RFA

Abbreviations: AS, active surveillance; ICER, incremental cost-effectiveness ratio; PT, partial thyroidectomy; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] Results may appear inexact due to rounding.

[b] RFA was less costly and more effective than partial thyroidectomy.

We also conducted 3 threshold analyses for symptomatic benign thyroid nodules and AFTNs to determine when RFA would no longer be cost-saving compared with partial thyroidectomy. For adults with symptomatic benign thyroid nodules, we found this to be the case when:

- The total cost of RFA was $4,026 per session (compared to $2,424 per session in the reference case)
- The probability of treatment success for RFA ablation was 0.53 (compared to 0.922 in the reference case). This means that RFA no longer generated savings when the likelihood of the procedure achieving a reduction of 50% or more of the nodule's initial volume at 1-year postprocedure was reduced to 53%.

- The average total hospital care costs associated with partial thyroidectomy were reduced to $2,711 per surgery (compared with $4,762 per surgery in the reference case)

For adults with AFTNs, we found this to be the case when:

- The total cost of RFA was $3,375 per session (compared to $2,424 per session in the reference case)
- The probability of treatment success for RFA ablation was 0.533 (compared to 0.764 in the reference case). This means that RFA no longer generated savings when the likelihood of the procedure resulting in normalization of TSH at 1-year post-procedure was reduced to 53.3%
- The average hospital care costs associated with partial thyroidectomy were reduced to $3,332 per surgery (compared with $4,762 per surgery in the reference case)

Discussion

Our reference case showed that RFA was the optimal strategy compared to standard care in all 3 of our populations of interest. In adults with symptomatic benign thyroid nodules and AFTNs, RFA was the dominant strategy (i.e., less costly and more effective) compared with partial thyroidectomy. In adults with small, low-risk papillary thyroid cancer, RFA was the dominant strategy (i.e., less costly and more effective) compared with partial thyroidectomy and was cost-effective compared with active surveillance, resulting in an ICER of $1,574 per QALY gained. Our reference case results remained robust across all scenario analyses.

Notably, across all 3 populations, RFA generated a small average increase in QALYs over a lifetime horizon while demonstrating a more substantial decrease in average total costs compared with partial thyroidectomy. This suggests that RFA for thyroid nodules may result in more substantially reduced costs to the public health payer rather than improvements to overall health-related quality of life outcomes for patients.

Because there was no treatment effect on survival for any strategy, incremental QALY estimates reflect only differences in health-related quality of life. However, in our probabilistic analyses, we found uncertainty associated with both our total and incremental QALY estimates across all 3 models, as reflected in the wide 95% credible intervals around these estimates. For incremental QALYs, the 95% credible intervals for all 3 models also spanned both negative and positive values (see Tables 28 and 29, and Appendix 8, Table A30). The uncertainty associated with our QALY estimates was attributable to a lack of appropriate utility data. Specifically, our analyses were limited by the availability of preference-based utilities that exactly matched the definitions of our post-treatment health states across all models. This limitation was also identified in the model-based studies[209,211] included in our economic evidence review. Many published studies have measured the quality of life of people with thyroid conditions who have undergone RFA treatment, but these studies largely used the thyroid-specific questionnaire Thyroid-Related Patient-Reported Outcome (ThyPRO). To date, there is no validated mapping methodology to convert ThyPRO scores to health utility values that can be used to inform economic evaluations. To address this uncertainty, we assumed a standard error of 10% for utility and disutility parameters, which contributed to the wide credible internals. When all utility parameters were held as fixed deterministic values, the credible intervals around QALY estimates narrowed substantially.

Nevertheless, based on leveraging the best available utility data, our reference case results aligned with the findings of our clinical evidence review, which found that overall, RFA may result in better quality of life compared with surgery across all our populations of interest.

Equity Considerations

Although the use of QALYs in cost-effectiveness analysis is compatible with the aim of maximizing health benefits, QALYs are unlikely to be the only goal for health care decision-makers or for the populations they serve. Addressing health disparities and equity considerations are examples of additional policy objectives. We did not conduct an equity-focused subgroup analysis due to limited data availability. However, it may be important to consider the following:

- The magnitude of the negative impact of post-thyroidectomy scarring on health-related quality of life may vary by sex and age.
- People living in rural areas or further from treatment centres may be burdened with higher out-of-pocket costs when it comes to accessing treatments and adhering to the duration and frequency of follow-up requirements.

Strengths and Limitations

Our primary economic evaluation provides comprehensive cost-effectiveness analyses of RFA versus current standard care strategies for adults with symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer from the perspective of the Ontario Ministry of Health. To ensure that the evidence we used was of high quality, we derived key clinical parameters from our clinical evidence review for all 3 populations of interest, where possible. We also obtained cost parameter inputs that best reflected actual expenditures in Ontario. Overall, we applied model assumptions that were considered reasonable and conservative and were verified by clinical experts to meet face validity.

As described previously, our analyses were associated with limitations similar to those faced by the studies included in our economic evidence review due to a lack of appropriate data on health-related quality of life that could be used to inform economic evaluations. However, based on the best available utility data, our reference case results aligned with those of the patient reported quality-of-life outcomes in our clinical evidence review. Last, although our model cost parameters provide our best estimates based on verified assumptions and best available data, some parameter values may not capture actual costs. For instance, we estimated the cost of physician services for performing RFA based on the billing fee associated with a similar procedure (J069). However, in practice this procedure (J069) may require less time and be less complex than an ablation procedure for thyroid conditions. To address this, we explored a scenario that assumed higher costs for RFA in all 3 models.

Conclusions

Our cost-effectiveness analyses showed that compared with partial thyroidectomy, RFA was the dominant strategy (i.e., less costly and more effective) in adults with symptomatic benign thyroid nodules and AFTNs. As well, RFA was the optimal strategy compared with partial thyroidectomy and active surveillance in adults with small, low-risk papillary thyroid cancer: it was less costly and more effective than partial thyroidectomy and was cost-effective compared with active surveillance, with an ICER of $1,574 per QALY gained.

Budget Impact Analysis

Research Question

1) What is the potential 5-year budget impact for the Ontario Ministry of Health of publicly funding radiofrequency ablation (RFA) for the treatment of symptomatic benign thyroid nodules in adults?
2) What is the potential 5-year budget impact for the Ontario Ministry of Health of publicly funding RFA for the treatment of autonomously functioning thyroid nodules (AFTNs) in adults?
3) What is the potential 5-year budget impact for the Ontario Ministry of Health of publicly funding RFA for the treatment of small, low-risk papillary thyroid cancer in adults?

Methods

Analytic Framework

We estimated the budget impact of publicly funding ultrasound-guided RFA using the cost difference between 2 scenarios: (1) current clinical practice without public funding for RFA (the current scenario), and (2) anticipated clinical practice with public funding for RFA (the new scenario). Figure 11 presents the model schematic.

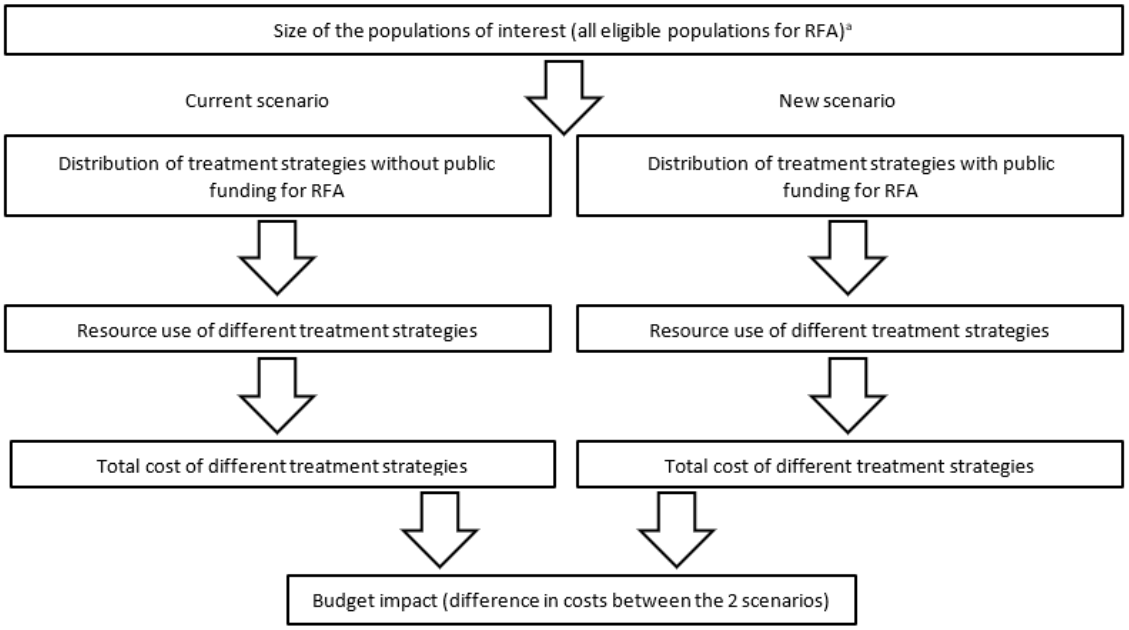

Figure 11: Schematic Model of Budget Impact

Flow chart describing the model for the budget impact analysis. Based on the size of the population of interest, we created 2 scenarios: the current scenario, which would explore the distribution of treatment strategies, resource use, and total costs without public funding for RFA, and the new scenario, which would explore the distribution of treatment strategies, resource use, and total costs with public funding for RFA. The budget impact would represent the difference in costs between the 2 scenarios.

Abbreviations: AFTN, autonomously functioning thyroid nodule; RFA, radiofrequency ablation.

[a] Our populations of interest for this budget impact analysis were adults with symptomatic benign thyroid nodules, adults with AFTNs, and adults with small, low-risk papillary thyroid cancer.

Key Assumptions

The main assumptions in our budget impact analysis included those used in our primary economic evaluation, as well as the following:

- All adults with symptomatic benign thyroid nodules and AFTNs who have undergone partial thyroidectomy in Ontario may be eligible for RFA.
- All adults with small, low-risk papillary thyroid cancer who have undergone partial thyroidectomy in Ontario or are under active surveillance may be eligible for RFA.
- In Ontario, adults with the classification cT1aN0M0 for papillary thyroid cancer (i.e., tumours 1 cm or less in maximum diameter with no regional lymph node involvement or distant metastasis) may be referred to active surveillance. We assumed that 20% of those referred would agree to undergo active surveillance (Antoine Eskander, MD, email communication, September 7, 2025).
- If publicly funded, RFA may be centralized to high-volume centres (defined as centres that receive an adequate volume of eligible patients to ensure sufficient experience and skills to select appropriate candidates and perform the procedure optimally with low morbidity and high efficiency). We assumed that each high-volume centre would perform approximately 100 RFA sessions per year for the treatment of thyroid conditions.

Population of Interest

Our populations of interest were adults with symptomatic benign thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer (Table 34). We estimated the size of our populations of interest based on the Ontario Ministry of Finance annual population projections from 2023 to 2051,[271] published epidemiology studies,[1,8,223,272] surgical volumes from health administrative databases via IntelliHealth Ontario, and consultations with clinical experts. These estimates were then verified for face validity by our clinical experts. Finally, we adjusted all of our populations of interest for annual population growth over the next 5 years based on Ontario Ministry of Finance population projections for the province.[271]

Table 34: Populations of Interest

Population, n	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Total population eligible for RFA	1,694	1,706	1,710	1,714	1,727	8,551
Symptomatic benign thyroid nodules	727	733	734	736	742	3,672
AFTNs	135	136	136	136	137	679
Small, low-risk papillary thyroid cancer	832	838	840	842	848	4,200
Partial thyroidectomy	661	666	668	669	674	3,339
Active surveillance	171	172	172	173	174	861

Abbreviations: AFTN, autonomously functioning thyroid nodule; RFA, radiofrequency ablation.

Symptomatic Benign Thyroid Nodules

We estimated the number of adults with symptomatic benign thyroid nodules who would be eligible for RFA based on the average annual volume of partial thyroidectomies performed for this population in Ontario from 2022 to 2024. To obtain this estimate, we used previously generated datasets from the Canadian Institute for Health Information Discharge Abstract Database and National Ambulatory Care Reporting System described in our Primary Economic Evaluation (see Cost Parameters and Appendix 9 for further details). Because this estimate included partial thyroidectomies performed for AFTNs as well, we calculated the difference after subtracting the estimated number of newly diagnosed AFTNs per year (see Autonomously Functioning Thyroid Nodules, below). Overall, we estimated that the annual number of adults with symptomatic benign thyroid nodules who would be eligible for RFA would range from 727 in year 1 to 742 in year 5, for a total of 3,672 over the next 5 years.

Autonomously Functioning Thyroid Nodules

We estimated the number of adults with AFTNs who would be eligible for RFA based on the reported incidence of solitary toxic adenomas (AFTNs that are symptomatic and causing overt hyperthyroidism) in an iodine-sufficient area of Sweden, which was found to be 1.0 per 100,000 per year.[223] Overall, we estimated that the annual number of adults with AFTNs eligible for RFA would range from 135 in year 1 to 137 in year 5, for a total of 679 over the next 5 years.

Small, Low-Risk Papillary Thyroid Cancer

We estimated the number of adults with small, low-risk papillary thyroid cancer eligible for RFA based on the average annual volume of partial thyroidectomies performed for this population in Ontario from 2022 to 2024 and the average number of adults with small, low-risk papillary thyroid cancer who agreed to undergo active surveillance.

To obtain the average annual volume of partial thyroidectomies performed for adults with small, low-risk papillary thyroid cancer, we used the same methods as described above to estimate surgical volumes for symptomatic benign thyroid nodules but filtered results instead using the Canadian version of the *International Classification of Diseases* (ICD-10-CA) disease code for thyroid cancer (C73, malignant neoplasm of the thyroid gland). We then accounted for the proportion of thyroid cancers that are papillary thyroid carcinomas (approximately 84%) and the proportion of papillary thyroid carcinomas that are 2 cm or less in maximum diameter (approximately 62.1%).[1,272]

To estimate the average number of adults with small, low-risk papillary thyroid cancer who would undergo active surveillance each year, we referred to the 2025 American Thyroid Association guidelines for differentiated thyroid cancer,[17] which recommend that active surveillance may be offered to some patients with the American Joint Committee on Cancer TNM (tumour, nodes, metastasis) staging classification cT1aN0M0 for papillary thyroid cancer (i.e., a tumour 1 cm or less in maximum diameter with no regional lymph node involvement or distant metastasis). We then approximated the annual number of people with small, low-risk papillary thyroid cancer under active surveillance in Ontario based on the following:

- Age-standardized incidence rate of thyroid cancer in Ontario in 2022 (22.6 per 100,000)[8]
- Proportion of thyroid cancer that is papillary thyroid cancer (approximately 84%)[1]

- Proportion of papillary thyroid cancer that is 1 cm or less in maximum diameter (approximately 33.4%)[272]
- The assumption that 20% of referred patients would agree to undergo active surveillance (Antoine Eskander, MD, email communication, September 7, 2025)

Overall, we estimated that the annual number of adults with small, low-risk papillary thyroid cancer who would be eligible for RFA would range from 832 in year 1 to 848 in year 5, for a total of 4,200 over the next 5 years.

Current Intervention Mix

At present, RFA for the treatment of symptomatic benign thyroid nodules and AFTNs is offered at 4 centres in Ontario.[26] Among these centres, 2 also offer RFA for small, low-risk papillary thyroid cancer. However, because RFA is not publicly funded and was paid for by philanthropic sources, research grants or patient self-pay, we did not consider its use for the treatment of symptomatic benign thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer to be part of our current intervention mix.

In our current intervention mix, we assumed that all adults with symptomatic benign thyroid nodules and AFTNs would be treated with partial thyroidectomy, and all adults with small, low-risk papillary thyroid cancer would be treated with partial thyroidectomy or undergo active surveillance (Table 34).

Uptake of the New Intervention and New Intervention Mix

The first RFA procedure for the treatment of thyroid nodules in Ontario took place in April 2023,[273] but diffusion of this minimally invasive, ultrasound-guided ablation technology has been slow. In the absence of public funding, only a small volume of RFA procedures have been performed since then.

If publicly funded, RFA may be centralized such that it is performed at centres that receive an adequate volume of eligible patients to ensure sufficient experience and skills to select appropriate candidates and perform the procedure optimally with low morbidity and high efficiency.[18] Existing guidelines[18] also suggest that these procedures should be performed by providers who have expertise with thyroid ultrasound and fine-needle biopsy. In Ontario, these providers may include otolaryngologists (ear, nose, and throat surgeons); general surgeons with a subspecialty in thyroid surgery; and interventional radiologists. Moreover, because RFA requires the use of ultrasound machines, this procedure is expected to be performed at centres that have this institutional resource.

Based on these considerations, we expect that in the first year of public funding, the uptake of RFA would continue to be concentrated at the 4 centres that are currently offering RFA, because they already have in place the required system (i.e., a Viva Combo RF Generator) and providers experienced in performing the procedure. In subsequent years, we expect that RFA would expand to other high-volume thyroid surgical centres that have staff surgeons who specialize in thyroid surgery or interventional radiologists. Assuming that each centre performs approximately 100 RFA sessions per year, this would correspond to an uptake of 25% in year 1. We then assumed a constant moderate increase in uptake of 20% in year 2 through year 4, reaching an uptake of 100% in year 5.

Tables 35 and 36 provide the estimated number of adults with symptomatic benign thyroid nodules and AFTNs in Ontario who are receiving RFA and partial thyroidectomy in the current scenario and our projected estimate for the use of RFA in Ontario over the next 4 years in the new scenario (i.e., with

public funding for RFA). Table 37 provides the estimated number of adults with small, low-risk papillary thyroid cancer in Ontario who are receiving RFA, partial thyroidectomy, and active surveillance in the current scenario and our projected estimate for the use of RFA in Ontario over the next 5 years in the new scenario. We assumed that uptake of RFA in the new scenario would displace proportionally the number of adults who chose partial thyroidectomy or active surveillance.

Table 35: Estimated Number of Adults With Symptomatic Benign Thyroid Nodules Receiving RFA and Partial Thyroidectomy in the Current and New Scenarios

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Current scenario						
RFA, n	0	0	0	0	0	0
Partial thyroidectomy, n	727	733	734	736	742	3,672
Total volume, n	727	733	734	736	742	3,672
New scenario[a]						
Uptake rate for RFA, %	0.25	0.45	0.65	0.85	1	–
RFA, n	182	330	477	625	742	2,356
Partial thyroidectomy, n	545	403	257	110	0	1,316
Total volume, n	727	733	734	736	742	3,672

Abbreviation: RFA, radiofrequency ablation.

[a] The volume of interventions was calculated from the total volume multiplied by the uptake rate for the new intervention. For example, in the new scenario, the total volume in year 1 is 727 and the uptake rate for RFA is 25%, so the volume of RFA in year 1 is 182 (727 × 25%).

Table 36: Estimated Number of Adults With AFTNs Receiving RFA and Partial Thyroidectomy in the Current and New Scenarios

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Current scenario						
RFA, n	0	0	0	0	0	0
Partial thyroidectomy, n	135	136	136	136	137	679
Total volume, n	135	136	136	136	137	679
New scenario[a]						
Uptake rate for RFA, %	0.25	0.45	0.65	0.85	1	–
RFA, n	34	61	88	116	137	436
Partial thyroidectomy, n	101	75	48	20	0	243
Total volume, n	135	136	136	136	137	679

Abbreviations: AFTN, autonomously functioning thyroid nodule; RFA, radiofrequency ablation.

[a] The volume of interventions was calculated from the total volume multiplied by the uptake rate for the new intervention. For example, in the new scenario, the total volume in year 1 is 135 and the uptake rate for RFA is 25%, so the volume of RFA in year 1 is 34 (135 × 25%).

Table 37: Estimated Number of Adults With Small, Low-Risk Papillary Thyroid Cancer Receiving RFA and Partial Thyroidectomy in the Current and New Scenarios

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Current scenario						
RFA, n	0	0	0	0	0	0
Partial thyroidectomy, n	661	666	668	669	674	3,339
Active surveillance, n	171	172	172	173	174	861
Total volume, n	832	838	840	842	848	4,200
New scenario[a]						
Uptake rate for RFA, %	0.25	0.45	0.65	0.85	1	–
RFA, n	208	377	546	716	848	2,695
Partial thyroidectomy, n	496	366	234	100	0	1,196
Active surveillance, n	128	95	60	26	0	309
Total volume, n	832	838	840	842	848	4,200

Abbreviations: RFA, radiofrequency ablation.

[a] We assumed that uptake of RFA in the new scenario would displace proportionally the number of people undergoing partial thyroidectomy and active surveillance.

Resources and Costs

We included all health care costs in our budget impact analysis by running our companion cost-effectiveness analyses for each population of interest (as previously described) over the time horizon of the budget impact analysis (without discounting) to obtain the relevant costs.

Internal Validation

The secondary health economist conducted formal internal validation. This process included checking for errors and ensuring the accuracy of parameter inputs and equations in the budget impact analysis.

Analysis

We conducted a reference case analysis and sensitivity analyses. Our reference case analysis represents the analysis with the most likely set of input parameters and model assumptions. Our sensitivity analyses explored how the results were affected by varying input parameters and model assumptions.

For adults with symptomatic benign thyroid nodules and AFTNs, we examined the following scenarios in our sensitivity analysis. Except for scenario 4, all scenarios were conducted for both populations:

- Scenario 1: Assumed that a higher proportion of patients undergoing RFA would require 1 additional ablation session (2 times that of the reference case, at 4.6%)
- Scenario 2: Assumed that 2.3% of patients undergoing RFA would require 2 additional ablation sessions
- Scenario 3: Assumed that the total cost for RFA per session would be higher by 25% ($3,030.38 per session versus $2,424.31 per session in the reference case)

- Scenario 4: Accounted for a false-negative rate of 3% in fine-needle aspiration cytology[235] for thyroid nodules by assuming a lower treatment success rate (at 89.2%) at 1 year after RFA in people with symptomatic benign thyroid nodules (this scenario applied only to the population with symptomatic benign thyroid nodules; AFTNs are almost always benign)
- Scenario 5: Assumed that all partial thyroidectomies for symptomatic benign thyroid nodules and AFTNs were performed as inpatient procedures in Ontario
- Scenario 6: Assumed that all partial thyroidectomies for symptomatic benign thyroid nodules and AFTNs were performed as outpatient procedures in Ontario
- Scenario 7: Assumed a lower uptake for RFA, starting at 20% in year 1, increasing by 15% each year, and reaching 80% in year 5

For adults with small, low-risk papillary thyroid cancer, we examined the following scenarios in our sensitivity analysis:

- Scenario 1: Assumed that a lower proportion of patients would achieve complete tumour disappearance with RFA at 85.97% (versus 95.28% in the reference case)[84]
- Scenario 2: Assumed higher costs associated with RFA, including a higher capital cost per session (3 times that of the reference case, at $121.50 per session) and a higher procedure cost for physicians performing the procedure (2 times that of the reference case, at $1,031.40 per session)
- Scenario 3: Assumed that all partial thyroidectomies for small, low-risk papillary thyroid cancer were performed as inpatient procedures in Ontario
- Scenario 4: Assumed that all partial thyroidectomies for small, low-risk papillary thyroid cancer were performed as outpatient procedures in Ontario
- Scenario 5: Assumed a lower uptake for RFA, starting at 20% in year 1, increasing by 15% each year, and reaching 80% in year 5

Results

Reference Case

Tables 38, 39, and 40 summarize the total costs associated with use of RFA for treatment of adults with symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer in Ontario over the next 5 years, respectively.

For adults with symptomatic benign thyroid nodules, the annual budget impact ranged from a cost saving of $0.45 million in year 1 to a cost saving of $1.62 million in year 5, for a total 5-year budget impact of $5.42 million in cost savings.

Table 38: Budget Impact Analysis Results, Symptomatic Benign Thyroid Nodules

	Budget impact, $ million[a]					
Scenario	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Total[b,c]**
Current scenario	4.32	4.36	4.38	4.39	4.44	21.90
RFA	0	0	0	0	0	0
Partial thyroidectomy	4.32	4.36	4.38	4.39	4.44	21.90
New scenario	3.87	3.56	3.26	2.98	2.81	16.48
RFA	0.63	1.16	1.72	2.31	2.80	8.62
Partial thyroidectomy	3.24	2.40	1.54	0.67	0.01	7.86
Budget impact[b,c]	−0.45	−0.80	−1.12	−1.42	−1.62	−5.42

Abbreviation: RFA, radiofrequency ablation.

[a] In 2025 Canadian dollars.

[b] Negative costs indicate savings.

[c] Results may appear inexact due to rounding. All costs were calculated using mean costs from the probabilistic results in the Primary Economic Evaluation.

For adults with AFTNs, the annual budget impact ranged from a cost saving of $0.06 million in year 1 to a cost saving of $0.19 million in year 5, for a total 5-year budget impact of $0.64 million in cost savings.

Table 39: Budget Impact Analysis Results, AFTNs

	Budget impact, $ million[a]					
Scenario	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Total[b,c]**
Current scenario	0.80	0.81	0.81	0.81	0.82	4.05
RFA	0	0	0	0	0	0
Partial thyroidectomy	0.80	0.81	0.81	0.81	0.82	4.05
New scenario	0.74	0.71	0.68	0.65	0.63	3.41
RFA	0.14	0.27	0.39	0.52	0.63	1.96
Partial thyroidectomy	0.60	0.44	0.28	0.12	0.00	1.45
Budget impact[b,c]	−0.06	−0.10	−0.13	−0.17	−0.19	−0.64

Abbreviations: AFTN, autonomously functioning thyroid nodule; RFA, radiofrequency ablation.

[a] In 2025 Canadian dollars.

[b] Negative costs indicate savings.

[c] Results may appear inexact due to rounding. All costs were calculated using mean costs from the probabilistic results in the Primary Economic Evaluation.

For adults with small, low-risk papillary thyroid cancer, the annual budget impact ranged from a cost saving of $0.32 million in year 1 to a cost saving of $1.26 million in year 5, for a total 5-year budget impact of $4.03 million in cost savings over the next 5 years.

Table 40: Budget Impact Analysis Results, Small, Low-Risk Papillary Thyroid Cancer

	Budget impact, $ million[a]					
Scenario	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Total[b,c]**
Current scenario	3.97	4.11	4.24	4.33	4.48	21.13
RFA	0	0	0	0	0	0
Partial thyroidectomy	3.89	4.01	4.12	4.17	4.28	20.47
Active surveillance	0.08	0.10	0.12	0.16	0.20	0.66
New scenario	3.65	3.54	3.42	3.27	3.22	17.10
RFA	0.68	1.26	1.87	2.50	3.03	9.33
Partial thyroidectomy	2.92	2.23	1.50	0.71	0.13	7.48
Active surveillance	0.06	0.06	0.05	0.06	0.06	0.29
Budget impact[b,c]	−0.32	−0.57	−0.82	−1.06	−1.26	−4.03

Abbreviation: RFA, radiofrequency ablation.

