MONASH University

AUSTRALIAN & NEW ZEALAND THYROID CANCER REGISTRY

2022 ANNUAL REPORT

AUSTRALIAN & NEW ZEALAND
THYROID CANCER
REGISTRY

CONTENTS

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AUSTRALIAN & NEW ZEALAND ENDOCRINE SURGEONS

THE AUSTRALIAN THYROID FOUNDATION LTD

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AUSTRALIAN & NEW ZEALAND THYROID CANCER REGISTRY

FOREWORD

FROM THE CLINICAL LEAD OF THE ANZTCR

It gives me great pleasure to introduce the fifth annual report of the Australian and New Zealand Thyroid Cancer Registry for 2022.

The registry continues to grow exponentially and demonstrates in this annual report, its primary purpose of improving outcomes for thyroid cancer patients.

There has been significant growth in patient numbers, sites and surgeons contributing to the registry. The results contained in this report indicate a high-quality outcome for our patients, particularly across the 12 key quality indicators.

A new feature presented in this annual report is the funnel plot benchmarking for sites.

We continue to enjoy the strong support of Australian and New Zealand Endocrine Surgeons (ANZES), Endocrinologists, ENT/Head and Neck Surgeons, Nuclear Medicine Physicians, and Data Managers.

Over the past 12 months there has been increasing utilisation of the registry for a variety of research projects including patient reported outcomes and experience measures.

I particularly would like to thank all our contributors for keeping the data in the registry so up to date, which has enabled this important analysis. I wish to thank Professor John Zalcberg, Professor Jeremy Millar, Dr Liane Ioannou and Benjamin Brown, from the Cancer Research Program at Monash University. Further, our strong and committed Steering Committee remain integral to the success of the ANZTCR.

This registry is now well established and is an important achievement as a key quality initiative for thyroid cancer patients. Finally, I would like to express my appreciation to our contributing patients, the Australian Thyroid Foundation, and our funders

Professor Jonathan Serpell
Clinical Lead, ANZTCR
Director, Department of General Surgery, Alfred Health
Director, Breast, Endocrine and General Surgery Unit, Alfred Health

FROM THE PRESIDENT OF ANZES

We are very proud to present the ANZTCR Report for 2022. The registry continues to mature and now involves 42 separate Hospital sites with 70 participating surgeons across Australasia.

It is particularly exciting to welcome contributions from Wellington Regional Hospital and Waikato Hospital in New Zealand/Aotearoa. This annual report represents the culmination of the extraordinary efforts of Surgeons, Data Managers and Registry staff at Monash University focussed on ensuring high quality surgery and optimal outcomes for thyroid cancer patients in our region. It is this careful and deliberate evaluation of our results which will maintain excellence and help to improve on it further.

I would also encourage our contributing surgeons to take advantage of this great resource, to study this remarkable dataset and to answer the questions which will help to better cancer care.

Associate Professor Mark Sywak
President,
Australian and New Zealand Endocrine Surgeons

EXECUTIVE SUMMARY

The ANZTCR was established in 2017 as a clinical quality registry to collect the diagnosis, treatment and outcome data of individuals diagnosed with thyroid cancer, in both public and private health services. This report presents key findings from the ANZTCR's first five years of data collection.

In 2022, the ANZTCR embarked on a new endeavour to produce our first round of benchmarked reports. This report is the first annual report produced from the ANZTCR to contain benchmarked data. The ANZTCR also expanded the collection of patient-reported outcome and experience measures to feedback to sites alongside clinical data up to five years post-surgery.

- As of 31st December 2022, a total of 42 hospitals across Australia and New Zealand were participating in the ANZTCR, with 70 contributing surgeons.
- As of 31st December 2022, there were 2480 participants in the ANZTCR, comprising 72% females and 28% males; at least some follow-up data was available for 100% of participants.
- The median age of participants was 52 years for females and 57 years for males (median overall age 53 years).
- Diagnosis of thyroid cancer was based on histology (63%), cytology (36%) and histology of metastasis (1%).
- At diagnosis, 40% of participants had at least one specified comorbidity, 3% had previously been exposed to upper body radiation and 4% had previous thyroid surgery.
- During diagnostic work-up, 92% of participants had an ultrasound, 88% had fine needle aspiration cytology (FNA) and 1% had a core biopsy; 22% underwent a computed tomography (CT) scan, 4% had a thyroid nuclear scan, 6% a positron emission tomography (PET) scan. 40 of 50 participants with evidence of voice abnormality prior to diagnosis underwent a laryngeal examination.
- The majority of participants underwent a total thyroidectomy (53%), or hemithyroidectomy (41%), with 5% undergoing a different procedure. Of those participants who had a subsequent procedure 76% had a completion thyroidectomy.
- More than half (53%) of participants had a lymph node dissection; where known, 21% with therapeutic intent and 67% with prophylactic intent.
- Pathology data was available for 2252 participants, and included 94% with differentiated, 2% with medullary and 1% with poorly differentiated thyroid cancer. Lymph node metastases were reported in 30% of participants at the time of initial procedure, with distant metastases reported in 1%.
- For 28% of participants, the finding of cancer was incidental.
- Nerve integrity monitoring was used during the initial procedure in 76% of participants. Twenty-nine participants had recurrent laryngeal nerves (RLN) damaged or sacrificed during their procedure (1%).
- Surgical complications reported in the registry included temporary RLN palsy (4%); with haemorrhage, infection and seroma reported in less than 1%.
- Postoperative treatment included medical supplementation with calcium (57%) and vitamin D (12%).
- All twelve clinical quality indicators are reported using benchmarked data for the first time.