[a] In 2025 Canadian dollars.

[b] Negative costs indicate savings.

[c] Results may appear inexact due to rounding. All costs were calculated using mean costs from the probabilistic results in the Primary Economic Evaluation.

Opportunities for Cost Savings or a Reduction in Health Care Resource Use

Although RFA generated cost savings in our budget impact analyses for all populations, these costs should not be interpreted as a net savings to the Ministry of Health's overall budget. Rather, they are cost reductions to portions of the Ministry of Health's budget and represent a release of system pressures (i.e., hospital resources), allowing hospitals to reallocate some resources to other areas.

Sensitivity Analysis

Tables 41, 42, and 43 summarize the results of the scenario analyses conducted for our budget impact analyses for adults with symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer, respectively. Across all scenarios, publicly funding RFA generated cost savings for the province. Overall, our reference case budget impact results for all populations were most sensitive to the scenario that assumed higher overall RFA costs per session (by 25%). For adults with small, low-risk papillary thyroid cancer, the scenarios that assumed a lower RFA treatment success (scenario 1) and lower uptake rate (scenario 5) also resulted in notably smaller total cost savings over 5 years than in our reference case.

Table 41: Budget Impact Analysis Results, Scenario Analysis, Symptomatic Benign Thyroid Nodules

Scenario	Budget impact, $ million[a,b,c]					
	Year 1	Year 2	Year 3	Year 4	Year 5	Total[b,c]
Reference case	−0.45	−0.80	−1.12	−1.42	−1.62	−5.42
Scenario 1: Assumed that a higher proportion of patients undergoing RFA would require 1 additional ablation session	−0.44	−0.79	−1.10	−1.38	−1.58	−5.30
Scenario 2: Assumed that 2.3% of patients undergoing RFA would require 2 additional ablation sessions	−0.43	−0.77	−1.07	−1.35	−1.55	−5.17
Scenario 3: Assumed higher total costs for RFA (by 25%)	−0.34	−0.60	−0.82	−1.02	−1.14	−3.92
Scenario 4: Accounted for a false negative rate of 3% in FNA cytology	−0.42	−0.75	−1.05	−1.32	−1.51	−5.04
Scenario 5: Assumed that all partial thyroidectomies were performed as inpatient procedures in Ontario	−0.52	−0.93	−1.30	−1.65	−1.90	−6.31
Scenario 6: Assumed that all partial thyroidectomies were performed as outpatient procedures in Ontario	−0.37	−0.66	−0.91	−1.14	−1.29	−4.38
Scenario 7: Assumed a lower uptake for RFA, starting at 20% in year 1, increasing by 15% each year, and reaching 80% in year 5	−0.36	−0.63	−0.86	−1.08	−2.19	−5.12

Abbreviations: FNA, fine-needle aspiration; RFA, radiofrequency ablation.

[a] In 2025 Canadian dollars.

[b] Negative costs indicate savings.

[c] Results may appear inexact due to rounding. All costs were calculated using mean costs from the probabilistic results in the Primary Economic Evaluation.

Table 42: Budget Impact Analysis Results, Scenario Analysis, AFTNs

Scenario[a]	Budget impact, $ million[b,c,d]					
	Year 1	Year 2	Year 3	Year 4	Year 5	Total[c,d]
Reference case	−0.06	−0.10	−0.13	−0.17	−0.19	−0.64
Scenario 1: Assumed that a higher proportion of patients undergoing RFA would require 1 additional ablation session	−0.05	−0.09	−0.13	−0.16	−0.19	−0.63
Scenario 2: Assumed that 2.3% of patients undergoing RFA would require 2 additional ablation sessions	−0.05	−0.09	−0.13	−0.16	−0.18	−0.60
Scenario 3: Assumed higher total costs for RFA (by 25%)	−0.03	−0.06	−0.08	−0.09	−0.10	−0.36
Scenario 5: Assumed that all partial thyroidectomies were performed as inpatient procedures in Ontario	−0.07	−0.12	−0.16	−0.20	−0.23	−0.77
Scenario 6: Assumed that all partial thyroidectomies were performed as outpatient procedures in Ontario	−0.04	−0.07	−0.10	−0.12	−0.14	−0.48
Scenario 7: Assumed a lower uptake for RFA, starting at 20% in year 1, increasing by 15% each year, and reaching 80% in year 5	−0.04	−0.08	−0.10	−0.13	−0.15	−0.50

Abbreviations: AFTN, autonomously functioning thyroid nodule; RFA, radiofrequency ablation.

[a] Scenario 4 is not reported here; it applied only to benign symptomatic thyroid nodules.

[b] In 2025 Canadian dollars.

[c] Negative costs indicate savings.

[d] Results may appear inexact due to rounding. All costs were calculated using mean costs from the probabilistic results in the Primary Economic Evaluation.

Table 43: Budget Impact Analysis Results, Scenario Analysis, Small, Low-Risk Papillary Thyroid Cancer

Scenario	Budget impact, $ million[a,b,c]					
	Year 1	Year 2	Year 3	Year 4	Year 5	Total[b,c]
Reference case	−0.32	−0.57	−0.82	−1.06	−1.26	−4.03
Scenario 1: Assumed that a lower proportion of patients would achieve complete tumour disappearance with RFA	−0.21	−0.38	−0.55	−0.71	−0.85	−2.71
Scenario 2: Assumed higher costs associated with RFA	−0.19	−0.34	−0.49	−0.63	−0.75	−2.40
Scenario 3: Assumed that all partial thyroidectomies for small, low-risk papillary thyroid cancer were performed as inpatient procedures in Ontario	−0.38	−0.68	−0.97	−1.27	−1.51	−4.81
Scenario 4: Assumed that all partial thyroidectomies for small, low-risk papillary thyroid cancer were performed as outpatient procedures in Ontario	−0.25	−0.44	−0.63	−0.82	−0.98	−3.12
Scenario 5: Assumed a lower uptake for RFA, starting at 20% in year 1, increasing by 15% each year, and reaching 80% in year 5	−0.25	−0.44	−0.63	−0.81	−1.01	−3.15

Abbreviation: RFA, radiofrequency ablation.

[a] In 2025 Canadian dollars.

[b] Negative costs indicate savings.

[c] Results may appear inexact due to rounding. All costs were calculated using mean costs from the probabilistic results in the Primary Economic Evaluation.

Discussion

The use of RFA is associated with substantially reduced up-front costs compared with partial thyroidectomy. This reduction in costs is attributed to shorter procedure time and health resource use requirements (e.g., RFA is performed in an outpatient setting under local anesthesia, whereas partial thyroidectomy is performed under general anesthesia and may require inpatient hospitalization and an overnight stay).

We based our estimates of the projected populations receiving RFA in the current and new scenarios on reasonable assumptions that achieved face validity, but only a proportion of each population of interest may be appropriate candidates for RFA treatment. For instance, RFA is contraindicated in people with nodules in areas that cannot be sufficiently visualized by ultrasound (e.g., in people with short necks or difficulty with neck extension), or with nodules that are in close proximity to important cervical structures, such as the carotid artery, jugular veins, or nerves.[18,274] People with large nodules (e.g., > 5 cm in diameter) may also not be ideal candidates for treatment with ablation technologies, because they may require multiple sessions to resolve symptoms (Antoine Eskander, MD, telephone communication, March 26, 2025). Furthermore, because people undergo ultrasound-guided ablation treatment in a conscious state, they may need to be able to tolerate a low degree of discomfort and cooperate with the physician while the ablation procedure is being performed.[18] Finally, some people may simply not want an intervention to address their symptoms.[18] As such, it is an important consideration that not all people who are eligible for RFA will choose to receive this intervention.

In our budget impact analysis for adults with small, low-risk papillary thyroid cancer, we assumed that if RFA were publicly funded, it would displace proportionally the number of people receiving partial thyroidectomy and active surveillance. In practice, the decision for a treatment option (i.e., partial thyroidectomy, active surveillance, or RFA) may be based on various clinical factors and should

be made jointly between physician and patient. As such, the number of people currently receiving partial thyroidectomy and active surveillance may not decrease proportionally as modelled if publicly funded RFA becomes available to this population.

Strengths and Limitations

We derived the estimates for our budget impact analysis by running cost-effectiveness analyses for each of our populations of interest, the key parameters of which were obtained from our clinical evidence review and local Canadian sources. Further, we verified our model assumptions and estimates with clinical experts who had expertise in the use of RFA and thyroid oncology and surgery. We also estimated the size of our populations of interest based on local datasets generated using health administrative databases maintained by the Canadian Institute for Health Information, and on recent epidemiology studies.

An important limitation is that we were unable to evaluate equity considerations in our budget impact analyses. This is an important consideration for implementation, because we expect that RFA may be centralized to high-volume centres if publicly funded, and this may impose access barriers for people who live in rural areas or far from these centres. As well, the implementation of RFA province-wide may require additional up-front costs that have not been accounted for in our analyses. These may include the cost of physician training to perform RFA, the cost of physician education for referring physicians, and the cost of developing a quality-assurance program around this procedure.

Conclusions

We estimate that publicly funding RFA in Ontario for the treatment of adults with symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer would lead to cost savings of $5.42 million, $0.64 million, and $4.03 million over the next 5 years.

Preferences and Values Evidence

Objective

The objective of this analysis was to explore the underlying values, needs, and priorities of those who have lived experience of symptomatic benign thyroid nodules, cystic thyroid nodules, autonomously functioning thyroid nodules (AFTNs), or small, low-risk papillary thyroid cancer, as well as the preferences and perceptions of patients, care partners, and health care providers with respect to ablative technologies.

Background

Exploring patient preferences and values provides a unique source of information about people's experiences of a health condition and the health technologies or interventions used to manage or treat that health condition. It includes the impact of the condition and its treatment on the person with the health condition, their family and other care partners, and the person's personal environment. Engagement also provides insights into how a health condition is managed by the province's health system.

Information shared from lived experience can also identify gaps or limitations in published research (e.g., outcomes important to those with lived experience that are not reflected in the literature).[275-277] Additionally, lived experience can provide information and perspectives on the ethical and social values implications of health technologies or interventions.

Because the needs, preferences, priorities, and values of those with lived experience in Ontario are important to consider in understanding the impact of a technology or intervention in people's lives, we may speak directly with people who live with a given health condition, including those with experience of the technology or intervention we are exploring.

For this analysis, we examined the preferences and values of people with symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer in 2 ways:

- A review by Ontario Health of the quantitative evidence on patient, care partner, and health care provider preferences and values
- Direct engagement by Ontario Health with people who have symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer through interviews

Quantitative Evidence

Research Question

What is the relative preference of patients and health care providers for ablative technologies for the treatment of symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer in adults?

Methods

Literature Search

We performed a literature search for quantitative evidence of preferences and values on March 12, 2025, to retrieve studies published from database inception until the search date. We used the Ovid interface to search MEDLINE and the EBSCOhost interface to search the Cumulative Index to Nursing & Allied Health Literature (CINAHL).

The search was based on the population and intervention of the clinical search strategy with a methodological filter applied to limit retrieval to quantitative evidence of preferences and values (modified from Selva et al[278]). The final search strategy was peer-reviewed using the PRESS Checklist.[28]

We created database auto-alerts in MEDLINE and CINAHL and monitored them until October 31, 2025. See Appendix 2 for our literature search strategies, including all search terms.

Eligibility Criteria

Studies

Inclusion Criteria

- English-language full-text publications
- Studies published from database inception to March 12, 2025
- Studies of patient and health care provider preferences for ablative technologies to manage symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer that used quantitative measures:
  - Utility measures: direct techniques (standard gamble, time trade-off, rating scales), conjoint analysis (discrete choice experiment, contingent valuation and willingness-to-pay, probability trade-off), or indirect techniques (prescored multiattributable instruments such as the 36-Item Short Form Health Survey, EQ-5D, Health Utilities Index)
  - Nonutility quantitative measures: direct-choice techniques, decision aids, surveys, questionnaires

Exclusion Criteria

- Qualitative studies, editorials, commentaries, case reports, conferences abstracts, letters

Participants

Inclusion Criteria

- Adults with symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer

Exclusion Criteria

- Children (< 18 years of age)
- Pregnant people

Interventions

Inclusion Criteria

- Thermal ablation, including radiofrequency ablation (RFA), microwave ablation, laser ablation, and high-intensity focused ultrasound ablation
- Chemical ablation, including ethanol
- Nanosecond pulsed-field ablation

Exclusion Criteria

- Nonablative technologies

Comparators

Inclusion Criteria

- Surgery
- Active surveillance
- Other ablative technologies (e.g., RFA vs. microwave ablation)

Exclusion Criteria

- One versus multiple treatments with the same ablative technology (e.g., 1 vs. 2 RFA sessions)
- One versus multiple treatments with different ablative technologies (e.g., RFA vs. RFA and microwave ablation)

Outcome Measures

- Any quantitative outcomes related to satisfaction, preferences, and values

Timing

- Presence of symptomatic benign thyroid nodules, cystic thyroid nodules, AFTNs, or small, low-risk papillary thyroid cancer that warrants intervention

Setting

- Outpatient

Literature Screening

A single reviewer conducted an initial screening of titles and abstracts using Covidence[29] and then obtained the full texts of studies that appeared eligible for review according to the inclusion criteria. The same reviewer then examined the full-text articles and selected studies eligible for inclusion. The reviewer also examined reference lists and consulted content experts for any additional relevant studies not identified through the search.

Data Extraction

We extracted relevant data on study design and characteristics using a data form to collect information about results and PICOTS (population, intervention, comparator, timing, setting).

Statistical Analysis

Results are summarized narratively. No additional statistical analyses were conducted beyond those reported in the primary studies.

Critical Appraisal of Evidence

We did not undertake a formal critical appraisal of the included studies.

Results

Literature Search

The literature search of the quantitative evidence of preferences and values yielded 231 citations, including grey literature results and after removing duplicates, published between database inception and March 12, 2025. We identified 2 additional studies from other sources, including database alerts (monitored until October 31, 2025). In total, we identified 2 observational studies that met our inclusion criteria. Figure 12 presents the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the literature search for quantitative evidence of preferences and values.

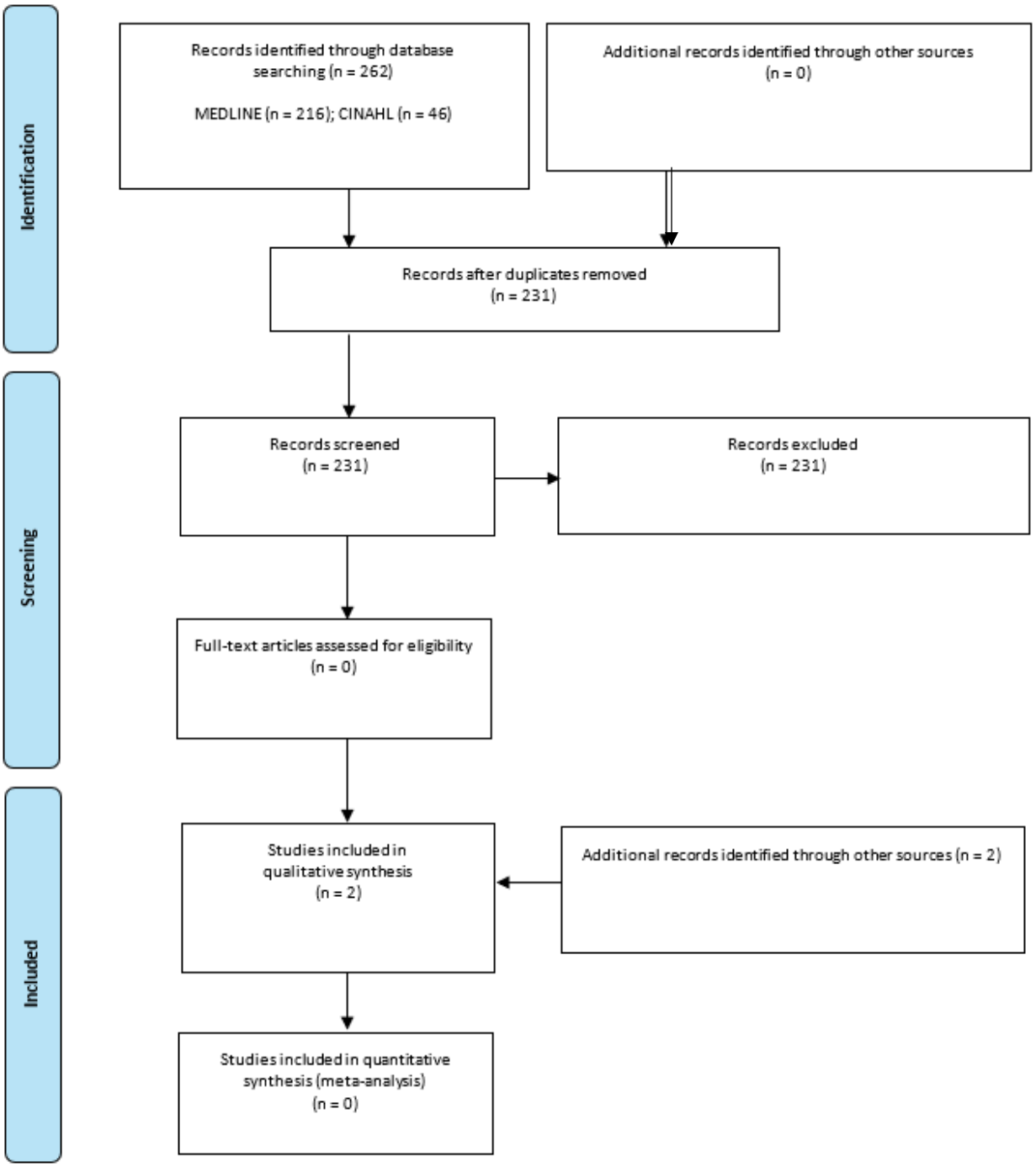

Figure 12: PRISMA Flow Diagram – Quantitative Evidence of Preferences and Values Review

PRISMA flow diagram showing the quantitative evidence of preferences and values review. The literature search for quantitative evidence of preferences and values yielded 231 citations, including grey literature results and after removing duplicates, published between database inception and March 12, 2025. We screened the abstracts of the 231 identified studies and excluded 231. We identified 2 additional studies from other sources. In the end, we included 2 articles in the qualitative synthesis.

Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Source: Adapted from Page et al.[40]

Characteristics of Included Studies

Two studies met the inclusion criteria.[279,280] The first included study was an online survey that explored physician and patient insights and preferences related to current interventions for thyroid nodules.[279] The survey was developed using the EVIdence based Decision-Making (EVIDEM) multicriteria decision analysis framework. The EVIDEM core model encompassed 5 categories of 13 quantitative criteria, and the contextual tool consisted of 4 qualitative criteria. The quantitative criteria were as follows:

- Disease severity
- Size of affected population
- Unmet needs
- Comparative efficacy or effectiveness
- Comparative safety or tolerability
- Comparative patient perceived health
- Type of preventive benefits
- Type of therapeutic benefit
- Comparative cost of intervention
- Comparative other medical costs
- Comparative nonmedical costs
- Quality of evidence
- Clinical practice guidelines

In the first part of the survey,[279] the authors captured participants' perspectives on which criterion contributed the most to the value of health care interventions by weight. They used a 5-point weighting scale (1 = lowest relative importance, 5 = highest relative importance). In the second part of the survey, the authors asked participants to appraise their preferences on the actual intervention for thyroid nodules using 2 scoring scales: 0 to 5 for noncomparative criteria and −5 to +5 for comparative criteria. A higher score indicated better performance. The third part of the survey included qualitative contextual criteria, which participants used to indicate a negative, neutral, or positive impact on their decision about the intervention using a numerical scale (−1, 0, and 1). However, the qualitative part of the survey was not linked to the quantitative results, and because qualitive preferences were out of scope for this health technology assessment, we have not elaborated on these results.

The survey was administered from November 20, 2018, to June 30, 2019.[279] After the survey closed, valid data were available from 105 participants. Data from 31 physicians and 48 patients who had ever had thyroid disease were included in the analysis. People who had had no previous thyroid disease were excluded. The mean of weights (importance) for each criterion and its standard deviation were normalized to sum to 1.

The second included study[280] was a cross-sectional study that involved participants completing a time trade-off instrument to estimate the quality-adjusted life-year (QALY) weights of common treatment scenarios for papillary thyroid microcarcinoma. The time trade-off instrument consisted of preference assessments for 10 health states related to papillary thyroid microcarcinoma, including 4 uncomplicated treatment scenarios (active surveillance, RFA, partial thyroidectomy, total thyroidectomy) and

6 complicated treatment scenarios (temporary and permanent unilateral or bilateral vocal cord palsy, permanent hypocalcemia, cancer progression). These health states were created by thyroid cancer survivors, cancer survivor care partners, and physicians.

Participants were included if they had a personal history of thyroid cancer, were fluent in English, and were 18 years of age or older.[280] Participants were excluded if they lacked the mental capacity to answer the study questions. All participants were enrolled between August 2022 and September 2024.

For each of the 10 thyroid cancer health states, participants were presented with 1 vignette describing the health state and another describing perfect health.[280] They were asked to indicate how many months or years of a 10-year survival time in the described health state they would be willing to give up to live with perfect health. A QALY weight was derived for each vignette, where 0 represented death and 1 represented perfect health. The study authors collected data from 101 thyroid cancer survivors. They compared QALY weights using within-subject measures analysis of variance and paired them using Wilcoxon rank-sum tests.

Results

Physician and Patient Preferences for Thyroid Nodule Interventions

For physicians, comparative effectiveness (mean ± standard deviation 0.089 ± 0.010) was the most important criterion, followed by type of therapeutic benefit (0.088 ± 0.011) and disease severity (0.088 ± 0.011).[279] For patients, comparative effectiveness (0.086 ± 0.010) was also the most important criterion, followed by type of therapeutic benefit (0.085 ± 0.010) and comparative patient-perceived health (0.085 ± 0.008).

Physicians weighted comparative safety and unmet needs more highly than patients (0.086 ± 0.011 vs. 0.079 ± 0.014 and 0.085 ± 0.013 vs. 0.079 ± 0.015, respectively).[279] In contrast, patients weighted type of preventive benefits and comparative patient-perceived health more highly than physicians (0.084 ± 0.012 vs. 0.072 ± 0.018 and 0.085 ± 0.008 vs. 0.074 ± 0.021, respectively).

Both physicians and patients gave comparative effectiveness the highest score (0.829 ± 0.227 and 0.838 ± 0.191, respectively).[279] However, 4 criteria received a higher score from patients compared to physicians: type of therapeutic benefit (0.704 ± 0.244 vs. 0.516 ± 0.192); type of preventive benefit (0.675 ± 0.147 vs. 0.561 ± 0.285); comparative safety (0.694 ± 0.216 vs. 0.587 ± 0.267); and clinical practice guidelines (0.583 ± 0.206 vs. 0.419 ± 0.215).

Patient-Derived QALY Weights for Papillary Thyroid Microcarcinoma

Mean QALY weights for uncomplicated treatment scenarios ranged from 0.975 to 0.992 and did not show a statistically significant difference between treatments ($P = .15$).[280] Treatment complications resulted in statistically significant lower QALY weights for RFA, partial thyroidectomy, and total thyroidectomy ($P < .01$), but not for active surveillance ($P = .72$).

Discussion

The perspectives of physicians and patients are important when selecting appropriate treatments for thyroid disease. At present, RFA is the only ablative technology for thyroid disease that is available for clinical use in Ontario. It is being used judiciously as an alternative treatment option for patients with

symptomatic benign nodules or small, low-risk papillary thyroid cancer, especially for those who have declined surgery, cannot undergo surgery, or are anxious about active surveillance. RFA may offer patients better quality of life than surgery because it does not cause hypothyroidism and there is no need for lifelong thyroid hormone replacement therapy.

Conclusions

For the treatment of thyroid nodules, both physicians and patients rated effectiveness as the top criterion. Physicians preferred interventions that were safe and effective; patients prioritized quality of life after the intervention. For papillary thyroid microcarcinoma, patient preferences were driven by an aversion to treatment complications rather than an inclination toward the experience of the treatments themselves. These perspectives highlight the need for shared decision-making; physicians should engage patients in discussions about the risks, benefits, and long-term impacts of interventions to treat thyroid nodules.

Direct Patient Engagement

Methods

Partnership Plan

The partnership plan for this health technology assessment focused on consultation to examine the experiences of people with thyroid nodules. We engaged people via telephone interviews.

We used a qualitative interview, because this method of engagement allowed us to explore the meaning of central themes in the experiences of people with thyroid nodules, their journey to diagnosis, and their treatment.[281] The sensitive nature of exploring people's experiences of a health condition and their quality of life further are other factors that support our choice of an interview methodology.

Participant Outreach

We used an approach called purposive sampling,[282-285] which involves actively reaching out to people with direct experience of the health condition and health technology or intervention being reviewed. We approached clinical experts to assist us in identifying and connecting with people who had thyroid nodules. Our interview recruitment poster was shared with thyroid support organizations throughout Ontario.

Inclusion Criteria

We sought to speak with adults with lived experience of thyroid nodules.

Exclusion Criteria

We did not set exclusion criteria for participants who otherwise met the inclusion criteria.

Participants

For this project, we spoke with 11 participants who had thyroid nodules and were living in Ontario. Among them, 6 had undergone RFA, 3 had undergone thyroidectomy, and 2 were receiving active monitoring or surveillance.

Approach

At the beginning of the interview, we explained the role of our organization, the purpose of this health technology assessment, the risks of participation, and how participants' personal health information would be protected. We gave this information to participants both verbally and in a letter of information (Appendix 10) if requested. We then obtained participants' verbal consent before starting the interview. With participants' consent, we audiorecorded and then transcribed the interviews.

Interviews lasted approximately 30 to 60 minutes. The interviews were semistructured and consisted of a series of open-ended questions. Questions were based on a list developed by the Health Technology Assessment International Interest Group on Patient and Citizen Involvement in Health Technology Assessment.[286] Questions focused on the impact of thyroid nodules, the journey to diagnosis, and perceptions regarding ablative technologies. See Appendix 11 for our interview guide.

Data Extraction and Analysis

We used a modified version of a grounded-theory methodology to analyze interview transcripts. The grounded-theory approach allowed us to organize and compare information on experiences across participants. This method consists of a repetitive process of obtaining, documenting, and analyzing responses while simultaneously collecting, analyzing, and comparing information.[287,288] We used the qualitative data analysis software program NVivo[289] to identify and interpret patterns in the data. The patterns we identified allowed us to highlight the impact of thyroid nodules on the people we interviewed.

Results

Diagnosis Journey

Participants described a range of symptoms that led to their diagnosis, including enlarging or visible lumps on the thyroid, persistent fatigue, sensitivity to cold, weight gain, and metabolic changes such as elevated cholesterol. These concerns prompted them to seek medical care, where thyroid nodules were ultimately identified.

> *I had been monitoring a lump on my thyroid. It was getting larger and larger, and I was getting more fatigued. I had rapid weight gain of 8 pounds in 3 weeks, and I'm always cold. I contacted my primary health care practitioner … and an ultrasound of my thyroid showed 2 nodules.*

> *For a couple of years, I was telling the doctor I was exhausted all the time, and then I started gaining weight and my cholesterol got really high … they sent me for a scan and told me that I had 2 or 3 nodules.*

> *I had physical symptoms, in that I had a very enlarged nodule in the front of my throat, which was visible to the naked eye. You could not miss it.*

Impact on Mental Health

Participants reported that thyroid nodules and their symptoms affected their mental health. Anxiety was common, stemming from concerns about the potential for cancer and from the effects of thyroid dysfunction.

> *Some of my symptoms were constant anxiety and fight or flight.*

> *My thyroid wasn't functioning properly, which added anxiety … I felt anxious and nervous.*

> *My concern is the thought of [the nodules] changing, becoming cancerous.*

Some participants noted feeling self-conscious or experiencing lower self-esteem because of the visible lump on their neck, while others reported mood changes that further affected their well-being.

> *And all of these things affect your mood. You start to feel depressed. It affects your self-esteem … because I felt very self-conscious as a female with a lump that almost looked double the size … It makes me feel very self-conscious.*

> *I was quite irritable, and I was having trouble focusing.*

Impact on Quality of Life

Participants described how the symptoms associated with thyroid dysfunction affected multiple aspects of their daily lives and their overall quality of life. Many experienced persistent fatigue and weakness that limited their ability to remain active. Some reported mobility challenges because of comorbid conditions such as arthritis, which compounded the physical strain. Fatigue often forced them to rest or sleep during the day, even though they were typically energetic people, disrupting their usual routines and activities. Others described a constant sensitivity to cold that affected their comfort and daily functioning.

> *I'm an active person. I'm up at 4:00 in the morning. I go to bed at 9:00 at night. So having to stop and sleep during the day is not normal behaviour. That impacts all parts of my life.*

> *I'm always cold, even in this heat wave. I've been wearing a jacket because I'm freezing cold.*

> *I've got arthritis along with that. So between the arthritis and the fatigue, I have a lot of difficulty walking, so I use crutches a lot.*

Physical symptoms also disrupted essential daily activities, such as eating and sleeping, and had a noticeable impact on participants' emotional well-being. Pain and discomfort when swallowing made eating difficult, sometimes forcing participants to stop mid-meal and limiting their ability to enjoy food or participate in social meals. Some also experienced weight fluctuations and changes to their voice, which further affected their confidence and comfort. In addition, many described ongoing anxiety, restlessness, and disturbed sleep related to their symptoms. The combination of physical discomfort,

restricted mobility, and emotional strain contributed to an overall decline in well-being and quality of life.

> *It affects my quality of life because unfortunately eating is a big function … it's very difficult to eat. And so sometimes I would have to stop eating because it's too uncomfortable to swallow. It feels like you're going to choke.*

> *Just the living in constant anxiety, sleepless, sweating at night. It was rough.*

> *I had rapid weight gain of 8 pounds in 3 weeks, which is horrifying. I'm always cold. There was a great pressure on the base of my throat. My voice was hoarse.*

Impact on Employment

Participants described how their symptoms negatively affected their work life. Managing their condition often required them to miss several days of work each month, and the limited number of available sick days created additional strain. They also noted that fatigue associated with their thyroid condition reduced their productivity and made it difficult to concentrate during meetings and other work tasks.

> *I was missing work. We're only allowed so many days, and you know when your symptoms start creeping up, I was missing work probably 3 to 4 times a month as the cyst was getting bigger.*

> *I was exhausted. I could barely stay awake through meetings.*

Participants also reported negative social experiences in the workplace related to their symptoms, which further affected their overall work experience.

> *Going into work, people just don't want to be near you if you're coughing. And I would say to them, "No, I'm not sick … I don't have a cold or a flu or anything. But I have this thyroid issue."*

Conventional Treatment Options

Active Surveillance (Monitoring)

Some participants explained that, based on their health care provider's recommendation, they were monitoring the growth of their thyroid nodules rather than treating them immediately. Although they had been prescribed medication to manage their thyroid function, the nodules themselves would not be actively treated unless they reached a size for which interventions such as surgery or ablation were advised. This "watchful waiting" approach caused anxiety for some participants, who expressed concern that their untreated nodules could eventually become cancerous.

> *For the thyroid, there was no cancer or anything, so they weren't treating the nodules. Not much happened over the next 5 years.*

> *I'm on medication for thyroid, but they're not doing anything on the nodules, [and] they are continuously getting larger.*

> *It's just a matter of monitoring. As I feel my symptoms change, I ask my doctor for another ultrasound … my concern is the thought of them [nodules] changing, becoming cancerous.*

Surgery

Some participants reflected on their experiences undergoing surgery to remove part or all of their thyroid. They discussed the challenges that followed – particularly the need to rely on lifelong medication to replace lost thyroid function. Recovery time was generally a few days, but experiences varied. Some people reported minimal and short-term side effects, but others described longer-term consequences, such as changes or difficulties with their vocal cords.

> *The fallout from having had a total thyroidectomy is being dependent on medications. And I no longer can absorb nutrients properly, so I have to take vitamins 3 different times every day.*

> *I wasn't really feeling very good when I came out of the hospital. It took me about maybe a week to 10 days to recover … it wasn't really pain, but I had discomfort in my chest area.*

> *One of the results of the surgery was that my vocal cords were twisted in the healing process. So even now I can't talk for long because my voice just disappears for a couple of hours.*

One participant shared feeling self-conscious about the scar left after surgery, noting that they often chose to cover it when they were outdoors.

> *I did go on a holiday, and I was very conscious about the scar tissue. So, I covered it up and I used a lot of cream on the scar.*

Ablative Technology (RFA)

Awareness

Awareness of RFA as a treatment for thyroid nodules varied widely among participants. Some were informed about the procedure by their health care providers and identified as suitable candidates, although they noted access issues such as lack of coverage under health insurance.

> *We discussed the radiofrequency ablation. And because I didn't have cancer, I was a good candidate for it, but he [the doctor] also mentioned that it wasn't covered by OHIP.*

> *The doctor recommended [RFA] to me at the hospital.*

However, many participants relied on self-directed research to learn about RFA. They reported reading online resources, discovering international use of the procedure, and initiating discussions with their providers. Some noted that their doctors were unfamiliar with RFA or did not acknowledge their inquiries, requiring participants to actively advocate for themselves. Others had little to no awareness of

RFA or other ablative treatments, highlighting substantial variability in knowledge and communication about available options.

> *I started doing research online about what you can do with the nodule. So most of the research that I did online was [United States]–based, and they have radiofrequency ablation. And I thought that was a great technique.*
>
> *I had to do all the research, I had to call … So I guess you have to advocate for yourself, because nobody else will.*
>
> *They [the doctors] had never mentioned it [RFA]. I looked a little bit up about it, but I really don't know much about it.*

Preference for Ablative Techniques

Participants expressed a preference for ablative techniques such as RFA because of its minimally invasive nature. They viewed surgery as a more invasive option associated with higher risk of complications and longer recovery times. Several participants also shared that they were reluctant to have their thyroid removed, because this would require lifelong medication to replace its function.

> *It was the minimally invasive part of [RFA], the fact that it's a sort of in and out procedure. You're not even in the hospital for very long.*
>
> *The other option would be surgery to cut out half of my gland. Why would I want to remove half of my thyroid gland? The thyroid is a very important organ in the body. It's responsible for a lot of different functions and I wouldn't want to just cut half of it away.*
>
> *I didn't want to have to take medication for the rest of my life … so that was probably my main factor for looking for an alternative solution, which would be the RFA.*

Some participants also emphasized that the shorter recovery time associated with RFA compared to surgery influenced their decision to pursue the procedure. They appreciated that shorter hospital stays and quicker recovery allowed them to return to their normal routines more easily, without the need to arrange childcare or take extended time off work. For participants with compromised immune systems, the reduced hospital exposure also meant a lower risk of infection, which they viewed as an important advantage of RFA. Furthermore, some participants who had undergone surgery noted that they would have preferred nonsurgical options such as RFA if they had been aware of them.

> *[RFA has] quick recovery time and it wouldn't impact my life the same way as a surgery would. [For surgery], the recovery time would have been much longer and would have impacted my life more because I am still working.*
>
> *I don't have to worry about who's going to look after my kids when I sit in a hospital and take time off from work. Not everyone has those abilities, whereas with RFA, you're in and out. I take 1 day off and can go back to work the next day.*

> *I picked RFA because I don't want to stay in a hospital for an unprecedented amount of time and then worry about risk of infection, which is way higher for people like me, who are on immunosuppressants.*

> *If there's an option not to have surgery – that is proven effective and would work for me – I would have certainly explored it. But I didn't get an option.*

Scarring was also mentioned as 1 of the factors influencing participants' preference for RFA over surgery. They noted that the minimally invasive nature of RFA resulted in little to no visible scarring, which made the procedure more appealing compared to surgical options that often leave a noticeable mark on the neck.

> *Conventional surgery would have left a scar. I'm not a vain person, but I didn't really want to have a scar.*

> *As a female, you don't want to scar … with this procedure [RFA], it is noninvasive, not risky, and there's no scarring.*

Experience With RFA and Impact

Participants who underwent RFA described the procedure as quick and associated with a short recovery period. They noted that any bruising or swelling resolved quickly and that the overall experience was largely pain-free.

> *I did not feel pain throughout the procedure at all. And I think I left within not even like 30 minutes after the procedure.*

> *It was an excellent experience because I did not have to sleep in the hospital for 1 night. I went in on the day, she did the ablation, and that whole procedure from start to finish took approximately 45 minutes.*

> *One day after the procedure you can see the discolouring and bruising is already starting to wear off. By the fourth day it was pretty much gone, and I went back to work as normal.*

Participants also reflected on the positive impact of RFA on their overall health and daily functioning. Many reported that most, if not all, of their symptoms improved after treatment. Swallowing became easier and pain-free, and those who had struggled with weight management noted improvements in metabolism, making it easier to lose weight. Participants also described having more energy and less fatigue after the procedure, which contributed to an enhanced quality of life.

> *When I swallow, I don't feel it [pain] anymore. Swallowing was my biggest problem. I haven't had that problem since I did the RFA.*

> *I struggled to lose weight before, but since I received the ablation technique, now I can lose weight … I've got more energy and my metabolism seems to have improved.*

They further highlighted the relief of not needing lifelong medication after RFA. Some contrasted their experience with that of family members who had undergone thyroidectomy and struggled to manage their health postsurgery, expressing gratitude for a less invasive alternative. Many also reported a visible reduction in the size of their nodules after treatment. This improvement was particularly meaningful for those who shared that the lump on their neck had made them feel self-conscious.

> *I did come off medication that day [after RFA] and right away, just the fact I was off the medication was a huge relief for me.*
>
> *I feel very lucky having the ability to go through this [RFA], because family members who did not have that option and had to have the thyroidectomy experience long-term problems.*
>
> *Since I've had the procedure [RFA], that nodule reduced significantly. The size of my neck has reduced. It was almost like a tennis ball. It was that visible … This makes a woman feel very self-conscious. And so, to be able to do this procedure, it really makes a big difference to women.*

Barriers to Accessing RFA

Lack of Awareness

As noted in the previous section, awareness of RFA among participants varied widely. Although some were informed about the procedure by their health care providers, many relied on self-directed research, discovering information online and initiating conversations with their doctors. Several participants noted that their providers were unfamiliar with RFA or did not acknowledge their inquiries, requiring them to advocate for themselves. Others had little to no knowledge of RFA or other ablative treatments, highlighting substantial gaps in awareness and communication about available options.

> *The doctors that I saw weren't aware that RFA was something that could treat thyroid nodules.*

Cost

Participants consistently identified cost as the primary barrier to accessing RFA treatment. They noted that many people would likely choose RFA over surgery if it were more affordable or covered by provincial health insurance. A few participants said that their procedures were covered by the hospital, acknowledging that they would not have been able to afford it otherwise. Conversely, those who paid out of pocket said that although they recognized the high cost would be a limiting factor for many, they viewed the expense as worthwhile given the positive treatment experience and substantial improvement in their symptoms and quality of life.

> *I think if most people had the option, I think they would all go for RFA. But in today's society, who has that kind of money just sitting around? Not for procedures. It's very difficult.*
>
> *In my case, you can say that it's unaffordable. The cost was covered by the hospital – that's why I did it. If I had to pay for it, I couldn't afford it.*

> *It's an expensive procedure and I'm not somebody who generally gets elective surgeries. It was really because it was the best option for me … I wish it would be offered to more people without having to pay out of pocket because I think it is a really good solution rather than having a thyroidectomy.*

Geographic Barriers

Some participants who lived outside major urban centres noted that they had to arrange transportation to and from the hospital for their RFA procedure. Although they found this manageable in their own cases, they acknowledged that access would likely be more difficult for people living in rural or remote areas. They emphasized that RFA being available in only 1 major city limited access for many across the province. They expressed a desire for the procedure to be offered in more locations, suggesting that expanding geographic availability would help to ensure equitable access to this treatment.

> *I'm based in [urban city], so it's an hour-long drive for me [to get RFA]. I just had to find somebody to drive me home after, which was manageable.*

> *It would be nice if more places offered [RFA] … I can still get there, but if someone's in a remote town, it would be challenging.*

Discussion

All of the participants we interviewed had personal experience with thyroid nodules and their management. People's experiences reflected diverse needs and treatment preferences. Active surveillance and medication were common initial approaches, but they generated anxiety for some because of concerns about leaving nodules untreated. Although surgery is effective, participants viewed it as invasive and associated with scarring, longer recovery, and the need for lifelong medication. In contrast, participants valued RFA for its minimally invasive nature, short recovery time, reduced scarring, and largely pain-free experience. Those who underwent RFA reported substantial improvements in symptoms and expressed relief at not needing lifelong medication. However, barriers such as high cost, limited geographic availability, and variable awareness highlight the need to expand access to this treatment option.

A limitation of this study was the lack of participants with experience in ablative techniques other than RFA. As well, although we made efforts to include both urban and rural perspectives, representation from Northern Ontario was limited.

Conclusions

Thyroid nodules have a negative impact on people's physical and emotional well-being, affecting daily activities, work, and overall quality of life. Minimally invasive treatments such as RFA were particularly appreciated by participants for their effectiveness, short recovery time, limited scarring, and reduced reliance on lifelong medication. However, access to RFA remains limited by factors such as cost, geographic availability, and inconsistent awareness, emphasizing the need to improve accessibility and increase education about this treatment option.

Preferences and Values Evidence Discussion

The quantitative evidence showed that people prioritized quality of life after interventions for thyroid nodules and were averse to treatment complications for papillary thyroid cancer. These results align with the findings of the direct patient engagement, in which people reported the positive impact of RFA on their overall health and quality of life.

Preferences and Values Evidence Conclusions

In our review of the quantitative evidence of preferences and values, effectiveness was the top priority for both physicians and patients when evaluating interventions for thyroid nodules. However, patients placed more value on quality of life after the intervention; physicians focused more on safety and unmet needs. Treatment complications substantially reduced patients' quality of life, except for active surveillance.

The people we interviewed noted that thyroid nodules had a negative impact on their physical and emotional well-being, affecting their daily activities, work, and overall quality of life. They expressed a preference for minimally invasive treatment options such as RFA, highlighting its advantages compared to traditional thyroidectomy, which included shorter recovery times and less reliance on lifelong medication as a result of preserved thyroid function.

Conclusions of the Health Technology Assessment

Compared with surgery, radiofrequency ablation (RFA) may be as effective in reducing nodule volume, improving symptoms, and avoiding nodule regrowth, and it may result in better quality of life in adults with symptomatic benign thyroid nodules. Compared with ethanol ablation, RFA may be as effective in reducing nodule volume and improving symptoms in adults with cystic thyroid nodules. Compared with before the intervention, RFA may reduce nodule volume, normalize thyroid-stimulating hormone levels, and improve symptoms in adults with autonomously functioning thyroid nodules (AFTNs). Compared with surgery, RFA may be as effective in terms of tumour disappearance but have a lower tumour recurrence rate in adults with small, low-risk papillary thyroid cancer; it may require less surgical time and a shorter length of hospital stay, and it may be associated with less postprocedural pain and better quality of life. Thermal ablation technologies are reasonably safe and have comparable safety profiles; they may not result in hypothyroidism and may lead to fewer adverse events than surgery. The effectiveness and safety of the different thermal ablation technologies may be similar, but the evidence is inconclusive. Chemical ablation is a safe procedure associated with minimal adverse events.

In adults with symptomatic benign thyroid nodules and AFTNs, RFA is more effective and less costly than surgery. In adults with small, low-risk papillary thyroid cancer, RFA is more effective and less costly than surgery and cost-effective compared with active surveillance at an incremental cost-effectiveness ratio of $1,574 per QALY gained. Publicly funding RFA in Ontario for adults with symptomatic benign thyroid nodules, AFTNs, and small, low-risk papillary thyroid cancer would lead to cost savings of $5.42 million, $0.62 million, and $4.03 million over the next 5 years, respectively.

Thyroid nodules have a negative impact on people's physical and emotional well-being, affecting daily activities, work, and overall quality of life. Minimally invasive treatments such as RFA were particularly appreciated for their effectiveness, short recovery time, limited scarring, and reduced reliance on lifelong medication. However, access to RFA is limited by factors such as cost, geographic availability, and inconsistent awareness, emphasizing the need to improve accessibility and increase awareness about this treatment option.

Abbreviations

AFTN: autonomously functioning thyroid nodule

CCI: Canadian Classification of Health Interventions

CDA: Canada's Drug Agency

CHEERS: Consolidated Health Economic Evaluation Reporting Standards

CI: confidence interval

CIHI: Canadian Institute for Health Information

CMG: case-mix group

DAD: Discharge Abstract Database

EVIDEM: EVIdence based DEcision-Making model

GRADE: Grading of Recommendations Assessment, Development, and Evaluation

HIFU: high-intensity focused ultrasound

ICD-10-CA: International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada

ICER: incremental cost-effectiveness ratio

MINORS: Methodological Index for Non-Randomized Studies

NACRS: National Ambulatory Care Reporting System

NHS EED: National Health Service Economic Evaluation Database

NICE: National Institute for Health and Care Excellence

NMB: net monetary benefit

NNT: number needed to treat

OHIP: Ontario Health Insurance Plan

OR: odds ratio

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses

PTMC: papillary thyroid microcarcinoma

QALY: quality-adjusted life-year

RCT: randomized controlled trial

RFA: radiofrequency ablation

RIW: resource intensity weight

ROBINS-I: Risk of Bias in Non-randomized Studies of Interventions

ROBIS: Risk of Bias in Systematic Reviews

RR: relative risk

SD: standard deviation

SMD: standardized mean difference

ThyPRO: Thyroid-Related Patient-Reported Outcome

TSH: thyroid-stimulating hormone

WTP: willingness-to-pay

Glossary

Adverse event: An adverse event is an unexpected medical problem that happens during treatment for a health condition. Adverse events may be caused by something other than the treatment.

Budget impact analysis: A budget impact analysis estimates the financial impact of adopting a new health care intervention on the current budget (i.e., the affordability of the new intervention). It is based on predictions of how changes in the intervention mix will impact the level of health care spending for a specific population. Budget impact analyses are typically conducted for a short-term period (e.g., 5 years). The budget impact, sometimes referred to as the net budget impact, is the estimated cost difference between the current scenario (i.e., the anticipated amount of spending for a specific population without using the new intervention) and the new scenario (i.e., the anticipated amount of spending for a specific population following the introduction of the new intervention).

Cost-effective: A health care intervention is considered cost-effective when it provides additional benefits, compared with relevant alternatives, at an additional cost that is acceptable to a decision-maker based on the maximum willingness-to-pay value.

Cost-effectiveness acceptability curve: In economic evaluations, a cost-effectiveness acceptability curve is a graphical representation of the results of a probabilistic analysis. It illustrates the probability of health care interventions being cost-effective over a range of willingness-to-pay values. Willingness-to-pay values are plotted on the horizontal axis of the graph, and the probability of the intervention of interest and its comparator(s) being cost-effective at corresponding willingness-to-pay values is plotted on the vertical axis.

Cost-effectiveness analysis: Used broadly, "cost-effectiveness analysis" may refer to an economic evaluation used to compare the benefits of 2 or more health care interventions with their costs. It may encompass several types of analysis (e.g., cost-effectiveness analysis, cost–utility analysis). Used more specifically, "cost-effectiveness analysis" may refer to a type of economic evaluation in which the main outcome measure is the incremental cost per natural unit of health (e.g., life-year, symptom-free day) gained.

Cost-effectiveness plane: In economic evaluations, a cost-effectiveness plane is a graph used to show the differences in cost and effectiveness between a health care intervention and its comparator(s). Differences in effects are plotted on the horizontal axis, and differences in costs are plotted on the vertical axis.

Cost–utility analysis: A cost–utility analysis is a type of economic evaluation used to compare the benefits of 2 or more health care interventions with their costs. The benefits are measured using quality-adjusted life-years, which capture both the quality and quantity of life. In a cost–utility analysis, the main outcome measure is the incremental cost per quality-adjusted life-year gained.

Discounting: Discounting is a method used in economic evaluations to adjust for the differential timing of the costs incurred and the benefits generated by a health care intervention over time. Discounting reflects the concept of positive time preference, whereby future costs and benefits are reduced to reflect their present value. The health technology assessments conducted by Ontario Health use an annual discount rate of 1.5% for both future costs and future benefits.

Disutility: A disutility is a decrease in utility (i.e., a decrease in preference for a particular health outcome) typically resulting from a particular health condition (e.g., experiencing a symptom or complication).

Dominant: A health care intervention is considered dominant when it is more effective and less costly than its comparator(s).

EQ-5D: The EQ-5D is a generic health-related quality-of-life classification system widely used in clinical studies. In economic evaluations, it is used as an indirect method of obtaining health state preferences (i.e., utility values). The EQ-5D questionnaire consists of 5 questions relating to different domains of quality of life: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. For each domain, there are 3 response options: no problems, some problems, or severe problems. A newer instrument, the EQ-5D-5L, includes 5 response options for each domain. A scoring table is used to convert EQ-5D scores to utility values.

Equity: Unlike the notion of equality, equity is not about treating everyone the same way.[290] It denotes fairness and justice in process and in results. Equitable outcomes often require differential treatment and resource redistribution to achieve a level playing field among all individuals and communities. This requires recognizing and addressing barriers to opportunities for all to thrive in our society.

Health-related quality of life: Health-related quality of life is a measure of the impact of a health care intervention on a person's health. It includes the dimensions of physiology, function, social life, cognition, emotions, sleep and rest, energy and vitality, health perception, and general life satisfaction.

Health state: A health state is a particular status of health (e.g., sick, well, dead). A health state is associated with some amount of benefit and may be associated with specific costs. Benefit is captured through individual or societal preferences for the time spent in each health state and is expressed in quality-adjusted weights called utility values. In a Markov model, a finite number of mutually exclusive health states are used to represent discrete states of health.

Incremental cost: The incremental cost is the additional cost, typically per person, of a health care intervention versus a comparator.

Incremental cost-effectiveness ratio: The incremental cost-effectiveness ratio (ICER) is a summary measure that indicates, for a given health care intervention, how much more a health care consumer must pay to get an additional unit of benefit relative to an alternative intervention. It is obtained by dividing the incremental cost by the incremental effectiveness. Incremental cost-effectiveness ratios are typically presented as the cost per life-year gained or the cost per quality-adjusted life-year gained.

Incremental net benefit: Incremental net benefit is a summary measure of cost-effectiveness. It incorporates the differences in cost and effect between 2 health care interventions and the willingness-to-pay value. Net health benefit is calculated as the difference in effect minus the difference in cost divided by the willingness-to-pay value. Net monetary benefit is calculated as the willingness-to-pay value multiplied by the difference in effect minus the difference in cost. An intervention can be considered cost-effective if either the net health or net monetary benefit is greater than zero.

Markov model: A Markov model is a type of decision-analytic model used in economic evaluations to estimate the costs and health outcomes (e.g., quality-adjusted life-years gained) associated with using a particular health care intervention. Markov models are useful for clinical problems that involve events of

interest that may recur over time (e.g., stroke). A Markov model consists of mutually exclusive, exhaustive health states. Patients remain in a given health state for a certain period of time before moving to another health state based on transition probabilities. The health states and events modelled may be associated with specific costs and health outcomes.

Ministry of Health perspective: The perspective adopted in economic evaluations determines the types of costs and health benefits to include. Ontario Health develops health technology assessment reports from the perspective of the Ontario Ministry of Health. This perspective includes all costs and health benefits attributable to the Ministry of Health, such as treatment costs (e.g., drugs, administration, monitoring, hospital stays) and costs associated with managing adverse events caused by treatments. This perspective does not include out-of-pocket costs incurred by patients related to obtaining care (e.g., transportation) or loss of productivity (e.g., absenteeism).

Probabilistic analysis: A probabilistic analysis (also known as a probabilistic sensitivity analysis) is used in economic models to explore uncertainty in several parameters simultaneously and is done using Monte Carlo simulation. Model inputs are defined as a distribution of possible values. In each iteration, model inputs are obtained by randomly sampling from each distribution, and a single estimate of cost and effectiveness is generated. This process is repeated many times (e.g., 10,000 times) to estimate the number of times (i.e., the probability) that the health care intervention of interest is cost-effective.

Quality-adjusted life-year: The quality-adjusted life-year (QALY) is a generic health outcome measure commonly used in cost–utility analyses to reflect the quantity and quality of life-years lived. The life-years lived are adjusted for quality of life using individual or societal preferences (i.e., utility values) for being in a particular health state. One year of perfect health is represented by 1 quality-adjusted life-year.

Reference case: The reference case is a preferred set of methods and principles that provide the guidelines for economic evaluations. Its purpose is to standardize the approach of conducting and reporting economic evaluations, so that results can be compared across studies.

Scenario analysis: A scenario analysis is used to explore uncertainty in the results of an economic evaluation. It is done by observing the potential impact of different scenarios on the cost-effectiveness of a health care intervention. Scenario analyses involve varying structural assumptions from the reference case.

Sensitivity analysis: Every economic evaluation contains some degree of uncertainty, and results can vary depending on the values taken by key parameters and the assumptions made. Sensitivity analysis allows these factors to be varied and shows the impact of these variations on the results of the evaluation. There are various types of sensitivity analysis, including deterministic, probabilistic, and scenario.

Societal perspective: The perspective adopted in an economic evaluation determines the types of costs and health benefits to include. The societal perspective reflects the broader economy and is the aggregation of all perspectives (e.g., health care payer and patient perspectives). It considers the full effect of a health condition on society, including all costs (regardless of who pays) and all benefits (regardless of who benefits).

Time horizon: In economic evaluations, the time horizon is the time frame over which costs and benefits are examined and calculated. The relevant time horizon is chosen based on the nature of the disease

and health care intervention being assessed, as well as the purpose of the analysis. For instance, a lifetime horizon would be chosen to capture the long-term health and cost consequences over a patient's lifetime.

Time trade-off: In economic evaluations, time trade-off is a direct method of measuring people's preferences for various health states. In a time-trade off, respondents are asked about their preference for either (a) living with a chronic health condition for a certain amount of time, followed by death, or (b) living in optimal health but for less time than in scenario (a). That is, respondents decide how much time in good health they would be willing to "trade off" for more time spent in poorer health. Respondents are surveyed repeatedly, with the amount of time spent in optimal health varying each time until they are indifferent about their choice.

Uptake rate: In instances where 2 technologies are being compared, the uptake rate is the rate at which a new technology is adopted. When a new technology is adopted, it may be used in addition to an existing technology, or it may replace an existing technology.

Utility: A utility is a value that represents a person's preference for various health states. Typically, utility values are anchored at 0 (death) and 1 (perfect health). In some scoring systems, a negative utility value indicates a state of health valued as being worse than death. Utility values can be aggregated over time to derive quality-adjusted life-years, a common outcome measure in economic evaluations.

Visual analogue scale: The visual analogue scale (VAS) is a direct method of measuring people's preferences for various health states. Respondents are first asked to rank a series of health states from least to most preferable. Then, they are asked to place the health states on a scale with intervals reflecting the differences in preference among the given health states. The scale ranges from 0 (worst imaginable health) to 100 (best imaginable health). The value of a respondent's preference for each health state is given by their placement of each health state on the scale.

Willingness-to-pay value: A willingness-to-pay value is the monetary value a health care consumer is willing to pay for added health benefits. When conducting a cost–utility analysis, the willingness-to-pay value represents the cost a consumer is willing to pay for an additional quality-adjusted life-year. If the incremental cost-effectiveness ratio is less than the willingness-to-pay value, the health care intervention of interest is considered cost-effective. If the incremental cost-effectiveness ratio is more than the willingness-to-pay value, the intervention is considered not to be cost-effective.

Appendices

Appendix 1: Clinical Practice Guidelines for Ablative Technologies

Table A1: Guideline Recommendations on Indications for Ablative Technologies in Symptomatic Benign Thyroid Nodules and Small, Low-Risk Papillary Thyroid Cancer

Title, date	Recommendations
2025 American Thyroid Association management guidelines for adult patients with differentiated thyroid cancer,[17] 2025	• Ultrasound-guided percutaneous ablation may be considered as an alternative to active surveillance or resection for cT1aN0M0 PTC in selected patients • Shared clinical decision-making between the patient and clinical team regarding the risks and benefits of this approach is essential **(Conditional recommendation, Low-certainty evidence)**
Radiofrequency ablation for recurrent thyroid cancers: 2025 Korean Society of Thyroid Radiology guideline,[291] 2025	• RFA can be performed with a curative or palliative intent for recurrent thyroid cancers at the thyroidectomy bed, neck dissection site, and metastatic cervical lymph nodes for patients who refuse surgery or who are at high surgical risk **(Evidence level: High; Strength of recommendation: Strong)** • RFA for curative intent should be considered when complete removal of the tumour is possible in patients with recurrent thyroid cancer and a limited number (≤ 3) of small tumours (size ≤ 2 cm) **(Evidence level: Moderate; Strength of recommendation: Strong)** • For palliative intent, RFA can be used when the resulting volume reduction can reduce symptoms and improve the patient's quality of life **(Evidence level: Low; Strength of recommendation: Weak)**
Brazilian consensus on the application of thermal ablation for treatment of thyroid nodules: a task force statement by the Brazilian Society of Interventional Radiology and Endovascular Surgery (SOBRICE), Brazilian Society of Head and Neck Surgery (SBCCP), and Brazilian Society of Endocrinology and Metabolism (SBEM),[292] 2024	• Ultrasound-guided ablation procedures can serve as a primary alternative to surgery in patients experiencing compressive and/or aesthetic symptoms due to benign thyroid nodules • Thermal ablation procedures, while not as effective as surgery or radioiodine therapy in normalizing thyroid function, can be a safe therapeutic option for patients with hyperfunctioning (autonomous/Plummer) thyroid nodules who are unable to undergo first-line therapies due to contraindications • Ultrasound-guided ablation procedures may be considered as a second-line treatment for patients with primary thyroid carcinoma up to 1 cm in size and a favourable location when surgery or active surveillance is not feasible • Ultrasound-guided ablation procedures may be considered for patients with recurrent metastatic papillary carcinoma with a favourable location who are not suitable for or who decline surgery • Chemical (ethanol) ablation is recommended for cystic or predominantly cystic nodules with more than 50% liquid content causing symptoms or cosmetic concerns, but it is not recommended for solid or predominantly solid nodules
General principles for the safe performance, training, and adoption of ablation techniques for benign thyroid nodules: an American Thyroid Association statement,[18] 2023	• Thermal ablation for benign nodules is most appropriate for patients with compressive and/or cosmetic complaints that can be clearly attributed to a single or dominant nodule • Patients with AFTNs causing subclinical or overt hyperthyroidism can also be successfully treated with ablative techniques • Ethanol ablation is indicated for purely cystic nodules or those nodules that are > 20% cystic
2023 European Thyroid Association clinical practice guidelines for thyroid nodule management,[10] 2023	• Consider thermal ablation for the treatment of solid benign thyroid nodules that cause local symptoms as an alternative to surgery and for cystic lesions that relapse after ethanol ablation **(Strength of recommendation: Strong; Quality of evidence: Low)** • Consider ethanol ablation as the first-line treatment for pure or dominantly cystic thyroid lesions **(Strength of recommendation: Strong; Quality of evidence: Moderate)**

Title, date	Recommendations
Italian guidelines for the management of non-functioning benign and locally symptomatic thyroid nodules,[293] 2023	• Consider thermal ablation as an alternative option to surgery for patients with a symptomatic, solid, benign, single, or dominant thyroid nodule **(Weak recommendation, Very low quality of evidence)**
Radiofrequency ablation and related ultrasound-guided ablation technologies for treatment of benign and malignant thyroid disease: an international multidisciplinary consensus statement of the American Head and Neck Society Endocrine Surgery Section with the Asia Pacific Society of Thyroid Surgery, Associazione Medici Endocrinologi, British Association of Endocrine and Thyroid Surgeons, European Thyroid Association, Italian Society of Endocrine Surgery Units, Korean Society of Thyroid Radiology, Latin American Thyroid Society, and Thyroid Nodules Therapies Association,[20] 2022	• Ultrasound-guided ablation procedures may be used as a first-line alternative to surgery for patients with benign thyroid nodules contributing to compressive and/or cosmetic symptoms • Although less efficacious than surgery or radioactive iodine in normalizing thyroid function, thermal ablation procedures can be a safe therapeutic alternative in patients with an autonomously functional thyroid nodule and contraindications to first-line techniques • Ultrasound-guided ablation procedures may be considered in patients with suitable primary papillary microcarcinoma who are unfit for surgery or decline surgery or active surveillance • Ultrasound-guided ablation procedures may be considered in patients with suitable recurrent PTC who are unfit for surgery or decline surgery or active surveillance
Percutaneous ultrasound-guided microwave ablation for symptomatic benign thyroid nodules (UK NICE interventional procedure guidance 743),[294] 2022	• Evidence on the safety of percutaneous ultrasound-guided microwave ablation for symptomatic benign thyroid nodules shows some well-recognized complications. Evidence on efficacy is adequate. Therefore, this procedure can be used provided standard arrangements are in place for clinical governance, consent, and audit
Radiofrequency ablation of benign thyroid nodules: recommendations from the Asian Conference on Tumor Ablation Task Force,[295] 2021	• RFA is indicated for patients with benign, nonfunctioning thyroid nodules with symptoms or cosmetic issues • RFA may be indicated for AFTNs that are toxic or pretoxic
European Thyroid Association and Cardiovascular and Interventional Radiological Society of Europe 2021 clinical practice guideline for the use of minimally invasive treatments in malignant thyroid lesions,[296] 2021	• Consider the use of image-guided thermal ablation for patients with low-risk PTMC, mainly if the patient is at surgical risk, is expected to have short life expectancy, has comorbidities that need to be prioritized before thyroid surgery, or is unwilling to undergo surgery or active surveillance **(Strength of recommendation: Strong; Quality of evidence: Low; Strong agreement [11/11, 100%])** • Abstain from using ethanol ablation and HIFU for PTMC treatment, due to insufficient evidence and technical limitations **(Strength of recommendation: Strong; Quality of evidence: Very low; Strong agreement [11/11, 100%])**

Title, date	Recommendations
Non-surgical and non-radioiodine techniques for ablation of benign thyroid nodules: consensus statement and recommendation (Thyroid section [German Society for Endocrinology], Thyroid Working Committee [German Society for Nuclear Medicine], and the German Association of Endocrine Surgeons [CAEK] for the German Society of General and Visceral Surgery [DGAV]), 2020[297]	Indications for thermal ablation techniques may be **(Weak recommendation, low or very low quality of evidence)**: • Symptomatic nodules: A symptomatic nodule is defined by symptoms caused by the nodule, including dysphagia, feeling of oppression, cough, and pain. Other causes of these symptoms have to be excluded prior to therapy. A scoring system for a subjective evaluation of the severity of the complaints should be used • Benign nodules with cosmetic indication: – Prerequisite: visible nodule/swelling – A validated scoring system for subjective evaluation should be used • Autonomously functioning nodules: – Prerequisite: relevant functional activity (TSH < 0.3 mU/mL without therapy with thyroid hormones) proven by ^{99m}Tc pertechnetate/^{123}I scan (uptake under suppression, if necessary) – In selected patients who are not suitable for surgery or radioiodine therapy and are at risk for iodine contamination with iodine-containing contrast agents, potentially resulting in heart arrhythmia (especially atrial fibrillation); if patients who are in need of therapy refuse conventional therapies (surgery, radioiodine therapy) Indications for ethanol/polidocanol ablation may be **(Weak recommendation, low or very low quality of evidence)**: • Recurrent cysts; in case of pure cysts, polidocanol may be used alternatively • Benign thyroid nodules with large cystic parts • Autonomous thyroid nodules in patients with multimorbidity who are not amenable to conventional therapies (radioiodine therapy, surgery) • Autonomous thyroid nodules in patients who refuse conventional therapies Recommended against any therapeutic intervention (thermal ablation or surgery) for ‘‘sonographically visible nodules per se without symptoms or hyperfunction and without suspicion or evidence of malignancy”

Title, date	Recommendations
2020 European Thyroid Association clinical practice guideline for the use of image-guided ablation in benign thyroid nodules,[4] 2020	• In adult patients with benign thyroid nodules that cause pressure symptoms and/or cosmetic concerns and decline surgery, image-guided thermal ablation should be considered as a cost- and risk-effective alternative option to surgical treatment or observation alone **(Strong recommendation, Low quality of evidence)** • We recommend against the use of thermal ablation for asymptomatic lesions **(Strong recommendation, Moderate quality of evidence)** • We recommend against thermal ablation for nodules with high-risk ultrasound features (EU-TIRADS class 5) **(Strong recommendation, Moderate quality of evidence)** • Based on direct comparison studies, and balance between efficacy and side effects, laser ablation and RFA are recommended as first-line thermal ablation treatment modalities **(Strong recommendation, Moderate quality of evidence)** • Based on studies to date, microwave ablation should be considered a second-line thermal ablation procedure in patients who are not suitable for or decline other thermal ablation procedures, or for participants in protocolled clinical studies **(Strong recommendation, Low quality of evidence)** • Based on its lower efficacy, higher cost, and limited reported trial evidence, as compared to RFA and laser ablation, HIFU should be considered only for selected nodules in patients who are not suitable for or decline other thermal ablation procedures, and for participants in protocolled studies **(Strong recommendation, Low quality of evidence)** • In multinodular goiters, due to lack of evidence of efficacy and the expected need of repeat treatment, thermal ablation should be restricted to patients with a well-defined dominant nodule or those who are not candidates for thyroid surgery or radioactive iodine treatment, as a palliative therapy option **(Strong recommendation, Low quality of evidence)** • Because of higher cost and complexity, as compared to aspiration and ethanol ablation, thermal ablation procedures are not recommended as a first-line treatment for pure or dominantly cystic thyroid lesions **(Strong recommendation, Moderate quality of evidence)** • Laser ablation and RFA should be considered therapeutic options for cystic lesions that relapse after ethanol ablation and for those that would remain symptomatic due to a large residual solid component **(Strong recommendation, Moderate quality of evidence)** • We recommend against thermal ablation as first-line treatment for large AFTNs. Due to the low rate of restoration of normal thyroid function, thermal ablation should be considered only for patients who decline or are not candidates for radioactive iodine therapy or surgery **(Strong recommendation, Moderate quality of evidence)** • Thermal ablation should be considered in young patients with small AFTNs and incomplete suppression of perinodular thyroid tissue due to the higher probability of normalization of thyroid function and the advantage of avoiding irradiation and restricting risk of late hypothyroidism **(Strong recommendation, Low quality of evidence)** • Treatment with a combination of laser ablation or RFA and radioactive iodine may be considered in selected patients with large AFTNs that cause local pressure symptoms in order to achieve a more rapid volume reduction and use of a lower radioactive iodine activity **(Weak recommendation, Low quality of evidence)**
Ethanol ablation of the thyroid nodules: 2018 consensus statement by the Korean Society of Thyroid Radiology,[298] 2019	• Ethanol ablation should be the first option for the treatment of pure cysts and predominantly cystic nodules that are not treated with simple aspiration • Ethanol ablation of solid nodules has limited therapeutic effect and may require multiple sessions • Long-term outcomes of ethanol ablation treatment of recurrent PTCs indicate that ethanol ablation is a secondary treatment option with some limitations, even though it can successfully decrease tumour volume • Unlike surgery, ethanol ablation is a safe procedure that is easy to repeat, is inexpensive, can be performed easily on an outpatient basis, and has only transient side effects

Title, date	Recommendations
2017 Thyroid radiofrequency ablation guideline: Korean Society of Thyroid Radiology,[225] 2018	• RFA is indicated for patients with benign thyroid nodules complaining of symptomatic or cosmetic problems **(Evidence level: Moderate; Grading of recommendation: Strong)** • RFA can be indicated for AFTNs, either toxic or pretoxic **(Evidence level: Moderate; Grading of recommendation: Weak)** • RFA can be performed for curative or palliative purposes in recurrent thyroid cancers at the thyroidectomy bed and cervical lymph nodes for patients at high surgical risk or who refuse surgery **(Evidence level: Moderate; Grading of recommendation: Strong)** • RFA is recommended as first-line treatment method for solid and predominantly solid nodules, although it is also effective treatment method to manage nonfunctioning thyroid nodules, regardless of the degree of solidity **(Evidence level: Moderate; Grading of recommendation: Strong)** • Ethanol ablation is recommended as first-line treatment method for cystic and predominantly cystic nodules. RFA can be recommended as a next step in cases with incomplete resolved symptoms or recurrence following ethanol ablation **(Evidence level: High; Grading of recommendation: Strong)**

Abbreviations: AFTN, autonomously functioning thyroid nodule; EU-TIRADS, European Thyroid Imaging Reporting and Data System; HIFU, high-intensity focused ultrasound; PTC, papillary thyroid carcinoma; PTMC, papillary thyroid microcarcinoma; RFA, radiofrequency ablation; TSH, thyroid-stimulating hormone.

Appendix 2: Literature Search Strategies

Clinical Evidence Search, Systematic Reviews

Database: EBM Reviews – Cochrane Database of Systematic Reviews <2005 to February 19, 2025>, EBM Reviews – NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1980 to 2025 Week 07>, Ovid MEDLINE ALL <1946 to February 19, 2025>
Search Date: February 19, 2025

Search Strategy:
1 Thyroid Nodule/ (29771)
2 (((thyroid* or benign) adj3 (nodule* or mass* or cyst* or lesion*)) or AFTN).ti,ab,kf. (146566)
3 Thyroid Cancer, Papillary/ (31303)
4 (thyroid* adj2 (cancer* or neoplasm* or carcinoma* or adenoma* or adenocarcinoma* or tumo?r* or malignan* or metasta*)).ti,ab,kf. (150915)
5 ((thyroid* adj5 (microcarcinoma* or papillar*)) or PTC or PTMC).ti,ab,kf. (67743)
6 or/1-5 (296340)
7 Ablation Techniques/ (32192)
8 High-Intensity Focused Ultrasound Ablation/ (9666)
9 Laser Therapy/ (48041)
10 Microwaves/ (52907)
11 exp Radiofrequency Ablation/ (95164)
12 ((ablat* adj5 (catheter* or HIFU or high-intensit* or laser* or microwave* or "micro wave" or therap* or ((nanosecond or nano second) adj3 (pulse* electric* or pulse* field*)) or radiofrequenc* or radio frequenc* or tech* or thermal* or ultrasound* or energy* or heat*)) or cryoablat* or nsPEF* or nsPFA* or RFA).ti,ab,kf. (206786)
13 Ethanol/ (398219)
14 Polidocanol/ (6174)
15 Injections, Intralesional/ (11352)
16 ((chemical* or ethanol* or polidocanol*) adj3 (ablat* or injection*)).ti,ab,kf. (13833)
17 or/7-16 (759529)
18 6 and 17 (8665)
19 Viva Combo RF Generator*.ti,ab,kf. (0)
20 (thyroid* adj3 ablat*).ti,ab,kf. (4886)
21 or/18-20 (11462)
22 exp Animals/ not Humans/ (10598009)
23 21 not 22 (11205)
24 limit 23 to english language [Limit not valid in CDSR; records were retained] (10386)
25 Case Reports/ or Comment.pt. or Editorial.pt. or (Letter not (Letter and Randomized Controlled Trial)).pt. or Congress.pt. (6826919)
26 24 not 25 (9442)
27 26 use coch,cleed (6)
28 (Systematic Reviews or Meta Analysis).pt. (213091)
29 Systematic Review/ or Systematic Reviews as Topic/ or Meta-Analysis/ or exp Meta-Analysis as Topic/ or exp Technology Assessment, Biomedical/ (1141638)
30 ((systematic* or methodologic*) adj3 (review* or overview*)).ti,ab,kf. (882514)

31 (meta analy* or metaanaly* or met analy* or metanaly* or meta review* or metareview* or health technolog* assess* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab,kf. (794213)
32 (evidence adj2 (review* or overview* or synthes#s)).ti,ab,kf. (113000)
33 (review of reviews or overview of reviews).ti,ab,kf. (3107)
34 umbrella review*.ti,ab,kf. (5176)
35 GRADE Approach/ (5461)
36 ((pool* adj3 analy*) or published studies or published literature or hand search* or handsearch* or manual search* or ((database* or systematic*) adj2 search*) or reference list* or bibliograph* or relevant journals or data synthes* or data extraction* or data abstraction*).ti,ab,kf. (740956)
37 (medline or pubmed or medlars or embase or cinahl or web of science or ovid or ebsco* or scopus).ab. (914430)
38 cochrane.ti,ab,kf. (381552)
39 (meta regress* or metaregress*).ti,ab,kf. (39616)
40 (((integrative or collaborative or quantitative) adj3 (review* or overview* or synthes*)) or (research adj3 overview*)).ti,ab,kf. (46747)
41 (cochrane or (health adj2 technology assessment) or evidence report or systematic review*).jw. (80196)
42 ((comparative adj3 (efficacy or effectiveness)) or relative effectiveness or ((indirect or indirect treatment or mixed-treatment) adj comparison*)).ti,ab,kf. (66688)
43 or/28-42 (2140934)
44 exp Guideline/ (40146)
45 Consensus/ (133787)
46 (guideline* or guidance or consensus or position statement* or position paper* or standards or recommendation* or policy statement* or association statement or practice parameter* or "American Thyroid Association" or "North American Society for Interventional Thyroidology").ti. (541258)
47 or/44-46 (644672)
48 43 or 47 (2717301)
49 26 and 48 (769)
50 49 use medall (284)
51 27 or 50 (290)
52 thyroid nodule/ (29771)
53 (((thyroid* or benign) adj3 (nodule* or mass* or cyst* or lesion*)) or AFTN).tw,kw,kf. (147038)
54 exp thyroid tumor/ (113057)
55 (thyroid* adj2 (cancer* or neoplasm* or carcinoma* or adenoma* or adenocarcinoma* or tumo?r* or malignan* or metasta*)).tw,kw,kf. (152352)
56 ((thyroid* adj5 (microcarcinoma* or papillar*)) or PTC or PTMC).tw,kw,kf. (68464)
57 or/52-56 (318382)
58 exp ablation therapy/ (76183)
59 high intensity focused ultrasound/ (7184)
60 laser therapy/ (48041)
61 microwave radiation/ (52900)
62 exp radiofrequency ablation/ (95164)
63 ((ablat* adj5 (catheter* or HIFU or high-intensit* or laser* or microwave* or "micro wave" or therap* or ((nanosecond or nano second) adj3 (pulse* electric* or pulse* field*)) or radiofrequenc* or radio frequenc* or tech* or thermal* or ultrasound* or energy* or heat*)) or cryoablat* or nsPEF* or nsPFA* or RFA).tw,kw,kf,dv,dm,mv. (207906)
64 polidocanol/ (6174)

65 intralesional drug administration/ (3782)
66 ((chemical* or ethanol* or polidocanol*) adj3 (ablat* or injection*)).tw,kw,kf,dv,dm,mv. (13973)
67 or/58-66 (364535)
68 57 and 67 (8097)
69 Viva Combo RF Generator*.tw,kw,kf. (0)
70 (thyroid* adj3 ablat*).tw,kw,kf. (5006)
71 or/68-70 (10962)
72 (exp animal/ or nonhuman/) not exp human/ (12385374)
73 71 not 72 (10721)
74 limit 73 to english language [Limit not valid in CDSR; records were retained] (9944)
75 Case Report/ or Comment/ or Editorial/ or (letter.pt. not (letter.pt. and randomized controlled trial/)) or conference abstract.pt. or conference review.pt. (12105380)
76 74 not 75 (7009)
77 Systematic review/ or "systematic review (topic)"/ or exp Meta Analysis/ or "Meta Analysis (Topic)"/ or Biomedical Technology Assessment/ (1110672)
78 (meta analy* or metaanaly* or health technolog* assess* or systematic review*).hw. (1115865)
79 ((systematic* or methodologic*) adj3 (review* or overview*)).tw,kw,kf. (893292)
80 (meta analy* or metaanaly* or met analy* or metanaly* or meta review* or metareview* or health technolog* assess* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).tw,kw,kf. (802231)
81 (evidence adj2 (review* or overview* or synthes#s)).tw,kw,kf. (115516)
82 (review of reviews or overview of reviews).tw,kw,kf. (3334)
83 umbrella review*.tw,kw,kf. (5210)
84 ((pool* adj3 analy*) or published studies or published literature or hand search* or handsearch* or manual search* or ((database* or systematic*) adj2 search*) or reference list* or bibliograph* or relevant journals or data synthes* or data extraction* or data abstraction*).tw,kw,kf. (750477)
85 (medline or pubmed or medlars or embase or cinahl or web of science or ovid or ebsco* or scopus).ab. (914430)
86 cochrane.tw,kw,kf. (385009)
87 (meta regress* or metaregress*).tw,kw,kf. (40649)
88 (((integrative or collaborative or quantitative) adj3 (review* or overview* or synthes*)) or (research adj3 overview*)).tw,kw,kf. (47887)
89 (cochrane or (health adj2 technology assessment) or evidence report or systematic review*).jw. (80196)
90 ((comparative adj3 (efficacy or effectiveness)) or relative effectiveness or ((indirect or indirect treatment or mixed-treatment) adj comparison*)).tw,kw,kf. (68051)
91 or/77-90 (2145314)
92 practice guideline/ (629845)
93 consensus/ (133787)
94 (guideline* or guidance or consensus or position statement* or position paper* or standards or recommendation* or policy statement* or association statement or practice parameter* or "American Thyroid Association" or "North American Society for Interventional Thyroidology").ti. (541258)
95 or/92-94 (1104966)
96 91 or 95 (3132851)
97 76 and 96 (788)
98 97 use emez (487)
99 51 or 98 (777)
100 99 use medall (284)

101 99 use emez (487)
102 99 use coch (3)
103 99 use cleed (3)
104 remove duplicates from 99 (526)

Clinical Evidence Search, Primary Studies

Database: EBM Reviews – Cochrane Central Register of Controlled Trials <May 2025>, EBM Reviews – NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1980 to 2025 Week 23>, Ovid MEDLINE ALL <1946 to June 06, 2025>
Search Date: June 9, 2025

Search Strategy:
1 Thyroid Nodule/ (30574)
2 (((thyroid* or benign) adj3 (nodule* or mass* or cyst* or lesion*)) or AFTN).ti,ab,kf. (150726)
3 Thyroid Cancer, Papillary/ (32279)
4 (thyroid* adj2 (cancer* or neoplasm* or carcinoma* or adenoma* or adenocarcinoma* or tumo?r* or malignan* or metasta*)).ti,ab,kf. (155520)
5 ((thyroid* adj5 (microcarcinoma* or papillar*)) or PTC or PTMC).ti,ab,kf. (69902)
6 or/1-5 (305400)
7 Ablation Techniques/ (33190)
8 High-Intensity Focused Ultrasound Ablation/ (9955)
9 Laser Therapy/ (51527)
10 Microwaves/ (54325)
11 exp Radiofrequency Ablation/ (99365)
12 ((ablat* adj5 (catheter* or HIFU or high-intensit* or laser* or microwave* or "micro wave" or therap* or ((nanosecond or nano second) adj3 (pulse* electric* or pulse* field*)) or radiofrequenc* or radio frequenc* or tech* or thermal* or ultrasound* or energy* or heat*)) or cryoablat* or nsPEF* or nsPFA* or RFA).ti,ab,kf. (220672)
13 Ethanol/ (408446)
14 Polidocanol/ (6463)
15 Injections, Intralesional/ (12298)
16 ((chemical* or ethanol* or polidocanol*) adj3 (ablat* or injection*)).ti,ab,kf. (14527)
17 or/7-16 (790718)
18 6 and 17 (9087)
19 Viva Combo RF Generator*.ti,ab,kf. (0)
20 (thyroid* adj3 ablat*).ti,ab,kf. (5128)
21 or/18-20 (11984)
22 exp Animals/ not Humans/ (10749767)
23 21 not 22 (11726)
24 limit 23 to english language (10876)
25 Case Reports/ or Comment.pt. or Editorial.pt. or (Letter not (Letter and Randomized Controlled Trial)).pt. or Congress.pt. (6915042)
26 24 not 25 (9901)
27 26 use cctr,cleed (317)
28 Clinical Trials as Topic/ (382109)
29 controlled clinical trials as topic/ (19987)
30 exp Randomized Controlled Trials as Topic/ (536550)
31 controlled clinical trial.pt. (95699)

32 randomized controlled trial.pt. (640833)
33 Pragmatic Clinical Trial.pt. (2714)
34 Random Allocation/ (234668)
35 Single-Blind Method/ (121828)
36 Double-Blind Method/ (582382)
37 Placebos/ (475887)
38 trial.ti. (1261731)
39 (random* or sham or placebo* or RCT*1).ti,ab,kf. (5695710)
40 ((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,kf. (851058)
41 ((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,kf. (8255)
42 or/28-41 (6845659)
43 26 and 42 (993)
44 43 use medall (307)
45 27 or 44 (624)
46 limit 45 to yr="2022 -Current" (130)
47 thyroid nodule/ (30574)
48 (((thyroid* or benign) adj3 (nodule* or mass* or cyst* or lesion*)) or AFTN).tw,kw,kf. (151209)
49 exp thyroid tumor/ (115225)
50 (thyroid* adj2 (cancer* or neoplasm* or carcinoma* or adenoma* or adenocarcinoma* or tumo?r* or malignan* or metasta*)).tw,kw,kf. (157114)
51 ((thyroid* adj5 (microcarcinoma* or papillar*)) or PTC or PTMC).tw,kw,kf. (70646)
52 or/47-51 (327959)
53 exp ablation therapy/ (78118)
54 high intensity focused ultrasound/ (7313)
55 laser therapy/ (51527)
56 microwave radiation/ (54318)
57 exp radiofrequency ablation/ (99365)
58 ((ablat* adj5 (catheter* or HIFU or high-intensit* or laser* or microwave* or "micro wave" or therap* or ((nanosecond or nano second) adj3 (pulse* electric* or pulse* field*)) or radiofrequenc* or radio frequenc* or tech* or thermal* or ultrasound* or energy* or heat*)) or cryoablat* or nsPEF* or nsPFA* or RFA).tw,kw,kf,dv,dm,mv. (222311)
59 polidocanol/ (6463)
60 intralesional drug administration/ (3845)
61 ((chemical* or ethanol* or polidocanol*) adj3 (ablat* or injection*)).tw,kw,kf,dv,dm,mv. (14646)
62 or/53-61 (385236)
63 52 and 62 (8502)
64 Viva Combo RF Generator*.tw,kw,kf. (0)
65 (thyroid* adj3 ablat*).tw,kw,kf. (5252)
66 or/63-65 (11469)
67 (exp animal/ or nonhuman/) not exp human/ (12580310)
68 66 not 67 (11226)
69 limit 68 to english language (10420)
70 Case Report/ or Comment/ or Editorial/ or (letter.pt. not (letter.pt. and randomized controlled trial/)) or conference abstract.pt. or conference review.pt. (12325425)
71 69 not 70 (7430)
72 "clinical trial (topic)"/ (136314)
73 "controlled clinical trial (topic)"/ (13654)
74 "randomized controlled trial (topic)"/ (293921)

75 randomization/ (234668)
76 Single Blind Procedure/ (59267)
77 Double Blind Procedure/ (229051)
78 placebo/ (413208)
79 trial.ti. (1261731)
80 (random* or sham or placebo* or RCT*1).tw,kw,kf. (5762417)
81 ((singl* or doubl*) adj (blind* or dumm* or mask*)).tw,kw,kf. (886209)
82 ((tripl* or trebl*) adj (blind* or dumm* or mask*)).tw,kw,kf. (8335)
83 or/72-82 (6510363)
84 71 and 83 (827)
85 limit 84 to yr="2022 -Current" (216)
86 85 use emez (106)
87 46 or 86 (236)
88 87 use medall (74)
89 87 use emez (106)
90 87 use cctr (56)
91 87 use cleed (0)
92 remove duplicates from 87 (152)
93 92 use medall,emez (111)

Economic Evidence Search

Database: EBM Reviews – Cochrane Central Register of Controlled Trials <December 2024>, EBM Reviews – Cochrane Database of Systematic Reviews <2005 to February 19, 2025>, EBM Reviews – NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1980 to 2025 Week 08>, Ovid MEDLINE ALL <1946 to February 25, 2025>
Search Date: February 25, 2025

Search Strategy:
1 Thyroid Nodule/ (30029)
2 (((thyroid* or benign) adj3 (nodule* or mass* or cyst* or lesion*)) or AFTN).ti,ab,kf. (148230)
3 Thyroid Cancer, Papillary/ (31481)
4 (thyroid* adj2 (cancer* or neoplasm* or carcinoma* or adenoma* or adenocarcinoma* or tumo?r* or malignan* or metasta*)).ti,ab,kf. (152917)
5 ((thyroid* adj5 (microcarcinoma* or papillar*)) or PTC or PTMC).ti,ab,kf. (68745)
6 or/1-5 (300445)
7 Ablation Techniques/ (32444)
8 High-Intensity Focused Ultrasound Ablation/ (9769)
9 Laser Therapy/ (50890)
10 Microwaves/ (53293)
11 exp Radiofrequency Ablation/ (97829)
12 ((ablat* adj5 (catheter* or HIFU or high-intensit* or laser* or microwave* or "micro wave" or therap* or ((nanosecond or nano second) adj3 (pulse* electric* or pulse* field*)) or radiofrequenc* or radio frequenc* or tech* or thermal* or ultrasound* or energy* or heat*)) or cryoablat* or nsPEF* or nsPFA* or RFA).ti,ab,kf. (216118)
13 Ethanol/ (402752)
14 Polidocanol/ (6366)
15 Injections, Intralesional/ (12218)
16 ((chemical* or ethanol* or polidocanol*) adj3 (ablat* or injection*)).ti,ab,kf. (14293)

17 or/7-16 (778083)
18 6 and 17 (8929)
19 Viva Combo RF Generator*.ti,ab,kf. (0)
20 (thyroid* adj3 ablat*).ti,ab,kf. (5073)
21 or/18-20 (11820)
22 exp Animals/ not Humans/ (10607472)
23 21 not 22 (11563)
24 Case Reports/ or Comment.pt. or Editorial.pt. or (Letter not (Letter and Randomized Controlled Trial)).pt. or Congress.pt. (6848512)
25 23 not 24 (10560)
26 limit 25 to english language [Limit not valid in CDSR; records were retained] (9783)
27 26 use coch,cleed (6)
28 economics/ (263776)
29 economics, medical/ or economics, pharmaceutical/ or exp economics, hospital/ or economics, nursing/ or economics, dental/ (1137751)
30 economics.fs. (481445)
31 (econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*).ti,ab,kf. (1434065)
32 exp "costs and cost analysis"/ (729986)
33 (cost or costs or costing or costly).ti. (359302)
34 cost effective*.ti,ab,kf. (515623)
35 (cost* adj2 (util* or efficacy* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog* or increment*)).ab,kf. (341972)
36 models, economic/ (17226)
37 markov chains/ or monte carlo method/ (118173)
38 (decision adj1 (tree* or analy* or model*)).ti,ab,kf. (78868)
39 (markov or markow or monte carlo).ti,ab,kf. (197412)
40 quality-adjusted life years/ (62653)
41 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).ti,ab,kf. (127335)
42 ((adjusted adj1 (quality or life)) or (willing* adj2 pay) or sensitivity analys*s).ti,ab,kf. (234511)
43 or/28-42 (3726480)
44 26 and 43 (472)
45 44 use medall,cctr (157)
46 27 or 45 (163)
47 thyroid nodule/ (30029)
48 (((thyroid* or benign) adj3 (nodule* or mass* or cyst* or lesion*)) or AFTN).tw,kw,kf. (148749)
49 (thyroid* adj2 (cancer* or neoplasm* or carcinoma* or adenoma* or adenocarcinoma* or tumo?r* or malignan* or metasta*)).tw,kw,kf. (154532)
50 ((thyroid* adj5 (microcarcinoma* or papillar*)) or PTC or PTMC).tw,kw,kf. (69501)
51 or/47-50 (299853)
52 exp ablation therapy/ (76371)
53 high intensity focused ultrasound/ (7195)
54 laser therapy/ (50890)
55 microwave radiation/ (53286)
56 exp radiofrequency ablation/ (97829)
57 ((ablat* adj5 (catheter* or HIFU or high-intensit* or laser* or microwave* or "micro wave" or therap* or ((nanosecond or nano second) adj3 (pulse* electric* or pulse* field*)) or radiofrequenc* or

radio frequenc* or tech* or thermal* or ultrasound* or energy* or heat*)) or cryoablat* or nsPEF* or nsPFA* or RFA).tw,kw,kf,dv,dm,mv. (217897)
58 polidocanol/ (6366)
59 intralesional drug administration/ (3790)
60 ((chemical* or ethanol* or polidocanol*) adj3 (ablat* or injection*)).tw,kw,kf,dv,dm,mv. (14443)
61 or/52-60 (378304)
62 51 and 61 (8101)
63 Viva Combo RF Generator*.tw,kw,kf. (0)
64 (thyroid* adj3 ablat*).tw,kw,kf. (5201)
65 or/62-64 (11080)
66 (exp animal/ or nonhuman/) not exp human/ (12396874)
67 65 not 66 (10841)
68 Case Report/ or Comment/ or Editorial/ or (letter.pt. not (letter.pt. and randomized controlled trial/)) or conference abstract.pt. or conference review.pt. (12130814)
69 67 not 68 (7911)
70 limit 69 to english language [Limit not valid in CDSR; records were retained] (7188)
71 Economics/ (263776)
72 Health Economics/ or Pharmacoeconomics/ or Drug Cost/ or Drug Formulary/ (159510)
73 Economic Aspect/ or exp Economic Evaluation/ (605237)
74 (econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*).tw,kw,kf. (1454830)
75 exp "Cost"/ (729986)
76 (cost or costs or costing or costly).ti. (359302)
77 cost effective*.tw,kw,kf. (524657)
78 (cost* adj2 (util* or efficac* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog* or increment*)).ab,kw,kf. (352590)
79 Monte Carlo Method/ (90883)
80 (decision adj1 (tree* or analy* or model*)).tw,kw,kf. (82324)
81 (markov or markow or monte carlo).tw,kw,kf. (200909)
82 Quality-Adjusted Life Years/ (62653)
83 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).tw,kw,kf. (130713)
84 ((adjusted adj1 (quality or life)) or (willing* adj2 pay) or sensitivity analys*s).tw,kw,kf. (255704)
85 or/71-84 (3215470)
86 70 and 85 (388)
87 86 use emez (211)
88 46 or 87 (374)
89 88 use medall (130)
90 88 use emez (211)
91 88 use cleed (3)
92 88 use cctr (27)
93 88 use coch (3)
94 remove duplicates from 88 (257)

Quantitative Evidence of Preferences and Values Search

Database: Ovid MEDLINE ALL <1946 to March 10, 2025>
Search Date: March 12, 2025

Search Strategy:

1 Thyroid Nodule/ (8549)
2 (((thyroid* or benign) adj3 (nodule* or mass* or cyst* or lesion*)) or AFTN).ti,ab,kf. (62261)
3 Thyroid Cancer, Papillary/ (7879)
4 (thyroid* adj2 (cancer* or neoplasm* or carcinoma* or adenoma* or adenocarcinoma* or tumo?r* or malignan* or metasta*)).ti,ab,kf. (65793)
5 ((thyroid* adj5 (microcarcinoma* or papillar*)) or PTC or PTMC).ti,ab,kf. (27981)
6 or/1-5 (126035)
7 Ablation Techniques/ (3831)
8 High-Intensity Focused Ultrasound Ablation/ (2497)
9 Laser Therapy/ (41989)
10 Microwaves/ (20895)
11 exp Radiofrequency Ablation/ (44216)
12 ((ablat* adj5 (catheter* or HIFU or high-intensit* or laser* or microwave* or "micro wave" or therap* or ((nanosecond or nano second) adj3 (pulse* electric* or pulse* field*)) or radiofrequenc* or radio frequenc* or tech* or thermal* or ultrasound* or energy* or heat*)) or cryoablat* or nsPEF* or nsPFA* or RFA).ti,ab,kf. (81044)
13 Ethanol/ (99533)
14 Polidocanol/ (1274)
15 Injections, Intralesional/ (7576)
16 ((chemical* or ethanol* or polidocanol*) adj3 (ablat* or injection*)).ti,ab,kf. (5866)
17 or/7-16 (260862)
18 6 and 17 (3089)
19 Viva Combo RF Generator*.ti,ab,kf. (0)
20 (thyroid* adj3 ablat*).ti,ab,kf. (1975)
21 or/18-20 (4232)
22 Attitude to Health/ (85584)
23 Health Knowledge, Attitudes, Practice/ (135205)
24 Patient Participation/ (30864)
25 Patient Preference/ (11796)
26 Attitude of Health Personnel/ (137857)
27 *Professional-Patient Relations/ (12596)
28 *Physician-Patient Relations/ (37979)
29 Choice Behavior/ (36272)
30 (choice or choices or value* or valuation* or knowledg*).ti. (353679)
31 (preference* or expectation* or attitude* or acceptab* or point of view).ti,ab,kf. (828483)
32 ((clinician* or doctor* or (health* adj2 worker*) or patient*1 or personal or physician* or practitioner* or professional*1 or provider* or user*1 or women or men) adj2 (participation or perspective* or perception* or misperception* or perceiv* or view* or understand* or misunderstand* or value*1 or knowledg*)).ti,ab,kf. (211112)
33 health perception*.ti,ab,kf. (3715)
34 *Decision Making/ (48349)
35 (clinician* or doctor* or (health* adj2 worker*) or patient*1 or personal or physician* or practitioner* or professional*1 or provider* or user*1 or women or men).ti. (3244448)
36 34 and 35 (8807)
37 (decision* and mak*).ti. (42807)
38 (decision mak* or decisions mak*).ti,ab,kf. (253985)
39 37 or 38 (255726)

40 (clinician* or doctor* or (health* adj2 worker*) or patient*1 or personal or physician* or practitioner* or professional*1 or provider* or user*1 or women or men).ti,ab,kf. (10856271)
41 39 and 40 (161632)
42 (discrete choice* or decision board* or decision analy* or decision-support or decision tool* or decision aid* or latent class* or decision* conflict* or decision* regret*).ti,ab,kf. (60903)
43 Decision Support Techniques/ (23352)
44 (health and utilit*).ti. (2198)
45 (gamble* or prospect theory or health utilit* or utility value* or utility score* or utility estimate* or health state or feeling thermometer* or best-worst scaling or time trade-off or TTO or probability trade-off).ti,ab,kf. (19011)
46 (preference based or preference score* or preference elicitation or multiattribute or multi attribute).ti,ab,kf. (4417)
47 or/22-33,36,41-46 (1750029)
48 21 and 47 (245)
49 Case Reports/ or Comment.pt. or Editorial.pt. or (Letter not (Letter and Randomized Controlled Trial)).pt. or Congress.pt. (4609240)
50 48 not 49 (229)
51 exp Animals/ not Humans/ (5315121)
52 50 not 51 (229)
53 limit 52 to english language (216)

CINAHL

#	Query	Results
S1	(MH "Thyroid Nodule")	1,118
S2	TI(((thyroid* or benign) n3 (nodule* or mass* or cyst* or lesion*)) or AFTN)	3,263
S3	AB(((thyroid* or benign) n3 (nodule* or mass* or cyst* or lesion*)) or AFTN)	9,067
S4	(MH "Thyroid Neoplasms")	7,876
S5	TI(thyroid* n2 (cancer* or neoplasm* or carcinoma* or adenoma* or adenocarcinoma* or tumo?r* or malignan* or metasta*))	7,098
S6	AB(thyroid* n2 (cancer* or neoplasm* or carcinoma* or adenoma* or adenocarcinoma* or tumo?r* or malignan* or metasta*))	6,568
S7	TI((thyroid* N5 (microcarcinoma* or papillar*)) or PTC or PTMC)	2,234
S8	AB((thyroid* N5 (microcarcinoma* or papillar*)) or PTC or PTMC)	2,799
S9	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8	21,257
S10	(MH "Ablation Techniques")	3,433
S11	(MH "Laser Therapy")	10,227
S12	(MH "Microwaves")	1,489
S13	(MH "Radiofrequency Ablation")	1,325
S14	TI((ablat* N5 (catheter* or HIFU or high-intensit* or laser* or microwave* or "micro wave" or therap* or ((nanosecond or nano second) adj3 (pulse* electric* or pulse* field*)) or radiofrequenc* or radio frequenc* or tech* or thermal* or ultrasound* or energy* or heat*)) or cryoablat* or nsPEF* or nsPFA* or RFA)	14,921
S15	AB((ablat* N5 (catheter* or HIFU or high-intensit* or laser* or microwave* or "micro wave" or therap* or ((nanosecond or nano second) adj3 (pulse* electric* or pulse* field*)) or radiofrequenc* or radio frequenc* or tech* or thermal* or ultrasound* or energy* or heat*)) or cryoablat* or nsPEF* or nsPFA* or RFA)	14,781
S16	(MH "Ethanol")	11,892
S17	(MH "Injections, Intralesional")	1,224

S18 TI((chemical* or ethanol* or polidocanol*) N3 (ablat* or injection*)) 338
S19 AB((chemical* or ethanol* or polidocanol*) N3 (ablat* or injection*)) 687
S20 S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 48,161
S21 S9 AND S20 603
S22 TI(Viva Combo RF Generator*) 0
S23 AB(Viva Combo RF Generator*) 0
S24 TI(thyroid* N3 ablat*) 218
S25 AB(thyroid* N3 ablat*) 239
S26 S21 OR S22 OR S23 OR S24 OR S25 793
S27 (MH "Attitude to Health") 50,607
S28 (MH "Health Knowledge") 43,186
S29 (MH "Consumer Participation") 25,114
S30 (MH "Patient Preference") 3,922
S31 (MH "Attitude of Health Personnel") 59,878
S32 (MM "Professional-Patient Relations") 15,122
S33 (MM "Physician-Patient Relations") 17,581
S34 (MM "Nurse-Patient Relations") 15,174
S35 TI (choice or choices or value* or valuation* or knowledg*) 128,279
S36 (preference* or expectation* or attitude* or acceptab* or point of view) 592,960
S37 ((clinician* or doctor* or (health* N2 worker*) or nurse or nurses or patient or patients or personal or physician* or practitioner* or professional or professionals or provider* or user or users or women or men) N2 (knowledg* or misperception* or misunderstand* or participation or perceiv* or perception* or perspective* or understand* or value or values or view*)) 194,961
S38 health perception* 5,762
S39 (MH "Decision Making, Shared") 4,874
S40 (MH "Decision Making, Patient") 15,995
S41 (MH "Decision Making, Family") 4,406
S42 (MM "Decision Making") 27,245
S43 TI (clinician* or doctor* or (health* N2 worker*) or nurse or nurses or patient or patients or personal or physician* or practitioner* or professional or professionals or provider* or user or users or women or men)1,516,529
S44 S42 AND S43 5,808
S45 TI (decision* and mak*) 23,741
S46 (decision mak* or decisions mak*) 193,132
S47 S45 OR S46 193,372
S48 (clinician* or doctor* or (health* N2 worker*) or nurse or nurses or patient or patients or personal or physician* or practitioner* or professional or professionals or provider* or user or users or women or men)3,969,971
S49 S47 AND S48 136,459
S50 (discrete choice* or decision board* or decision analy* or decision support or decision tool* or decision aid* or latent class* or decision* conflict* or decision* regret*) 40,241
S51 (MH "Decision Support Techniques") 7,945
S52 TI (health and utilit*) 1,305
S53 (gamble* or prospect theory or health utilit* or utility value* or utility score* or utility estimate* or health state or feeling thermometer* or best worst scaling or time trade off or TTO or probability trade off) 19,768
S54 (preference based or preference score* or preference elicitation or multiattribute or multi attribute) 1,953

S55 S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S44 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 984,450
S56 S26 AND S55 48
S57 PT (Case Study or Commentary or Editorial or Letter or Proceedings) 1,299,902
S58 S56 NOT S57 46
S59 S56 NOT S57 46

Grey Literature Search

Performed on: March 3–7, 2025

Websites searched: Alberta Health Evidence Reviews, BC Health Technology Assessments, Canadian Agency for Drugs and Technologies in Health (CADTH), Institut national d'excellence en santé et en services sociaux (INESSS), Institute of Health Economics (IHE), University Of Calgary Health Technology Assessment Unit, Ontario Health Technology Assessment Committee (OHTAC), McGill University Health Centre Health Technology Assessment Unit, Centre Hospitalier de l'Université de Quebec–Université Laval, Contextualized Health Research Synthesis Program of Newfoundland (CHRSP), Health Canada Medical Device Database, International HTA Database (INAHTA), Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Centers, Centers for Medicare and Medicaid Services Technology Assessments, Veterans Affairs Health Services Research and Development, Institute for Clinical and Economic Review, Oregon Health Authority Health Evidence Review Commission, Washington State Health Care Authority Health Technology Reviews, National Institute for Health and Care Excellence (NICE), National Health Service England (NHS), Healthcare Improvement Scotland, Health Technology Wales, Ireland Health Information and Quality Authority Health Technology Assessments, Adelaide Health Technology Assessment, Australian Government Medical Services Advisory Committee, Monash Health Centre for Clinical Effectiveness, The Sax Institute, Australian Government Department of Health and Aged Care, Australian Safety and Efficacy Register of New Interventional Procedures–Surgical (ASERNIP-S), Pharmac, Italian National Agency for Regional Health Services (Aegnas), Belgian Health Care Knowledge Centre, Ludwig Boltzmann Institute for Health Technology Assessment (Austria), Regional Health Technology Assessment Centre (HTA-centrum), Swedish Agency for Health Technology Assessment and Assessment of Social Services, Norwegian Institute of Public Health – Health Technology Assessments, Danish Health Technology Council, Ministry of Health Malaysia – Health Technology Assessment Section, Tuft's Cost-Effectiveness Analysis Registry, Sick Kids PEDE Database, PROSPERO, EUnetHTA, clinicaltrials.gov

Keywords: thyroid, thyroid nodule, thyroid cancer, papillary, ablation, ablate, ablative, Viva RF, thyroïde, l'ablation

Clinical results (included in PRISMA): 4
Economic results (included in PRISMA): 0
Ongoing HTAs (PROSPERO/EUnetHTA): 42
Ongoing clinical trials: 57

Appendix 3: Critical Appraisal of Clinical Evidence

Table A2: Risk of Bias[a] Among Systematic Reviews (ROBIS Tool)

	Phase 2				Phase 3
Author, year	Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	Risk of bias in the review
Bandeira-Echtler et al, 2014[41]	Low	Low	Low	Low	Low
Benaim et al, 2023[42]	Low[b]	Low	Low	Low	Low
Bernardi et al, 2021[43]	Low[b]	Low	Low	Low	Low
Cesareo et al, 2020[45]	Low[b]	Low	High[c]	High[d]	High
Cesareo et al, 2022[44]	Low[b]	High[e]	High[f]	Low	High
Cesareo et al, 2022[46]	Low[b]	High[g]	High[h]	High[d]	High
Chen et al, 2016[47]	Low[b]	Low	Low	Low	Low
Cheong et al, 2022[48]	Low	Low	Low	Low	Low
Cho et al, 2019[49]	Low[b]	Low	Low	High[i]	High
Cho et al, 2020[50]	Low[b]	Low	Low	Low	Low
Cho et al, 2021[51]	Low[b]	Low	Low	Low[j]	Low
Choi and Jung, 2020[52]	Low[b]	High[g]	Low	Low	High
Chorti et al, 2023[53]	Low	Low	Low	Low	Low
Chung et al, 2017[55]	Low[b]	High[g]	High[k]	Low	High
Chung et al, 2020[54]	Low[b]	Low	High[k]	Low	High
Cui et al, 2019[56]	Low[b]	High[l,m]	High[k]	High[n]	High
Ding et al, 2023[57]	Low[b]	Low	High[o]	High[d,j]	High
Fan et al, 2024[58]	Low	Low	Low	High[p]	High
Fei et al, 2020[59]	Low[b]	Low	Low	Low	Low
Feng et al, 2023[60]	Low[b]	High[m]	High[k]	Low	High
Fontenot et al, 2015[61]	Low[b]	Low	High[q]	High[p]	High
Fuller et al, 2014[62]	Low[b]	High[m,r]	High[q]	High[d]	High
Gao et al, 2023[63]	Low	Low	Low	Low	Low
Guan et al, 2020[64]	Low	Low	Low	Low[j]	Low

	Phase 2				Phase 3
Author, year	**Study eligibility criteria**	**Identification and selection of studies**	**Data collection and study appraisal**	**Synthesis and findings**	**Risk of bias in the review**
Guo et al, 2021[65]	Low[b]	Low	High[k]	Low	High
Ha et al, 2015[66]	Low[b]	High[m]	High[s]	Low	High
Han et al, 2024[67]	Low[b]	High[e,m]	High[k]	Low	High
He et al, 2021[68]	Low	Low	Low	Low	Low
Hurtado Amezquita et al, 2023[69]	Low[b]	Low	Low	Low[j]	Low
Javid et al, 2024[70]	Low	Low	Low	Low	Low
Jeong and Baek, 2025[71]	Low[b]	Low	High[h]	High[i]	High
Ji et al, 2022[72]	Low[b]	High[e]	Low	High[j]	High
Kim et al, 2021[73]	Low[b]	Low	Low	Low[j]	Low
Kim et al, 2021[74]	Low[b]	Low	Low	Low	Low
Kong et al, 2024[75]	Low	High[f]	Low	Low	High
Lang and Wu, 2017[23]	Low[b]	High[f]	High[h,q]	Low	High
Ledesma-Leon et al, 2024[76]	Low	Low	High[t]	High[j,p]	High
Leon-Salas et al, 2023[77]	Low	Low	Low	Low	Low
Li et al, 2024[78]	Low[b]	Low	Low	Low	Low
Lim et al, 2025[79]	Low[b]	Low	Low	High[p]	High
Monpeyssen et al, 2021[80]	Low[b]	High[f,u]	High[q,v]	Low	High
Muhammad et al, 2021[81]	Low[b]	Low	High[q]	Low	High
Muhammad et al, 2022[82]	Low[b]	High[l]	High[q]	Low	High
Muhammad et al, 2022[83]	Low[b]	High[l]	Low	High[p]	High
Nguyen et al, 2025[84]	Low[b]	Low	Low	Low	Low
Nicolopoulos et al, 2024[85]	Low	Low	Low	Low	Low
Ntelis and Linos, 2021[86]	Low[b]	High[g,w]	High[w]	Low	High
Qafesha et al, 2025[87]	Low	Low	Low	Low	Low
Qian et al, 2024[88]	Low[b]	High[m]	High[k]	High[p]	High
Scappaticcio et al, 2024[89]	Low[b]	Low	High[x]	Low	High
Shen et al, 2020[90]	Low[b]	Low	Low	Low[j]	Low

	Phase 2				Phase 3
Author, year	**Study eligibility criteria**	**Identification and selection of studies**	**Data collection and study appraisal**	**Synthesis and findings**	**Risk of bias in the review**
Spartalis et al, 2020[91]	Low[b]	High[f,y]	High[h,q]	Low	High
Suh et al, 2016[92]	Low[b]	Low	High[k]	Low	High
Sui et al, 2017[93]	Low[b]	High[z]	High[k]	Low	High
Sun et al, 2022[95]	Low[b]	Low	High[k]	Low	High
Sun et al, 2024[94]	Low	Low	High[aa]	Low	High
Tong et al, 2019[96]	Low[b]	Low	High[k]	High[p]	High
Toraih et al, 2025[97]	Low[b]	Low	Low	Low	Low
Trimboli et al, 2020[98]	Low[b]	Low	Low	Low	Low
van Dijk et al, 2022[99]	Low[b]	High[g]	High[c]	High[p]	High
Wang et al, 2022[100]	Low[b]	Low	Low	High[p]	High
Wu and Chen, 2022[101]	Low[b]	Low	Low	Low	Low
Wu et al, 2022[102]	Low[b]	Low	High[k]	High[p]	High
Xu et al, 2024[104]	Low[b]	Low	High[k]	Low	High
Xu et al, 2024[103]	Low[b]	Low	Low	High[j,p]	High
Xu et al, 2024[105]	Low[b]	Low	High[k]	Low	High
Xue et al, 2022[106]	Low[b]	Low	Low	Low	Low
Xue et al, 2022[107]	Low[b]	Low	Low	Low	Low
Yang et al, 2021[108]	Low[b]	Low	Low	Low	Low
Yang et al, 2024[109]	Low[b]	Low	Low	High[p]	High
Yu et al, 2025[110]	Low	Low	High[k]	Low[j]	High
Yuan et al, 2024[111]	Low[b]	Low	Low	Low	Low
Zhang et al, 2024[112]	Low[b]	Low	Low	High[j,p]	High
Zhao et al, 2016[113]	Low[b]	Low	Low	Low	Low
Zheng et al, 2018[114]	Low[b]	Low	Low	High[f]	High
Zufry et al, 2024[115]	Low	Low	Low	Low	Low

Abbreviations: ROBIS, Risk of Bias in Systematic Reviews.

[a] Possible risk of bias levels: low, high, unclear.

[b] No information on predefined review protocol.

Notes continued on the next page.

Notes continued from the previous page.
[c] Unclear which risk of bias tool was used.
[d] Pooled studies with different comparators in meta-analyses.
[e] Limited or no information on search terms.
[f] No information on study designs of included studies.
[g] Included studies of unclear designs.
[h] No information on demographic characteristics of included studies.
[i] Outcomes of different ablative technologies were reported and discussed as *thermal ablation*, not separately.
[j] Pooled studies with different ablative technologies in meta-analyses, with no subgroup analyses by types of ablative technologies.
[k] Inappropriate risk-of-bias tool.
[l] No information on literature search date.
[m] Some nonrandomized studies were incorrectly identified as randomized controlled trials.
[n] Pooled studies on benign nodules and thyroid cancers in meta-analyses with no subgroup analyses.
[o] Unclear which risk-of-bias tool was used to assess the included nonrandomized trial.
[p] Limited or no exploration of the potential sources of heterogeneity in meta-analyses.
[q] No risk of bias assessment.
[r] One included study was not the intervention of interest of that review.
[s] No risk of bias assessment on observational studies.
[t] No risk of bias assessment on cross-sectional studies.
[u] No information on the literature search month.
[v] Discrepancy in the number of included studies in the text and flow diagram.
[w] Single reviewer in study selection and/or data extraction.
[x] No information on which National Heart, Lung and Blood Institute Quality Assessment Tool was used.
[y] No information on the number of reviewers.
[z] Unclear what "NG studies" were.
[aa] Inappropriate risk-of-bias tool for nonrandomized studies.

Table A3: Risk of Bias[a] Among Randomized Controlled Trials (Cochrane Risk-of-Bias Tool 2)

Author, year	Randomization process	Deviation from intended inteventions	Missing outcome data	Measurement of the outcome	Selection of the report result	Overall risk of bias
Chen et al, 2024[196]	Some concerns[b]	Low	Low	Some concerns/high[c]	Low	High

[a] Possible risk-of-bias levels: high, some concerns, low.

[b] The study stated that participants were randomized to either radiofrequency ablation or microwave ablation by an independent investigator. It is unclear if this was equivalent to allocation concealment.

[c] No blinding of outcome assessors and participants. Volume reduction and adverse events were assessed as having some concerns. Symptom improvement and cosmetic appearance improvement were assessed as having a high risk of bias.

Table A4: GRADE Evidence Profile for the Comparison of RFA and Surgery in Symptomatic Benign Thyroid Nodules

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Nodule volume reduction							
1 (RCT)	Very serious limitations (−2)[a]	No serious limitations	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
1 (nonrandomized study)	Very serious limitations (−2)[c,d]	No serious limitations	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Symptom improvement							
1 (nonrandomized study)	Very serious limitations (−2)[c,d]	Not applicable[e]	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Cosmetic appearance improvement							
1 (nonrandomized study)	Very serious limitations (−2)[c,d]	Not applicable[e]	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Thyroid function							
1 (nonrandomized study)	Very serious limitations (−2)[c,d]	Not applicable[e]	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Quality of life							
1 (nonrandomized study)	Very serious limitations (−2)[c,d]	Not applicable[e]	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Nodule recurrence rate							
1 (nonrandomized study)	Very serious limitations (−2)[c,d]	Not applicable[e]	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Adverse events							
1 (nonrandomized study)	Very serious limitations (−2)[c,d]	Not applicable[e]	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RCT, randomized controlled trial; RFA, radiofrequency ablation; ROBINS-I, Risk of Bias in Non-randomized Studies of Interventions.

[a] The RCT included in the systematic review was considered to have a very high risk of bias.

[b] Indirectness was downgraded in the GRADE table with a footnote stating, "imprecision downgraded due to study setting (China)." However, a study setting in China may limit generalizability rather than the precision or directness of the outcomes. Therefore, we did not downgrade these 2 domains unless otherwise stated.

[c] The ROBINS-I tool was used to assess risk of bias in the nonrandomized studies. As such, the GRADE for these studies started at High.

[d] Nonrandomized studies included in the systematic review were considered to have very high risk of bias.

[e] Evidence from a single study.

Adapted partially from Nicolopoulos et al (Austrian Institute of Health Technology Assessment).[85]

Table A5: GRADE Evidence Profile for the Comparison of Microwave Ablation and Surgery in Symptomatic Benign Thyroid Nodules

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Nodule volume reduction							
2 (RCTs)	Very serious limitations (−2)[a]	No serious limitations	No serious limitations[b]	Serious limitations (−1)[b,c]	Undetected	None	⨁ Very low
1 (nonrandomized study)	Very serious limitations (−2)[d,e]	No serious limitations	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Symptom improvement							
1 (RCT)	Very serious limitations (−2)[a]	No serious limitations	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
1 (nonrandomized study)	Very serious limitations (−2)[d,e]	No serious limitations	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Cosmetic appearance improvement							
1 (RCT)	Very serious limitations (−2)[a]	No serious limitations	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
1 (nonrandomized study)	Very serious limitations (−2)[d,e]	No serious limitations	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Thyroid function							
1 (RCT)	Very serious limitations (−2)[a]	No serious limitations	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
1 (nonrandomized study)	Very serious limitations (−2)[d,e]	No serious limitations	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Quality of life							
1 (RCT)	Very serious limitations (−2)[a]	Not applicable[f]	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low
Adverse events							
2 (RCTs)	Very serious limitations (−2)[a]	No serious limitations	No serious limitations[b]	Serious limitations (−1)[b,g]	Undetected	None	⨁ Very low
1 (nonrandomized study)	Very serious limitations (−2)[d,e]	No serious limitations	No serious limitations[b]	No serious limitations[b]	Undetected	None	⨁⨁ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RCT, randomized controlled trial; ROBINS-I, Risk of Bias in Non-randomized Studies of Interventions.

[a] The RCT included in the systematic review had a very high risk of bias.

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[b] Indirectness was downgraded in the GRADE table with a footnote stating, "imprecision downgraded due to study setting (China)." However, study setting in China may limit generalizability rather than the precision or directness of the outcomes. Therefore, we did not downgrade these 2 domains unless otherwise stated.

[c] Large variations in estimates at same follow-up timepoints.

[d] The ROBINS-I tool was used to assess risk of bias in nonrandomized studies. As such, the GRADE for these studies started at High.

[e] The nonrandomized studies included in the systematic review were considered to have very high risk of bias.

[f] Evidence from a single study.

[g] Adverse events were investigated only to 48 hours; this may not have been sufficient time to capture all relevant events related to the intervention or the comparator.

Adapted partially from Nicolopoulos et al (Austrian Institute of Health Technology Assessment).[85]

Table A6: GRADE Evidence Profile for the Comparison of HIFU and Surgery in Symptomatic Benign Thyroid Nodules

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Nodule volume reduction							
1 (nonrandomized study)	Very serious limitations (−2)[a,b]	Not applicable[c]	No serious limitations[d]	Serious limitations (−1)[d,e]	Undetected	None	⊕ Very low
Symptom improvement							
1 (nonrandomized study)	Very serious limitations (−2)[a,b]	Not applicable[c]	No serious limitations[d]	No serious limitations[d]	Undetected	None	⊕⊕ Low
Thyroid function							
1 (nonrandomized study)	Very serious limitations (−2)[a,b]	Not applicable[c]	No serious limitations[d]	No serious limitations[d]	Undetected	None	⊕⊕ Low
Adverse events							
1 (nonrandomized study)	Very serious limitations (−2)[a,b]	Not applicable[c]	No serious limitations[d]	No serious limitations[d]	Undetected	None	⊕⊕ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; HIFU, high-intensity focused ultrasound; ROBINS-I, Risk of Bias in Non-randomized Studies of Interventions.

[a] The ROBINS-I tool was used to assess risk of bias in nonrandomized studies. As such, the GRADE for these studies started at High.

[b] The nonrandomized studies included in the systematic review had a very high risk of bias.

[c] Evidence from a single study.

[d] Indirectness in the GRADE table with a footnote stating, "imprecision downgraded due to study setting (China)." However, study setting in China may limit generalizability rather than the precision or directness of the outcomes. Therefore, we did not downgrade these 2 domains unless otherwise stated.

[e] Large standard deviation.

Adapted partially from Nicolopoulos et al (Austrian Institute of Health Technology Assessment).[85]

Table A7: GRADE Evidence Profile for the Comparison of RFA and Microwave Ablation in Symptomatic Benign Thyroid Nodules

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Nodule volume reduction							
1 (RCT)	Serious limitations (−1)[a]	Not applicable[b]	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁⨁ Low
Symptom improvement							
1 (RCT)	Serious limitations (−1)[a]	Not applicable[b]	No serious limitations	Serious limitations (−1)[d]	Undetected	None	⨁⨁ Low
Cosmetic appearance improvement							
1 (RCT)	Serious limitations (−1)[a]	Not applicable[b]	No serious limitations	Serious limitations (−1)[d]	Undetected	None	⨁⨁ Low
Adverse events							
1 (RCT)	Serious limitations (−1)[a]	Not applicable[b]	No serious limitations	Serious limitations (−1)[d]	Undetected	None	⨁⨁ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RCT, randomized controlled trial; RFA, radiofrequency ablation.

[a] No allocation concealment, and no blinding of outcome assessors and participants.

[b] Evidence from a single study.

[c] An infinity as the upper confidence interval for the difference in volume reduction rate established noninferiority between RFA and microwave ablation with limited precision and showed that the true difference in treatment effect was unknown.

[d] The study sample size was calculated to provide adequate statistical power only for the primary outcome of volume reduction rate.

Table A8: GRADE Evidence Profile for the Comparison of Ethanol Ablation and RFA in Cystic Thyroid Nodules

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Nodule volume reduction							
2 (RCTs)	Serious limitations (−1)[a]	No serious limitations	No serious limitations	Serious limitations (−1)[b]	Undetected	None	⨁⨁ Low
Symptom improvement							
2 (RCTs)	Serious limitations (−1)[a]	No serious limitations	No serious limitations	Serious limitations (−1)[b]	Undetected	None	⨁⨁ Low
Cosmetic appearance improvement							
2 (RCTs)	Serious limitations (−1)[a]	No serious limitations	No serious limitations	Serious limitations (−1)[b]	Undetected	None	⨁⨁ Low
Adverse events							
2 (RCTs)	Serious limitations (−1)[a]	No serious limitations	No serious limitations	Serious limitations (−1)[b]	Undetected	None	⨁⨁ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RCT, randomized controlled trial; RFA, radiofrequency ablation.

[a] No information on randomization processes.

[b] Confidence intervals included null effects and appreciable risk and protection values.

Adapted partially from Leon-Salas et al.[77]

Table A9: GRADE Evidence Profile for the Comparison of After and Before RFA in AFTNs

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Nodule volume reduction							
10 (nonrandomized studies)	Serious limitations (−1)[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁⨁ Low
Symptom improvement							
5 (nonrandomized studies)	Serious limitations (−1)[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁⨁ Low
Cosmetic appearance improvement							
5 (nonrandomized studies)	Serious limitations (−1)[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁⨁ Low
Thyroid function							
10 (nonrandomized studies)	Serious limitations (−1)[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁⨁ Low
Adverse events							
10 (nonrandomized studies)	Serious limitations (−1)[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁⨁ Low

Abbreviations: AFTN, autonomously functioning thyroid nodule; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RFA, radiofrequency ablation; ROBINS-I, Risk of Bias in Non-randomized Studies of Interventions.

[a] The ROBINS-I tool was used to assess risk of bias in nonrandomized studies. As such, the GRADE for these studies started at High.

[b] All included studies were assessed to be at risk of confounding and selection bias.

[c] Small sample sizes: 9 to 44 for all outcomes.

Adapted partially from Javid et al.[70]

Table A10: GRADE Evidence Profile for the Comparison of RFA and Surgery in Small, Low-Risk Papillary Thyroid Cancer

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Tumour disappearance rate							
3 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
Tumour recurrence rate							
5 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
Surgical time							
7 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
Length of hospital stay							
6 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
Postprocedural pain							
2 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
Postprocedural quality of life							
2 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
Recurrent laryngeal nerve palsy or voice change							
7 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
Overall complications							
7 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RFA, radiofrequency ablation.

[a] Observational or nonrandomized studies started with a GRADE level of Low because of inherent limitations in study design (e.g., lack of randomization, lack of blinding, loss to follow-up). We did not lower the GRADE level further unless there were more substantial study limitations.

[b] Study quality was assessed as fair to high.

Adapted partially from Nguyen et al.[84]

Table A11: GRADE Evidence Profile for the Comparison of Microwave Ablation and Surgery in Small, Low-Risk Papillary Thyroid Cancer

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Tumour disappearance rate							
5 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁ Very low
Tumour recurrence rate							
7 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Surgical time							
7 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Length of hospital stay							
6 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Postprocedural pain							
3 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Postprocedural quality of life							
3 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Recurrent laryngeal nerve palsy or voice change							
8 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Overall complications							
8 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation.

[a] Observational or nonrandomized studies started with a GRADE level of Low because of inherent limitations in study design (e.g., lack of randomization, lack of blinding, loss to follow-up). We did not lower the GRADE level further unless there were more substantial study limitations.

[b] Study quality was assessed as fair to high.

[c] Large variances on estimates.

Adapted partially from Nguyen et al.[84]

Table A12: GRADE Evidence Profile for the Comparison of Laser Ablation and Surgery in Small, Low-Risk Papillary Thyroid Cancer

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Tumour disappearance rate							
1 (nonrandomized study)	No serious limitations[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Tumour recurrence rate							
1 (nonrandomized study)	No serious limitations[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Surgical time							
1 (nonrandomized study)	No serious limitations[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Length of hospital stay							
1 (nonrandomized study)	No serious limitations[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Recurrent laryngeal nerve palsy or voice change							
1 (nonrandomized study)	No serious limitations[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Overall complications							
1 (nonrandomized study)	No serious limitations[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation.

[a] Observational or nonrandomized studies started with a GRADE level of Low because of inherent limitations in study design (e.g., lack of randomization, lack of blinding, loss to follow-up). We did not lower the GRADE level further unless there were more substantial study limitations.

[b] Study quality was assessed as fair to high.

[c] Evidence from a single study.

Adapted partially from Nguyen et al.[84]

Table A13: GRADE Evidence Profile for the Comparison of RFA and Microwave Ablation in Small, Low-Risk Papillary Thyroid Cancer

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Tumour disappearance rate							
1 (nonrandomized study)	Serious limitations (−1)[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
Tumour recurrence rate							
4 (nonrandomized studies)	Serious limitations (−1)[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
Surgical time							
1 (nonrandomized study)	Serious limitations (−1)[a b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
Length of hospital stay							
Indirect evidence	Serious limitations (−1)[a,b,d]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
Postprocedural pain							
Indirect evidence	Serious limitations (−1)[a,b,d]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
Postprocedural quality of life							
Indirect evidence	Serious limitations (−1)[a,b,d]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
Recurrent laryngeal nerve palsy or voice change							
4 (nonrandomized studies)	Serious limitations (−1)[a,b,d]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
Overall complications							
4 (nonrandomized studies)	Serious limitations (−1)[a,b,d]	No serious limitations	No serious limitations	Serious limitations (−1)[e]	Undetected	None	⊕ Very low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RFA, radiofrequency ablation.

[a] Observational or nonrandomized studies started with a GRADE level of Low because of inherent limitations in study design (e.g., lack of randomization, lack of blinding, loss to follow-up). We did not lower the GRADE level further unless there were more substantial study limitations.

[b] All included studies were retrospective studies at high risk of recall bias and selection bias. There were potential differences in populations across studies at risk of confounding. Study quality was assessed as fair.

[c] Evidence from a single study.

[d] The validity of indirect evidence relies on the transitivity assumption (i.e., the studies making different direct comparisons must be sufficiently similar in all aspects other than the interventions being compared).

[e] Large variances in estimates.

Adapted partially from Nguyen et al.[84]

Table A14: GRADE Evidence Profile for the Comparison of Microwave Ablation and Laser Ablation in Small, Low-Risk Papillary Thyroid Cancer

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Tumour volume reduction							
1 (nonrandomized study)	Serious limitations (−1)[a,b]	Not applicable[c]	No serious limitations	Serious limitations (−1)[d]	Undetected	None	⨁ Very low
Tumour disappearance rate							
1 (nonrandomized study)	Serious limitations (−1)[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁ Very low
Tumour recurrence rate							
1 (nonrandomized study)	Serious limitations (−1)[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁ Very low
Surgical time							
1 (nonrandomized study)	Serious limitations (−1)[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁ Very low
Length of hospital stay							
1 (nonrandomized study)	Serious limitations (−1)[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁ Very low
Recurrent laryngeal nerve palsy or voice change							
1 (nonrandomized study)	Serious limitations (−1)[a,b]	Not applicable[c]	No serious limitations	No serious limitations	Undetected	None	⨁ Very low
Overall complications							
1 (nonrandomized study)	Serious limitations (−1)[a,b]	Not applicable[c]	No serious limitations	Serious limitations (−1)[d]	Undetected	None	⨁ Very low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation.

[a] Observational or nonrandomized studies started with a GRADE level of Low because of inherent limitations in study design (e.g., lack of randomization, lack of blinding, loss to follow-up). We did not lower the GRADE level further unless there were more substantial study limitations.

[b] All included retrospective studies were at high risk of recall bias and selection bias. Study quality was assessed as fair.

[c] Evidence from a single study.

[d] Large variances on estimates.

Adapted partially from Nguyen et al.[84]

Table A15: GRADE Evidence Profile for the Comparison of RFA and Laser Ablation in Small, Low-Risk Papillary Thyroid Cancer

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Tumour recurrence rate							
Indirect evidence	Serious limitations (−1)[a,b,c]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁ Very low
Surgical time							
Indirect evidence	Serious limitations (−1)[a,b,c]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁ Very low
Length of hospital stay							
Indirect evidence	Serious limitations (−1)[a,b,c]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁ Very low
Overall complications							
Indirect evidence	Serious limitations (−1)[a,b,c]	No serious limitations	No serious limitations	Serious limitations (−1)[d]	Undetected	None	⨁ Very low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RFA, radiofrequency ablation.

[a] The validity of indirect evidence relies on the transitivity assumption (i.e., the studies making different direct comparisons must be sufficiently similar in all aspects other than the interventions being compared).

[b] Observational or nonrandomized studies started with a GRADE level of Low because of inherent limitations in study design (e.g., lack of randomization, lack of blinding, loss to follow-up). We did not lower the GRADE level further unless there were more substantial study limitations.

[c] All included retrospective studies were at high risk of recall bias and selection bias. There were potential differences in populations across studies at risk of confounding. Study quality was assessed as fair.

[d] Large variances in estimates.

Adapted partially from Nguyen et al.[84]

Table A16: GRADE Evidence Profile for the Comparison of After and Before RFA in Small, Low-Risk Papillary Thyroid Cancer

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Tumour volume reduction							
15 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁ Very low
Tumour disappearance rate							
16 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁ Very low
Tumour recurrence rate							
19 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁ Very low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RFA, radiofrequency ablation.

[a] Observational or nonrandomized studies started with a GRADE level of Low because of inherent limitations in study design (e.g., lack of randomization, lack of blinding, loss to follow-up). We did not lower the GRADE level further unless there were more substantial study limitations.

[b] Study quality was assessed as fair to high.

[c] Large variances in estimates.

Adapted partially from Nguyen et al.[84]

Table A17: GRADE Evidence Profile for the Comparison of After and Before Microwave Ablation in Small, Low-Risk Papillary Thyroid Cancer

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Tumour volume reduction							
12 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁ Very low
Tumour disappearance rate							
12 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Tumour recurrence rate							
12 (nonrandomized studies)	No serious limitations[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁ Very low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation.

[a] Observational or nonrandomized studies started with a GRADE level of Low because of inherent limitations in study design (e.g., lack of randomization, lack of blinding, loss to follow-up). We did not lower the GRADE level further unless there were more substantial study limitations.

[b] Study quality was assessed as fair to high.

[c] Large variances in estimates.

Adapted partially from Nguyen et al.[84]

Table A18: GRADE Evidence Profile for the Comparison of After and Before Laser Ablation in Small, Low-Risk Papillary Thyroid Cancer

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Tumour volume reduction							
4 (nonrandomized studies)	Serious limitations (−1)[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁ Very low
Tumour disappearance rate							
6 (nonrandomized studies)	Serious limitations (−1)[a,b]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⨁ Very low
Tumour recurrence rate							
7 (nonrandomized studies)	Serious limitations (−1)[a,b]	No serious limitations	No serious limitations	Serious limitations (−1)[c]	Undetected	None	⨁ Very low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation.

[a] Observational or nonrandomized studies started with a GRADE level of Low because of inherent limitations in study design (e.g., lack of randomization, lack of blinding, loss to follow-up). We did not lower the GRADE level further unless there were more substantial study limitations.

[b] All included studies were retrospective studies at high risk of recall bias and selection bias. Study quality was assessed as fair to high.

[c] Large variances in estimates.

Adapted partially from Nguyen et al.[84]

Appendix 4: Selected Excluded Studies – Clinical Evidence

For transparency, we provide a list of full-text studies we reviewed that did not meet the inclusion criteria, along with the primary reason for exclusion.

Table A19: Selected Excluded Systematic Reviews

Citation	Primary reason for exclusion
Chen Z, Zhang W, He W. Ultrasound-guided thermal ablation for papillary thyroid microcarcinoma: a systematic review. Clin Endocrinol. 2023;98(3):297-305.	Included studies with designs that were not of interest
Guan SN, Zhang YX, Fu J, Deng FP, Xu EJ. Factors influencing absorption of benign thyroid nodules after microwave ablation based on AMSTARS meta-analysis. Rev Psiquiatria Clinica. 2023;50(3):13-9.	Included studies with designs that were not of interest
Li T, Lu B, Zhang Y, Sun Y. Meta-analysis of the application effect of different modalities of thermal ablation and surgical treatment in papillary thyroid microcarcinoma. Dis Markers. 2022;9714140.	Retracted
Lim JY, Kuo JH. Thyroid nodule radiofrequency ablation: complications and clinical follow-up. Tech Vasc Interv Radiol. 2022;25(2):100824	Narrative review
Min Y, Wang X, Chen H, Chen J, Xiang K, Yin G. Thermal ablation for papillary thyroid microcarcinoma: how far we have come? Cancer Manag Res. 2020;12:13369-79.	Narrative review
Wang JF, Wu T, Hu KP, Xu W, Zheng BW, Tong G, et al. Complications following radiofrequency ablation of benign thyroid nodules: a systematic review. Chin Med J. 2017;130(11):1361-70.	Included studies with designs that were not of interest
Yao JS, Zhang XH, Li ZG, Xi Y. Assessment of thermal ablation for treating Bethesda IV thyroid nodules: a systematic review and meta-analysis. Thyroid Res. 2025;18(1):2	Not a population of interest

Table A20: Selected Excluded Primary Studies

Citation	Primary reason for exclusion
Lee JY, Na DG, Sim JS, Sung JY, Cho SW, Park DJ, et al. A prospective clinical trial of radiofrequency ablation in patients with low-risk unifocal papillary thyroid microcarcinoma favoring active surveillance over surgery. Thyroid. 2024;34:1126-36.	Not a randomized controlled trial
Lou Q, Zhu YF, Ye ML. Treatment of cystic-solid thyroid nodules with ultrasound-guided radiofrequency ablation and enhancement of thyroid function. J Multidiscip Healthc. 2023;16:2773-9.	Not a comparator of interest
Zhang Y, Zhao Y, Han X, Chu X, Chen G, Liu C, et al. Microwave ablation versus radiofrequency ablation for benign non-functioning thyroid nodules: six-month results of a randomized controlled trial. Thyroid. 2022;32:A131-2.	Abstract

Appendix 5: Characteristics of Included Studies – Clinical Evidence

Table A21: Characteristics of Studies Included in the Selected Systematic Reviews

Author, year, country	Study design	Intervention	Comparator	No. patients (M/F); age, mean ± SD	Baseline nodule characteristics, mean ± SD	Follow-up duration	Notes
Studies included in the systematic review by Nicolopoulos et al (Austria Institute of Health Technology Assessment)[85] on symptomatic benign thyroid nodules							
Jin et al, 2021,[117] China	RCT	RFA or MWA	Thyroidectomy	MWA or RFA: 225; 43 ± 5 y Thyroidectomy: 225; 43 ± 5 y	Maximum diameter, cm RFA or MWA: 2.72 ± 0.82 Thyroidectomy: 3.21 ± 0.61	15 mo Loss to follow-up RFA or MWA: 11% Thyroidectomy: 12%	Separate data on MWA (n = 89) and RFA (n = 112) for volume reduction rate only
Yan et al, 2018,[118] China	RCT	MWA	Thyroidectomy	MWA: 57 (M 8/F 49); 45.8 ± 10.2 y Thyroidectomy: 51 (M 11/F 40); 46.2 ± 11.5 y	Diameter, cm MWA: 2.55 ± 1.13 Thyroidectomy: 2.34 ± 1.05	48 h Loss to follow-up NR	–
Zhi et al, 2018,[119] China	RCT	MWA	Thyroidectomy	MWA: 28 (M 20/F 8); 53.61 ± 8.76 y Thyroidectomy: 24 (M 14/F 10); 52.05 ± 11.95 y	Maximum diameter, cm MWA: 3.76 ± 1.06 Thyroidectomy: 4.36 ± 0.84 Volume, mL MWA: 17.11 ± 14.41 Thyroidectomy: 20.79 ± 14.00	12 mo Loss to follow-up MWA: 7% Thyroidectomy: 20%	–
Jin et al, 2018,[121] China	Retrospective, propensity-score matching, double-blinded	MWA	Thyroidectomy	*Before propensity matching* MWA: 156 (M 58/F 98); 36.7 ± 10.3 y Thyroidectomy: 124 (M 40/F 84); 45.4 ± 11.2 y *After propensity matching* MWA: 106 (M 31/F 75); 39.6 ± 11.2 y Thyroidectomy: 106 (M 28/F 78): 45.4 ± 11.2 y	Median (IQR) *Before propensity matching* Diameter, cm MWA: 28.2 (24.1–35.6) Thyroidectomy: 26.3 (23.2–32.1) Volume, mL MWA: 5.7 (3.8–10.3) Thyroidectomy: 4.6 (3.4–8.5) *After propensity matching* Diameter, cm MWA: 28.6 (24.1–35.3) Thyroidectomy: 28.2 (23.0–35.9) Volume, mL MWA: 5.7 (3.8–10.3) Thyroidectomy: 5.5 (3.5–9.6)	MWA: 12.8 mo Thyroidectomy: 12.6 mo Loss to follow-up NR	–

Author, year, country	Study design	Intervention	Comparator	No. patients (M/F); age, mean ± SD	Baseline nodule characteristics, mean ± SD	Follow-up duration	Notes
Lang et al, 2019,[23] China	Retrospective, propensity-score matching	HIFU	Lobectomy	*Before propensity matching* HIFU: 97 (M 12/F 85); 48 ± 12 y Lobectomy: 88 (M 25/F 63); 54 ± 15.17 y *After propensity matching* HIFU: 77 (M 12/F 65); 49 ± 13 y Lobectomy: 77 (M 17/F 60); 51 ± 14 y	*Before propensity matching* Dominant size, cm HIFU: 3.5 ± 1.1 Lobectomy: 3.9 ± 1.5 Dominant volume, mL HIFU: 25.2 ± 14.0 Lobectomy: 26.67 ± 13.9 *After propensity matching* Dominant size, cm HIFU: 4.0 ± 1.0 Lobectomy: 4.0 ± 1.0 Dominant volume, mL HIFU: 24.8 ± 14.5 Lobectomy: 24.0 ± 17.2	6 mo Loss to follow-up NR	–
Yan et al, 2023,[122] China	Retrospective, propensity-score matching	RFA	Thyroidectomy	Median age (IQR) *Before propensity matching* RFA: 49 (M 9/F 40); 65 (5.5) y Thyroidectomy: 181 (M 59/ F 122); 64 (6.0) y *After propensity matching* RFA: 49 (M 9/F 40); 65 (5.5) y Thyroidectomy: 49 (M 9/F 40); 64 (5.0) y	Median (IQR) *Before propensity matching* Largest diameter, cm RFA: 3.2 (1.5) Thyroidectomy: 4.1 (1.6) Volume, mL RFA: 7.4 (10.1) Thyroidectomy: 18.6 (22.0) *After propensity matching* Largest diameter, cm RFA: 3.2 (1.5) Thyroidectomy: 3.1 (1.2) Volume, mL RFA: 7.4 (10.1) Thyroidectomy: 7.1 (13.6)	Median (IQR) RFA: 27.3 (36.3) mo Thyroidectomy: 35.7 (25.9) mo Loss to follow-up NR	Elderly populations
Yue et al, 2016,[123] China	Retrospective, propensity-score matching	RFA	Thyroidectomy	*Before propensity matching* RFA: 137 (M 38/F 99); 48.3 ± 12.9 y Thyroidectomy: 267 (M 129/ F 138); 52.4 ± 12.7 y *After propensity matching* RFA: 108 (M 36/F 72); 50.8 ± 11.9 y Thyroidectomy: 108 (M 39/F 69); 49.8 ± 13.6 y	Median (IQR) *Before propensity matching* Volume, mL RFA: 5.7 (3.9–9.1) Thyroidectomy: 5.2 (1.4–11.2) *After propensity matching* Volume, mL RFA: 5.6 (3.9–8.7) Thyroidectomy: 5.3 (2.2–10.4)	6 mo Loss to follow-up NR	–

Author, year, country	Study design	Intervention	Comparator	No. patients (M/F); age, mean ± SD	Baseline nodule characteristics, mean ± SD	Follow-up duration	Notes
Studies included in the systematic review by Leon-Salas et al[77] on cystic thyroid nodules							
Baek et al, 2015,[125] Korea	RCT	EA	RFA	EA: 24 (M 6/F 18); 47.6 y RFA: 22 (M 3/F 19); 50.8 y	Diameter, cm EA: 3.6 ± 1.0 RFA: 3.0 ± 1.0 Volume, mL EA: 14.7 ± 13.7 RFA: 8.6 ± 9.4	6 mo Loss to follow-up RFA: 3 PEI: 1	Predominantly cystic thyroid nodules (50%–90% cystic portion)
Sung et al, 2013,[126] Korea	RCT	EA	RFA	EA: 25 (M 2/F 23); 45.0 ± 10.9 y RFA: 25 (M 3/F 22); 44.9 ± 10.6 y	Diameter, cm EA: 3.4 ± 1.0 (range 1.7–5.7) RFA: 3.0 ± 1.2 (range 1.8–6.2) Volume, mL EA: 12.2 ± 11.0 (range 1.9–39.0) RFA: 9.3 ± 11.7 (range 1.8–54.0)	6 mo	Predominantly cystic thyroid nodules (> 90% cystic portion)
Studies included in the systematic review by Javid et al[70] on AFTNs							
Bernardi et al, 2017,[129] Italy	Prospective noncomparative	RFA	–	30 (M 10/F 20); 69.1 ± 2.0 y	NR	12 mo	Single RFA session
Cesareo et al, 2018,[132] Italy	Prospective noncomparative	RFA	–	29 (M 18/F 11); 51.41 ± 15.5 y	NR	24 mo	Single RFA session
Dobnig and Amrein, 2018,[134] Austria	Prospective noncomparative	RFA	–	32; NR	NR	12 mo	Single RFA session
Vu et al, 2022,[136] Vietnam	Prospective noncomparative	RFA	–	17 (M 2/F 15); 46.47 ± 13.11 y	NR	24 mo	Single RFA session
Baek et al, 2009,[127] Korea	Retrospective noncomparative	RFA	–	9 (M 1/F 8); 47 ± 17 y	NR	11.0 ± 4.2 mo	Multiple RFA sessions
Bernardi et al, 2018,[128] Italy	Retrospective noncomparative	RFA	–	32; NR	NR	NR	Single RFA session
Cappelli et al, 2020,[130] Italy	Retrospective noncomparative	RFA	–	17 (M 6/F 11); 45.3 ± 18.0 y	NR	12 mo	Single RFA session
Cervelli et al, 2019,[131] Italy	Retrospective noncomparative	RFA	–	22 (M 2/F 20); 51.9 ± 13.9 y	NR	12 mo	Single RFA session
Deandrea et al, 2008,[133] Italy	Retrospective noncomparative	RFA	–	22; NR	NR	6 mo	Single RFA session
Sung et al, 2015,[135] Korea	Retrospective noncomparative	RFA	–	44 (M 2/F 42); 43 ± 14.7 y	NR	19.9 ± 12.6 mo	Multiple RFA sessions

Author, year, country	Study design	Intervention	Comparator	No. patients (M/F); age, mean ± SD	Baseline nodule characteristics, mean ± SD	Follow-up duration	Notes
Studies included in the systematic review by Nguyen et al[84] on papillary thyroid cancer							
Guo et al, 2024,[137] China	Prospective comparative	MWA	Surgery	MWA: 52 (M 9/F 43); NR Surgery: 71 (M 13/F 58); NR	Size, mm MWA: 12.9 ± 2.2 Surgery: 13.6 ± 5.6 Volume, mm^3 MWA: 660 ± 440 Surgery: 820 ± 560	12 mo	PTC
Zheng et al, 2023,[138] China	Prospective comparative	MWA	Surgery	MWA: 92 (M 16/F 76); NR Surgery: 106 (M 23/F 83); NR	Size, mm MWA: 8.1 ± 3.0 Surgery: 8.9 ± 3.3 Volume, mm^3 MWA: 230 ± 330 Surgery: 320 ± 370	13 mo	PTC, PTMC
Cao et al, 2021,[139] China	Retrospective comparative	RFA	MWA	RFA: 49 (M 7/F 42); 46.0 ± 14.0 y MWA: 123 (M 31/F 92); 46.0 ± 12.0 y	Size, mm RFA: 13.2 ± 2.8 MWA: 13.5 ± 2.8 Volume, mm^3 NR	25 mo	PTC
Cao et al, 2021,[140] China	Retrospective comparative	RFA	MWA	RFA: 183; NR MWA: 542; NR	Size, mm NR Volume, mm^3 NR	21 mo	PTMC
He et al, 2021,[141] China	Retrospective comparative	RFA	Surgery	RFA: 94 (M 23/F 71); 43.9 y Surgery: 110 (M 17/F 93); 43.8 y	Size, mm NR Volume, mm^3 RFA: 795 ± 480.2 Surgery: NR	NR	PTC
Li et al, 2018,[142] China	Retrospective comparative	MWA	Surgery	MWA: 46 (M 14/F 32); 43.6 ± 9.3 y Surgery: 46 (M 13/F 33); 49.6 ± 9.0 y	Size, mm MWA: 4.5 ± 1.6 Surgery: 4.3 ± 1.4 Volume, mm^3 MWA: 56.6 ± 48.8 Surgery: NR	42 mo	PTMC
Li et al, 2019,[143] China	Retrospective comparative	MWA	Surgery	MWA: 168 (M 36/F 132); 47.3 ± 10.7 y Surgery: 143 (M 29/F 114); 49.2 ± 11.4 y	Size, mm NR Volume, mm^3 MWA: 81.6 ± 10.0 Surgery: NR	12 mo	PTMC

Author, year, country	Study design	Intervention	Comparator	No. patients (M/F); age, mean ± SD	Baseline nodule characteristics, mean ± SD	Follow-up duration	Notes
Li et al, 2024,[144] China	Retrospective comparative	RFA	MWA	RFA: 346 (M 63/F 283); 37.3 ± 9.8 y MWA: 166 (M 38/F 128); 38.3 ± 9.9 y	Size, mm RFA: 1.3 ± 2.0 MWA: 1.0 ± 1.1 Volume, mm^3 NR	22 mo	PTMC
Song et al, 2021,[145] China	Retrospective comparative	RFA	Surgery	RFA: 115 (M 18/F 97); 44.9 ± 10.4 y Surgery: 103 (M 19/F 84); 45.4 ± 9.9 y	Size, mm RFA: 6.5 ± 1.9 Surgery: 6.9 ± 1.6 Volume, mm^3 RFA: 181.6 ± 156.5 Surgery: 198.2 ± 118.8	RFA: 26 mo Surgery: 29 mo	PTMC
Wang et al, 2021,[146] China	Retrospective comparative	MWA	Surgery	MWA: 63 (M 12/F 51); 43.6 ± 14.2 y Surgery: 83 (M 24/F 59); 43.2 ± 10.9 y	Size, mm MWA: 4.5 ± 1.1 Surgery: 4.5 ± 1.1 Volume, mm^3 MWA: 35.1 ± 26.8 Surgery: NR	24 mo	PTMC
Wei et al, 2022,[147] China	Retrospective comparative	MWA	Surgery	MWA: 350 (M 82/F 268); 44.0 ± 12.0 Surgery: 350 (M 83/F 267); 44.0 ± 12.0	Size, mm MWA: 8.0 ± 4.0 Surgery: 8.0 ± 4.0 Volume, mm^3 MWA: 200 ± 300 Surgery: NR	36 mo	PTC, PTMC
Xu et al, 2018,[148] China	Retrospective comparative	MWA	Surgery	MWA: 41 (M 12/F 29); 45.8 ± 10.2 y Surgery: 46 (M 16/F 30); 46.2 ± 11.5 y	Size, mm MWA: 8.9 ± 1.0 Surgery: 8.1 ± 1.2 Volume, mm^3 NR	NR	PTMC
Yan et al, 2021,[202] China	Retrospective comparative	RFA	Surgery	RFA: 332 (M 82/F 250); 44.1 ± 9.5 y Surgery: 332 (M 84/F 248); 43.8 ± 9.5 y	Size, mm RFA: 5.7 ± 2.2 Surgery: 5.5 ± 2.2 Volume, mm^3 RFA: 91.6 ± 107.5 Surgery: 86.4 ± 106.8	RFA: 47 mo Surgery: 51 mo	PTMC
Yan et al, 2023,[203] China	Retrospective comparative	RFA	MWA	RFA: 357 (M 98/F 259); 44.8 ± 10.4 y MWA: 117 (M 25/F 92); 45.8 ± 10.5 y	Size, mm NR Volume, mm^3 NR	77 mo	PTMC

Author, year, country	Study design	Intervention	Comparator	No. patients (M/F); age, mean ± SD	Baseline nodule characteristics, mean ± SD	Follow-up duration	Notes
Yan et al, 2023,[149] China	Retrospective comparative	RFA	Surgery	RFA: 44 (M 10/F 34); 44.3 ± 10.2 y Surgery: 53 (M 18/F 35); 41.6 ± 10.1 y	Size, mm RFA: 5.5 ± 2.3 Surgery: 6.0 ± 2.4 Volume, mm^3 RFA: 83.2 ± 111.3 Surgery: 110.0 ± 150.5	RFA: 74 mo Surgery: 22 mo	PTMC
Zeng et al, 2023,[150] China	Retrospective comparative	RFA	Surgery	RFA: 86 (M 41/F 45); 48.5 ± 7.4 y Surgery: 74 (M 28/F 46); 47.1 ± 6.8 y	Size, mm RFA: 5.4 ± 1.8 Surgery: 5.6 ± 1.8 Volume, mm^3 RFA: 50.5 ± 16.8 Surgery: 54.8 ± 17.2	NR	PTMC
Zhang et al, 2020,[152] China	Retrospective comparative	RFA	Surgery	RFA: 94 (M 24/F 70); 45.4 ± 10.8 y Surgery: 80 (M 20/F 60); 44.1 ± 9.6 y	Size, mm RFA: 6.1 ± 2.5 Surgery: 6.0 ± 1.5 Volume, mm^3 RFA: 175.9 ± 228.3 Surgery: 132.7 ± 94.1	64 mo	PTMC
Zhang et al, 2022,[151] China	Retrospective comparative	RFA	Surgery	RFA: 157 (M 60/F 97); 45.8 ± 9.9 y Surgery: 206 (M 105/F 101); 45.7 ± 10.8 y	Size, mm RFA: 5.3 ± 1.8 Surgery: 5.3 ± 1.8 Volume, mm^3 RFA: 58.3 ± 52.7 Surgery: 61.9 ± 54.1	30 mo	PTMC
Zhou et al, 2019,[153] China	Retrospective comparative	LA	Surgery	LA: 36 (M 14/F 22); 41.5 ± 11.3 y Surgery: 45 (M 17/F 28); 41.6 ± 9.6	Size, mm LA: 4.7 ± 1.4 Surgery: 5.0 ± 1.1 Volume, mm^3 LA: 43.3 ± 38.8 Surgery: 49.3 ± 30.4	LA: 36 mo Surgery: 28 mo	PTMC
Zhou et al, 2020,[154] China	Retrospective comparative	MWA	LA	MWA: 33 (M 7/F 26); 37.9 ± 10.1 y LA: 34 (M 11/F 23); 41.8 ± 13.4 y	Size, mm MWA: 5.0 ± 1.4 LA: 4.5 ± 1.6 Volume, mm^3 MWA: 38.5 ± 43.0 LA: 51.9 ± 40.8	30 mo	PTMC

Author, year, country	Study design	Intervention	Comparator	No. patients (M/F); age, mean ± SD	Baseline nodule characteristics, mean ± SD	Follow-up duration	Notes
Zu et al, 2021,[155] China	Retrospective comparative	MWA	Surgery	MWA: 320 (M 83/F 237); 45.0 ± 10.6 y Surgery: 324 (M 77/F 247); 43.9 ± 11.5 y	Size, mm MWA: 5.0 ± 1.9 Surgery: 5.1 ± 1.9 Volume, mm^3 MWA: 85.1 ± 89.1 Surgery: NR	94 mo	PTMC
Han et al, 2023,[156] China	Prospective noncomparative	MWA	–	1,278 (M 282/F 996); 44.3 ± 10.7 y	Size, mm: 6.1 ± 2.1 Volume, mm^3: 110.0 ± 110.0	36 mo	PTMC
Lim et al, 2022,[157] China	Prospective noncomparative	RFA	–	12 (M 2/F 10); 51.2 ± 11.0 y	Size, mm: 5.3 ± 1.5 Volume, mm^3: 172.5 ± 104.6	12 mo	PTMC
Teng et al, 2018,[158] China	Prospective noncomparative	MWA	–	15 (M 6/F 9); 48.0 ± 8.8 y	Size, mm: 5.8 ± 2.5 Volume, mm^3: 134.3 ± 129.8	42 mo	PTMC
Wang et al, 2014,[159] China	Prospective noncomparative	RFA	–	8 (M 1/F 7); 43.6 ± 9.3 y	Size, mm: 10.0 ± 6.1 Volume, mm^3: 206.0 ± 241.0	12 mo	PTC
Yue et al, 2014,[160] China	Prospective noncomparative	MWA	–	18 (M 6/F 12); 52.1 ± 13.6 y	Size, mm: 7.3 ± 3.0 Volume, mm^3: 89.5 ± 20.1	12 mo	PTMC
Yue et al, 2020,[161] China	Prospective noncomparative	MWA	–	119 (M 27/F 92); 48.7 ± 11.8 y	Size, mm: 6.9 ± 1.9 Volume, mm^3: 130.0 ± 90.0	17 mo	PTMC
Zhang et al, 2016,[162] China	Prospective noncomparative	RFA	–	92 (M 23/F 69); 44.7 ± 10.7 y	Size, mm: 5.5 ± 2.0 Volume, mm^3: 118.8 ± 106.9	9 mo	PTMC
Zheng et al, 2023,[163] China	Prospective noncomparative	MWA	–	461 (M 124/F 337); 43.0 ± 11.0 y	Size, mm: 6.0 ± 2.0 Volume, mm^3: 100.0 ± 100.0	26 mo	PTMC
Cao et al, 2020,[164] China	Retrospective noncomparative	MWA	–	14 (M 3/F 11); 46.9 ± 11.9 y	Size, mm: 11.8 ± 3.2 Volume, mm^3: 271.4 ± 195.9	24 mo	PTC
Cho et al, 2020,[165] Korea	Retrospective noncomparative	RFA	–	74 (M 8/F 66); 46.0 ± 12.0 y	Size, mm: 5.2 ± 1.4 Volume, mm^3: 59.8 ± 47.8	72 mo	PTMC
Ding et al, 2019,[166] China	Retrospective noncomparative	RFA	–	37 (M 8/F 29); 45.1 ± 13.0 y	Size, mm: 7.4 ± 4.1 Volume, mm^3: 120.0 ± 100.0	9 mo	PTMC
Dong et al, 2024,[167] China	Retrospective noncomparative	MWA	–	66 (M 13/F 53); 43.5 ± 8.7 y	Size, mm: 5.1 ± 3.0 Volume, mm^3: 43.8 ± 75.7	60 mo	PTMC
Guang et al, 2017,[168] China	Retrospective noncomparative	RFA	–	33 (M 11/F 22); 43.7 ± 10.7 y	Size, mm: 12.2 ± 5.1 Volume, mm^3: 405.8 ± 440.3	21 mo	PTC
Han et al, 2020,[169] China	Retrospective noncomparative	MWA	–	37 (M 17/F 20); 43.6 ± 13.8 y	Size, mm: 13.2 ± 5.9 Volume, mm^3: NR	11 mo	PTC

Author, year, country	Study design	Intervention	Comparator	No. patients (M/F); age, mean ± SD	Baseline nodule characteristics, mean ± SD	Follow-up duration	Notes
He et al, 2021,[170] China	Retrospective noncomparative	RFA	–	95 (M 24/F 71); 66.6 ± 4.4 y	Size, mm: 6.1 ± 2.0 Volume, mm^3: 107.3 ± 99.1	36 mo	PTMC
Ji et al, 2019,[171] China	Retrospective noncomparative	LA	–	37 (M 12/F 25); 43.9 ± 17.6 y	Size, mm: 5.1 ± 3.4 Volume, mm^3: 52.8 ± 30.6	18 mo	PTMC
Jing et al, 2024,[172] China	Retrospective noncomparative	RFA	–	592 (M 122/F 470); 43.9 ± 10.1 y	Size, mm: NR Volume, mm^3: 107.6 ± 96.0	40 mo	PTMC
Juan et al, 2022,[173] China	Retrospective noncomparative	LA	–	38 (M 12/F 26); 62.0 ± 2.4 y	Size, mm: 5.1 ± 1.0 Volume, mm^3: 40.7 ± 16.5	60 mo	PTMC
Kim et al, 2017,[174] Korea	Retrospective noncomparative	RFA	–	6 (M 2/F 4); 72.0 ± 6.6 y	Size, mm: 9.2 ± 2.8 Volume, mm^3: 215.3 ± 197.9	48 mo	PTMC
Lim et al, 2019,[175] Korea	Retrospective noncomparative	RFA	–	133 (M 19/F 114); 46.0 ± 12.0 y	Size, mm: 4.3 ± 1.4 Volume, mm^3: 30.0 ± 40.0	39 mo	PTMC
Mauri et al, 2016,[176] Italy	Retrospective noncomparative	LA	–	24 (M 11/F 13); 62.3 ± 13.2 y	Size, mm: 10.0 ± 5.0 Volume, mm^3: NR	30 mo	PTC
Offi et al, 2021,[177] Italy	Retrospective noncomparative	LA	–	10 (M 4/F 6); 40.2 ± 17.9 y	Size, mm: NR Volume, mm^3: 182.0 ± 345.0	NR	PTC
Peng et al, 2021,[178] China	Retrospective noncomparative	LA	–	105 (M 31/F 74); 44.1 ± 12.2 y	Size, mm: 6.3 ± 2.6 Volume, mm^3: 99.4 ± 84.0	65 mo	PTMC
Seo et al, 2021,[179] Korea	Retrospective noncomparative	RFA	–	5 (M 0/F 5); 40.4 ± 8.8 y	Size, mm: 5.0 ± 1.2 Volume, mm^3: NR	130 mo	PTMC
Song et al, 2020,[180] China	Retrospective noncomparative	RFA	–	112 (M 18/F 94); 44.9 ± 10.6 y	Size, mm: 6.5 ± 1.9 Volume, mm^3: 181.6	30 mo	PTMC
Teng et al, 2019,[181] China	Retrospective noncomparative	MWA	–	185 (M 40/F 145); 42.2 ± 11.7 y	Size, mm: 5.3 ± 1.9 Volume, mm^3: 100.1 ± 92.9	20 mo	PTMC
Teng et al, 2020,[182] China	Retrospective noncomparative	MWA	–	41 (M 13/F 28); 46.1 ± 8.9 y	Size, mm: 5.6 ± 2.1 Volume, mm^3: 61.3 ± 20.9	60 mo	PTMC
Wang et al, 2024,[183] China	Retrospective noncomparative	RFA	–	50 (M 7/F 43); 52.3 ± 7.3 y	Size, mm: 5.6 ± 1.6 Volume, mm^3: NR	12 mo	PTMC
Wu et al, 2020,[186] China	Retrospective noncomparative	RFA	–	198 (M 57/F 141); 42.5 ± 9.5 y	Size, mm: 6.3 ± 1.8 Volume, mm^3: 99.4 ± 84.0	26 mo	PTMC
Wu et al, 2021,[185] China	Retrospective noncomparative	MWA	–	106 (M 19/F 87); 44.4 ± 11.1 y	Size, mm: 7.7 ± 3.5 Volume, mm^3: 200.0 ± 300.0	42 mo	PTMC
Wu et al, 2022,[184] China	Retrospective noncomparative	MWA	–	69 (M 18/F 51); 45.5 ± 11.8 y	Size, mm: 8.4 ± 3.9 Volume, mm^3: 260.0 ± 350.0	36 mo	PTC

Author, year, country	Study design	Intervention	Comparator	No. patients (M/F); age, mean ± SD	Baseline nodule characteristics, mean ± SD	Follow-up duration	Notes
Yan et al, 2020,[188] China	Retrospective noncomparative	RFA	–	202 (M 50/F 152); 42.8 ± 10.1 y	Size, mm: 5.4 ± 1.6 Volume, mm^3: 102.3 ± 93.8	25 mo	PTMC
Yan et al, 2021,[187] China	Retrospective noncomparative	RFA	–	414 (M 91/F 323); 43.6 ± 9.8 y	Size, mm: 5.2 ± 1.6 Volume, mm^3: 92.7 ± 83.4	42 mo	PTMC
Yan et al, 2022,[189] China	Retrospective noncomparative	RFA	–	487 (M 106/F 381); 43.6 ± 9.7 y	Size, mm: 6.1 ± 1.9 Volume, mm^3: 96.2 ± 83.6	50 mo	PTMC
Zhang et al, 2018,[191] China	Retrospective noncomparative	LA	–	64 (M 23/F 41); 42.5 ± 12.3 y	Size, mm: 4.6 ± 1.5 Volume, mm^3: 41.0 ± 40.4	26 mo	PTMC
Zhang et al, 2019,[192] China	Retrospective noncomparative	RFA	–	30 (M 8/F 22); 44.1 ± 9.0 y	Size, mm: NR Volume, mm^3: 110.0 ± 170.0	18 mo	PTMC
Zhang et al, 2022,[190] China	Retrospective noncomparative	LA	–	72 (M 14/F 58); 39.2 ± 9.3 y	Size, mm: 5.1 ± 1.5 Volume, mm^3: 44.7 ± 13.7	18 mo	PTMC
Zhou et al, 2017,[194] China	Retrospective noncomparative	LA	–	30 (M 13/F 17); NR	Size, mm: 4.8 ± 1.2 Volume, mm^3: 43.7 ± 37.8	11 mo	PTMC
Zhou et al, 2019,[193] China	Retrospective noncomparative	MWA	–	14 (M 3/F 11); 45.1 ± 12.1 y	Size, mm: 10.1 ± 4.7 Volume, mm^3: 291.9 ± 255.6	9 mo	PTC
Zhu et al, 2021,[195] China	Retrospective noncomparative	RFA	–	102 (M 20/F 82); 43.0 ± 19.0 y	Size, mm: 5.0 ± 2.9 Volume, mm^3: 60.0 ± 90.0	60 mo	PTMC

Abbreviations: EA, ethanol ablation; HIFU, high-intensity focused ultrasound; IQR, interquartile range; LA, laser ablation; MWA, microwave ablation; NR, not reported; PTC, papillary thyroid carcinoma; PTMC, papillary thyroid microcarcinoma; RCT, randomized controlled trial; RFA, radiofrequency ablation; SD, standard deviation.
Note: Studies are ordered alphabetically and then by study design.

Table A22: Characteristics of the Identified Randomized Controlled Trial

Author, year, country	Population	Intervention	Comparator	No. patients (M/F); age, mean ± SD	Baseline nodule characteristics, mean ± SD	Follow-up duration	Notes
Chen et al, 2024,[196] China	Patients with predominantly solid benign thyroid nodules	RFA	MWA	RFA: 76 (M 56/F 20); 49.7 ± 13.1 y MWA: 76 (M 58/F 18); 46.4 ± 12.4 y	Diameter, cm RFA: 2.3 ± 0.7 MWA: 2.6 ± 0.8 Volume, mL RFA: 7.9 ± 7.8 MWA: 10.3 ± 9.9	2 y	–

Abbreviations: MWA, microwave ablation; RFA, radiofrequency ablation; SD, standard deviation.

Appendix 6: Ongoing Studies – Clinical Evidence

Table A23: Ongoing Systematic Reviews on Ablative Technologies for Thyroid Nodules or Papillary Thyroid Cancer[a]

PROSPERO registry	Title	Expected end date
CRD42024590653	Comparison of safety and efficacy of thyroid radiofrequency ablation and endoscopic thyroidectomy in the treatment of papillary thyroid microcarcinoma: a systematic review and meta-analysis	January 2025
CRD42024626727	Effect of thermal ablation and surgery on various outcomes in patients with thyroid cancer: an umbrella review of systematic reviews and meta-analyses of comparative studies	February 2025
CRD42025639370	Radiofrequency ablation compared to surgery as management option for papillary thyroid microcarcinoma: a systematic review, meta-analysis, and meta-regression	February 2025
CRD420250651356	Thermal ablation for papillary thyroid carcinoma in the isthmus: a systematic review and meta-analysis	March 2025
CRD42024629049	Ultrasound-guided thermal ablation versus surgery for low-risk papillary thyroid carcinoma: a systematic review and meta-analysis	April 2025
CRD420250652099	Radiofrequency ablation compared to conventional thyroidectomy in benign thyroid nodules: a meta-analysis and systematic review	June 2025
CRD42024617047	Efficacy and safety of thermal ablation for the treatment of papillary thyroid carcinoma with capsular invasion: a systematic review and meta-analysis	July 2025

[a] Included only systematic reviews with an expected end date in 2025 and beyond.

Table A24: Ongoing Clinical Studies on Ablative Technologies for Thyroid Nodules or Papillary Thyroid Cancer[a]

Clinicaltrial.gov ID	Title	Comparator	Enrollment	Study design	Expected completion
NCT04233398	High-intensity focused ultrasound treatment of benign thyroid nodules	Active surveillance	240	Randomized controlled trial	November 2024
NCT05189314	Radiofrequency ablation of benign thyroid nodules: clinical outcomes and quality of life study	Thyroidectomy	100	Prospective cohort	August 2026
NCT06316895	The clinical outcomes and prediction of thermal ablation for low-risk papillary thyroid carcinoma	Thyroid lobectomy	3,772	Prospective cohort	December 2029
NCT06426563	Microwave ablation vs. radiofrequency ablation for the treatment of moderate-sized benign thyroid nodules	Radiofrequency ablation	150	Randomized controlled trial	June 2028
NCT06607133	Thermal ablation vs. thyroidectomy for large benign thyroid nodules	Thyroidectomy	300	Prospective cohort	December 2027
NCT06725576	Ultrasound-guided microwave ablation vs. surgery for low-risk papillary thyroid carcinoma	Thyroidectomy	201	Prospective cohort	March 2025

[a] Included only comparative studies with a separate control group.

Appendix 7: Results of Applicability and Limitation Checklists for Studies Included in the Economic Literature Review

Table A25: Assessment of the Applicability of Studies Evaluating the Cost-Effectiveness of Ablative Technologies Versus Standard Care for Treatment of Adults With Symptomatic Benign Thyroid Nodules, Cystic Thyroid Nodules, AFTNs, or Small, Low-Risk Papillary Thyroid Cancer

Author, year, country	Is the study population appropriate for the review question?	Are the interventions appropriate for the review question?	Is the system in which the study was conducted sufficiently like the current Ontario context?	Is the perspective of the costs appropriate for the review question (e.g., Canadian public payer)?	Is the perspective of the outcomes appropriate for the review question?	Are all future costs and outcomes discounted appropriately (as per current CDA guidelines)?	Are QALYs derived using CDA's preferred methods, or is an appropriate social care–related equivalent used as an outcome? (If not, describe rationale and outcomes used in line with the analytical perspective taken)	Overall judgment[a]
Carlisle et al, 2025,[209] United States	Yes	Partially (RAI included as comparator, but not standard care in Canada)	Partially	Partially (perspective not explicitly reported)	Partially (perspective not explicitly reported)	Partially (all costs and outcomes discounted at 3%)	Partially (some health-related utility measures were derived from expert judgment or unclear source)	Partially applicable
Carlisle et al, 2024,[210] United States	Yes	Partially (surgery not included as a relevant comparator)	Partially	Yes	Yes	Partially (all costs and outcomes discounted at 3%)	No (study outcomes did not include QALYs)	Partially applicable
Kuo et al, 2023[211] United States	Yes	Yes	Partially	Yes	Yes	Partially (all costs and outcomes discounted at 3%)	Yes	Partially applicable
Yue et al, 2016,[123] China	Yes	Yes	No	Yes	Yes	NA	Yes	Partially applicable

Note: Response options for all items were "yes," "partially," "no," "unclear," and "NA" (not applicable).

Abbreviations: AFTN, autonomously functioning thyroid nodule; CDA, Canada's Drug Agency; NA, not applicable; QALY, quality-adjusted life-year; RAI, radioactive iodine.

[a] Overall judgment may be "directly applicable," "partially applicable," or "not applicable."

Table A26: Assessment of the Limitations of Studies Evaluating the Cost-Effectiveness of Ablative Technologies Versus Standard Care for Treatment of Adults With Symptomatic Benign Thyroid Nodules, Cystic Thyroid Nodules, AFTNs, or Small, Low-Risk Papillary Thyroid Cancer

Author, year, country	Does the model structure adequately reflect the nature of the health condition under evaluation?	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Are all important and relevant health outcomes included?	Are the clinical inputs[a] obtained from the best available sources?	Do the clinical inputs[a] match the estimates contained in the clinical sources?	Are all important and relevant (direct) costs included in the analysis?	Are the estimates of resource use obtained from the best available sources?	Are the unit costs of resources obtained from the best available sources?	Is an appropriate incremental analysis presented, or can it be calculated from the reported data?	Are all important and uncertain parameters subjected to appropriate sensitivity analysis?	Is there a potential conflict of interest?	Overall judgment[b]
Carlisle et al, 2025,[209] United States	Partially (model structure may not reflect AFTN management pathway in Canada)	No (time horizon was 2 years)	Partially (nodule volume reduction was not included as a health outcome)	Yes	Yes	Yes	Partially (cost of partial thyroidectomy appeared to be based on Medicare reimbursement rate for total thyroidectomy)	Partially	Yes	Yes	No	Potentially serious limitations
Carlisle et al, 2024,[210] United States	Yes	No (cancer progression for PTMC is typically very slow; as such, a lifetime time horizon may be needed to capture all important differences in costs and outcomes)	Yes	Yes	Yes	Partially (authors stated that a societal perspective was used; however, only direct costs were included in the analysis)	Yes	Yes	Partially (for incremental effectiveness, only NNT was reported; the mean incidence rate of cancer progression per strategy was not explicitly reported)	Yes	No	Minor limitations

Author, year, country	Does the model structure adequately reflect the nature of the health condition under evaluation?	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Are all important and relevant health outcomes included?	Are the clinical inputs[a] obtained from the best available sources?	Do the clinical inputs[a] match the estimates contained in the clinical sources?	Are all important and relevant (direct) costs included in the analysis?	Are the estimates of resource use obtained from the best available sources?	Are the unit costs of resources obtained from the best available sources?	Is an appropriate incremental analysis presented, or can it be calculated from the reported data?	Are all important and uncertain parameters subjected to appropriate sensitivity analysis?	Is there a potential conflict of interest?	Overall judgment[b]
Kuo et al, 2023,[211] United States	Yes	Yes	Yes	Yes	Yes	Unclear (it was unclear whether the costs of complications or postsurgical follow-up were accounted for)	Yes	Unclear (no source was provided for the cost of RFA)	Yes	Yes	No	Minor limitations
Yue et al, 2016,[123] China	NA (study was an economic evaluation conducted alongside a retrospective cohort study)	No (time horizon was 6 months)	Partially (nodule volume reduction was not included as a health outcome)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Potentially serious limitations

Note: Response options for all items were "yes," "partially," "no," "unclear," and "NA" (not applicable).

Abbreviations: AFTN, autonomously functioning thyroid nodule; NA, not applicable; NNT, number needed to treat; PTMC, papillary thyroid microcarcinoma; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] Clinical inputs include relative treatment effects, natural history, and utilities.

[b] Overall judgment may be "minor limitations," "potentially serious limitations," or "very serious limitations."

Appendix 8: Supplementary Tables

Table A27: Crude Estimate of the Prevalence of Symptomatic Cystic Thyroid Nodules

Parameter	Mean (95% CI)	Reference
Prevalence of thyroid nodules in general population	24.83 (21.44–28.55)	Mu et al, 2022[213]
Proportion of thyroid nodules that are cystic in tumour composition	0.067 (0.03–0.12)	Mu et al, 2022[213]
Proportion of thyroid nodules that cause compressive symptoms	0.05 (NA)[a]	Durante et al, 2018[7]
Crude prevalence of cystic thyroid nodules that cause compressive symptoms	0.0008	Calculated

Abbreviations: CI, confidence interval; NA, not applicable.

[a] Commonly accepted estimate.

Table A28 was created by digitizing the Kaplan–Meier curve on the 10-year cumulative incidence of nodule regrowth among ablated thyroid nodules from Park et al,[236] using the online platform Automeris.io. We created a dataset based on the digitized points, from which we estimated the annual probability of patients with regrown ablated nodules at each yearly interval.

Table A28: Annual Probability of Nodule Regrowth Among Ablated Thyroid Nodules Created From Digitized Points

Year	Cumulative incidence of nodule regrowth	Annual probability of nodule regrowth (given no regrowth in previous year)[a]	1 – Cumulative incidence of nodule regrowth up to year$_i$
1	0.0025	0.003	0.9975
2	0.046	0.044	0.954
3	0.08	0.036	0.92
4	0.11	0.033	0.89
5	0.12	0.011	0.88
6	0.14	0.023	0.86
7	0.15	0.012	0.85
8	0.17	0.024	0.83
9	0.19	0.024	0.81
10	0.21	0.025	0.79

[a] Calculated using the formula $P(event\ in\ year\ i | no\ event\ to\ year\ i-1) = \frac{R_{i-1}-R_i}{R_{i-1}}$, where $R_i = 1 - Cumulative\ incidence_i$ is the probability of nodule regrowth at year i.

Table A29 was created by digitizing the Kaplan–Meier curve on the 10-year cumulative incidence of tumour progression in small, low-risk papillary thyroid cancer under active surveillance from Ito et al,[248] using the online platform Automeris.io. We created a dataset based on the digitized points, from which we estimated the annual probability of tumour progression at each yearly interval.

Table A29: Annual Probability of Tumour Progression in Small, Low-Risk Papillary Thyroid Cancer Under Active Surveillance Created From Digitized Points

Year	Cumulative incidence of tumour progression	Annual probability of tumour progression (given no progression in previous year)[a]	1 – Cumulative incidence of tumour progression up to year$_i$
1	0.000	0.000	1
2	0.000	0.000	1.0000
3	0.021	0.021	0.9794
4	0.036	0.016	0.9637
5	0.039	0.003	0.9608
6	0.039	0.000	0.9608
7	0.039	0.000	0.9608
8	0.044	0.005	0.9559
9	0.054	0.010	0.9461
10	0.068	0.015	0.9324

[a] Calculated using the formula $P(event\ in\ year\ i | no\ event\ to\ year\ i-1) = \frac{T_{i-1}-T_i}{T_{i-1}}$, where $T_i = 1 - Cumulative\ incidence_i$ is the probability of tumour progression at year i.

Table A30: Detailed Breakdown of Postprocedure Costs Used in the Economic Models

Variable	Unit cost, $	Distribution (parameter 1, parameter 2)[a]	Duration or quantity	Total cost, $	Reference
Partial thyroidectomy					
Follow-up in year 1, symptomatic benign thyroid nodules and AFTNs	$61.11	NA	Per year	$61.11	Calculated
Physician visit (code: A244)	$27.00	Fixed	2	$54.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Follow-up in year 1,[b] small, low-risk PTC	$143.89	NA	Per year	$143.89	Calculated
Physician visit (code: A244)	$27.00	Fixed	2	$54.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroglobulin test (code: L609)	$11.78	Fixed	1	$11.78	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	1	$71.00	SoB for Physician Services[257]
Follow-up in year 2,[b] small, low-risk PTC	$45.89	NA	Per year	$45.89	Calculated
Physician visit (code: A244)	$27.00	Fixed	1	$27.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroglobulin test (code: L609)	$11.78	Fixed	1	$11.78	SoB for Laboratory Services[258]
Follow-up in years 3–5,[b] small, low-risk PTC	$57.78	NA	Per year	$57.78	Calculated
Physician visit (code: A244)	$27.00	Fixed	1	$27.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	0.33	$23.67	SoB for Physician Services[257]
Follow-up in all remaining years,[b] small, low-risk PTC	$48.31	NA	Per year	$48.31	Calculated
Physician visit (code: A244)	$27.00	Fixed	1	$27.00	SoB for Physician Services[257]

Variable	Unit cost, $	Distribution (parameter 1, parameter 2)[a]	Duration or quantity	Total cost, $	Reference
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	0.2	$14.20	SoB for Physician Services[257]
Total and completion thyroidectomy					
Follow-up in year 1[c]	$108.39	NA	Per year	$108.39	Calculated
Physician visit (code: A244)	$27.00	Fixed	2	$54.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroglobulin test (code: L609)	$11.78	Fixed	1	$11.78	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	0.5	$35.50	SoB for Physician Services[257]
Follow-up in year 2[c]	$81.39	NA	Per year	$81.39	Calculated
Physician visit (code: A244)	$27.00	Fixed	1	$27.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroglobulin test (code: L609)	$11.78	Fixed	1	$11.78	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	0.5	$35.50	SoB for Physician Services[257]
Follow-up in years 3–5[c]	$69.56	NA	Per year	$69.56	Calculated
Physician visit (code: A244)	$27.00	Fixed	1	$27.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroglobulin test (code: L609)	$11.78	Fixed	1	$11.78	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	0.33	$23.67	SoB for Physician Services[257]
Follow-up in all remaining years[c]	$45.89	NA	Per year	$45.89	Calculated
Physician visit (code: A244)	$27.00	Fixed	1	$27.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroglobulin test (code: L609)	$11.78	Fixed	1	$11.78	SoB for Laboratory Services[258]
RFA					
Follow-up in year 1, symptomatic benign thyroid nodules	$399.11	NA	Per year	$399.11	Calculated
Physician visit (code: A244)	$27.00	Fixed	4	$108.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	4	$284.00	SoB for Physician Services[257]
Follow-up in years 2–5, symptomatic benign thyroid nodules	$105.11	NA	Per year	$105.11	Calculated
Physician visit (code: A244)	$27.00	Fixed	1	$27.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	1	$71.00	SoB for Physician Services[257]
Follow-up in year 1, AFTNs	$413.33	NA	Per year	$413.33	Calculated
Physician visit (code: A244)	$27.00	Fixed	4	$108.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	3	$21.33	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	4	$284.00	SoB for Physician Services[257]
Follow-up in years 2–5, AFTNs	$119.33	NA	Per year	$119.33	Calculated
Physician visit (code: A244)	$27.00	Fixed	1	$27.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	3	$21.33	SoB for Laboratory Services[258]

Variable	Unit cost, $	Distribution (parameter 1, parameter 2)[a]	Duration or quantity	Total cost, $	Reference
Thyroid ultrasound (code: J105)	$71.00	Fixed	1	$71.00	SoB for Physician Services[257]
Follow-up in year 1, small, low-risk PTC	$410.89	NA	Per year	$410.89	Calculated
Physician visit (code: A244)	$27.00	Fixed	4	$108.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroglobulin test (code: L609)	$11.78	Fixed	1	$11.78	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	4	$284.00	SoB for Physician Services[257]
Follow-up in all remaining years, small, low-risk PTC	$116.89	NA	Per year	$116.89	Calculated
Physician visit (code: A244)	$27.00	Fixed	1	$27.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroglobulin test (code: L609)	$11.78	Fixed	1	$11.78	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	1	$71.00	SoB for Physician Services[257]
Active surveillance					
Active surveillance in years 1 and 2	$233.78	NA	Per year	$233.78	Calculated
Physician visit (code: A244)	$27.00	Fixed	2	$54.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	2	$14.22	SoB for Laboratory Services[258]
Thyroglobulin test (code: L609)	$11.78	Fixed	2	$23.56	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	2	$142.00	SoB for Physician Services[257]
Active surveillance in all remaining years	$116.89	NA	Per year	$116.89	Calculated
Physician visit (code: A244)	$27.00	Fixed	1	$27.00	SoB for Physician Services[257]
Thyroid function tests (codes: L341, L607)	$7.11	Fixed	1	$7.11	SoB for Laboratory Services[258]
Thyroglobulin test (code: L609)	$11.78	Fixed	1	$11.78	SoB for Laboratory Services[258]
Thyroid ultrasound (code: J105)	$71.00	Fixed	1	$71.00	SoB for Physician Services[257]

Abbreviations: CT, completion thyroidectomy; DAD, Discharge Abstract Database; FNA, fine-needle aspiration; NACRS, National Ambulatory Care Reporting System; ODB, Ontario Drug Benefit; ONA, Ontario Nurses' Association; PT, partial thyroidectomy; RFA, radiofrequency ablation; SoB, Schedule of Benefits; TT, total thyroidectomy.

[a] For beta distribution, parameter 1 = alpha, parameter 2 = beta; for gamma distribution, parameter 1 = alpha, parameter 2 = lambda.

[b] The follow-up strategy after partial thyroidectomy for adults with papillary thyroid cancer consists of 2 physician visits, bloodwork testing for thyroid function and thyroglobulin measurements, and thyroid ultrasound in year 1; 1 physician visit and bloodwork testing for thyroid function and thyroglobulin measurements in year 2; 1 annual physician visit, annual bloodwork testing for thyroid function, and 1 ultrasound over years 3 to 5; and 1 annual physician visit, annual bloodwork for thyroid function, and 1 ultrasound every 5 years for the rest of a person's life.[265]

[c] The follow-up strategy after total or completion thyroidectomy for adults with papillary thyroid cancer consists of 2 physician visits, bloodwork testing for thyroid function, and thyroglobulin measurements in year 1; 1 physician visit, bloodwork testing for thyroid function and thyroglobulin measurements, and 1 thyroid ultrasound in year 1; 1 annual physician visit, bloodwork testing for thyroid function and thyroglobulin measurements, and 1 thyroid ultrasound over years 3 to 5; and 1 annual physician visit and annual bloodwork testing for thyroid function and thyroglobulin measurements for the rest of a person's life.[265]

Table A31: Reference Case Analysis Results for Small, Low-Risk Papillary Thyroid Cancer (Expanded Table)

Strategy[a]	Average total costs (95% CrI), $	Average total effects (95% CrI), QALYs	Incremental costs, $	Incremental QALYs	ICER, $/QALY	
			Versus active surveillance		Versus active surveillance	Sequential ICER
Active surveillance	3,884 (3,854 to 3,915)	23.84 (23.32 to 24.32)	–	–	–	–
RFA	6,465 (6,295 to 6,807)	25.48 (19.81 to 28.73)	2,581 (2,408–2,920)	1.64 (–4.07 to 4.94)	1,574	1,574
Partial thyroidectomy	9,267 (8,645 to 9,922)	24.64 (18.75 to 28.22)	5,383 (4,790–6,005)	0.80 (–4.88 to 4.25)	6,729	Dominated[b] by RFA

Abbreviations: CrI, credible interval; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; RFA, radiofrequency ablation.

[a] Treatment strategies are ordered by average total costs, from lowest to highest.

[b] Dominated by RFA indicates that RFA is less costly and more effective than partial thyroidectomy.

Appendix 9: Methods for Obtaining Average Hospital Costs and Annual Volume of Thyroidectomies for Thyroid Nodules in Ontario

For adults with symptomatic benign thyroid nodules (including autonomously functioning thyroid nodules [AFTNs]), we estimated the following:

- The average inpatient and outpatient hospital costs of partial thyroidectomy
- The average surgical volume of inpatient and outpatient partial thyroidectomies from the Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD) and National Ambulatory Care Reporting System (NACRS), respectively, via the IntelliHealth Ontario repository

We used the relevant Canadian Classification of Health Interventions (CCI) code (1FU87^^) to generate separate datasets and capture all partial thyroidectomies performed in Ontario as inpatient and outpatient procedures from 2022 to 2024 for benign thyroid nodules. We then filtered them by age at discharge (18 years and older), and by International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada (ICD-10-CA) disease code for benign thyroid nodules (D34, benign neoplasm of the thyroid gland), which also captured AFTNs. Our outcome measures included resource intensity weights (RIWs) and total surgical volumes per year.

To estimate average hospital care costs, we used the case-mix group costing approach[299] by multiplying the average RIWs obtained from both datasets by the cost of a standard hospital stay in Ontario in fiscal year 2022/23 ($6,960), adjusted for inflation.

To estimate the ratio of outpatient to inpatient partial thyroidectomies in Ontario, we obtained the average annual surgical volumes of partial thyroidectomies in the generated datasets from the DAD and NACRS, respectively. Overall, we estimated that the average volume of partial thyroidectomies for symptomatic benign thyroid nodules and AFTNs was approximately 860 per year, of which 46% were performed as outpatient procedures.

To estimate the annual volume of partial thyroidectomies in Ontario performed for benign thyroid nodules, we averaged the yearly sum of partial thyroidectomies in the generated datasets from the DAD and NACRS from 2022 to 2024.

For adults with small, low-risk papillary thyroid cancer, we estimated the average inpatient hospital costs of total and completion thyroidectomies from the CIHI DAD via the IntelliHealth Ontario repository. We used the relevant CCI code (1FU89^^) to generate a dataset to capture all total and completion thyroidectomies performed in Ontario 2022 to 2024. We then filtered them by age at discharge (18 years and older), and by ICD-10-CA disease code for thyroid cancer (C73, malignant neoplasm of thyroid gland). Our outcome measures included RIWs.

Appendix 10: Letter of Information

Ontario Health is conducting a health technology assessment (HTA) of **Ablative Technologies for the Treatment of Thyroid Nodules.** The purpose is to better understand how this technique can be publicly funded in Ontario.

An important part of this review involves gathering perspectives of patients who have been diagnosed with thyroid nodules and who have/may have experience with ablative technologies.

What Do You Need From Me

- Willingness to share your story
- 30-40 minutes of your time for a phone interview
- Permission to audio- (not video-) record the interview

What Your Participation Involves

If you agree to share your experiences, you will be asked to have an interview with Ontario Health staff. Ontario Health staff will contact interested participants by collecting contact information (i.e., email address and/or phone number) to set up an interview. The interview will last about 30-40 minutes. It will be held over the telephone. With your permission, the interview will be audio-taped. The interviewer will ask you questions about your or your loved one's condition and your perspectives about your diagnosis and treatment options in Ontario. Participation is voluntary. You may refuse to participate, refuse to answer any questions or withdraw before or at any point during your interview. Withdrawal will in no way affect the care you receive.

Confidentiality

All information you share will be kept confidential and your privacy will be protected except as required by law. The results of this review will be published; however, no identifying information will be released or published. Any records containing information from your interview will be stored securely until project completion. After completion of the project, the records will be destroyed. If you are sending us personal information by email, please be aware that electronic communication is not always secure and can be vulnerable to interception.

Ontario Health is designated an "institution" by the *Freedom of Information and Protection of Privacy Act* (FIPPA) and is collecting your personal information pursuant to FIPPA and the *Connecting Care Act, 2019* to support the Health Technology Assessment Program. If you have any questions regarding Ontario Health's collection and use of personal information for the purposes of this program, please contact our Team Lead.

Risks to Participation

There are no known physical risks to participating. Some participants may experience discomfort or anxiety after speaking about their experience.

If you are interested, please contact us.

Appendix 11: Interview Guide

Diagnosis and Burden of Disease

- Can you tell me about how you first found out you had thyroid nodules? (Prompt: What symptoms, if any, led you to seek care? What kind of tests or appointments were involved?)
- How has living with thyroid nodules affected different parts of your life? (Prompt: Think about your daily routine, work, social activities, mental health, or relationships.)

Treatment

- What kinds of treatment options were offered or discussed with you? (Prompt: Surgery, monitoring, medication, ablative techniques, or others?)
- How did you first hear about ablative techniques as a treatment option for thyroid nodules? (Prompt: Was it through a doctor, online research, family/friends, or another source?)
- What would be the decision-making factors for you when considering traditional surgery versus ablative techniques? (cost, invasiveness, time off work, appearance/scarring, recovery time)

Ablative Technique Experience (if applicable)

Examples:

- Radiofrequency ablation (RFA)
- Microwave ablation (MWA)
- Laser ablation
- High-intensity focused ultrasound (HIFU)

- Can you describe your experience with the ablative technique? (Prompt: What was the procedure like? Did you need to stay in the hospital? What was recovery like?)
- What factors influenced your decision to choose ablative treatment instead of traditional surgery? (Prompt: Were you thinking about things like invasiveness, recovery time, risks, appearance, etc.?)
- How did the treatment affect your health and well-being afterward? (Prompt: Any changes physically, emotionally, or in your daily life – positive or negative?)
- Did you face any challenges or barriers in accessing this treatment? Location? (Prompt: Think about wait times, cost, availability, location, referrals, or other healthcare system issues.)

References

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About Us

We are an agency created by the Government of Ontario to connect, coordinate, and modernize our province's health care system. We work with partners, providers, and patients to make the health system more efficient so everyone in Ontario has an opportunity for better health and well-being.

Equity, Inclusion, Diversity and Anti-Racism

Ontario Health is committed to advancing equity, inclusion and diversity and addressing racism in the health care system. As part of this work, Ontario Health has developed an Equity, Inclusion, Diversity and Anti-Racism Framework, which builds on existing legislated commitments and relationships and recognizes the need for an intersectional approach.

Unlike the notion of equality, equity is not about sameness of treatment. It denotes fairness and justice in process and in results. Equitable outcomes often require differential treatment and resource redistribution to achieve a level playing field among all individuals and communities. This requires recognizing and addressing barriers to opportunities for all to thrive in our society.

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