FUNDING PARTNERS

The ANZTCR relies on funding grants from a range of sources to support its operations.

The ANZES membership has also made a very significant contribution to the ANZTCR, both through their participation in the registry, and through their financial support of the registry. The registry sincerely thanks the membership for their ongoing commitment and support to this important craft group initiative.

The ANZTCR is very privileged to have consistent industry supporters in Medtronic and Eisai Australia and New Zealand, which has supported the registry from its early days and has enabled it to increase its reach nationally, and now binationally.

Without these important funders, the ANZTCR and this report would not be possible.

AUSTRALIAN & NEW ZEALAND
ENDOCRINE SURGEONS

ENDORSEMENTS

The ANZTCR has the support from a variety of societies and organisations

The ANZTCR has been formally endorsed by:

AUSTRALIAN & NEW ZEALAND ENDOCRINE SURGEONS

Royal Australasian College of Surgeons

ASOHNS

THE AUSTRALIAN THYROID FOUNDATION LTD

MONASH University

endocrine society of australia

INTRODUCTION

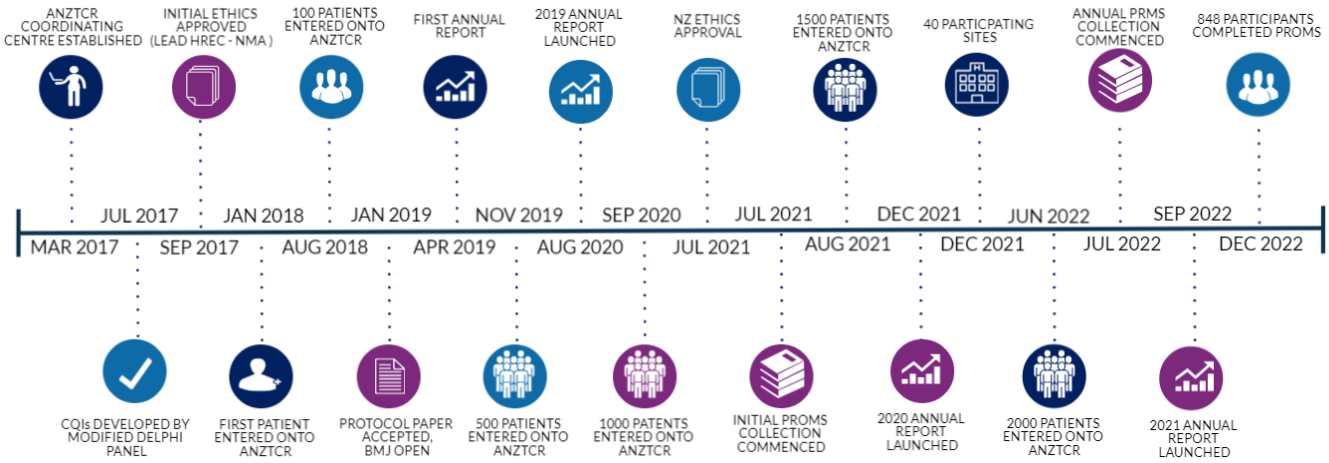
The ANZTCR is a clinical quality registry established in 2017 to monitor the quality of care provided to patients diagnosed with thyroid cancer. The ANZTCR collects the diagnosis, treatment and outcome data of individuals with thyroid cancer, in both public and private health services.

The ANZTCR conforms to the national operating principles for clinical quality registries as detailed in the 'Operating Principles and Technical Standards for Australian Clinical Quality Registries 2008'[1] and the 'Framework for Australian Clinical Registries 2014'[2] published by the Australian Commission for Safety and Quality in Healthcare (ACSQHC).

We report the first five years of data collection and benchmarked ANZTCR clinical quality indicator (CQI) outcomes.

MILESTONES

The ANZTCR milestones are highlighted in the diagram below:



REGISTRY GOVERNANCE

Steering Committee

The ANZTCR is led by a multidisciplinary steering committee which guides registry strategy and policy, monitors data collection and quality assurance, and produces data reports. Current membership includes representation from ANZES, the Australian Society of Otolaryngology Head and Neck Surgeons (ASOHNS), the Australian Thyroid Foundation, Endocrine Society of Australia (ESA) and Monash University.

The Steering Committee comprises representation from Australia and New Zealand, and includes representation of the following specialities and/or expertise:

- Surgery
- Endocrinology
- Radiation oncology
- Nuclear medicine
- Medical oncology
- Patient advocacy
- Data management
- Registry science

For a list of ANZTCR policies and procedures, please see Appendix G.

Monash University has custodianship of the data which includes accountability for the privacy, security and integrity of patient information held within the registry. Data is collected and managed using REDCap electronic data capture tools hosted and managed by Helix (Monash University). REDCap (Research Electronic Data Capture)[3] is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Management Committee

A Management Committee oversees the daily operations of the registry undertaken by the ANZTCR Coordinating Centre based at Monash University.

REGISTRY METHODOLOGY

PARTICIPANT RECRUITMENT

All patients newly diagnosed with thyroid cancer from a participating site are eligible to participate in the prospective registry.

Inclusion criteria

- All newly-diagnosed patients presenting to a participating hospital with a confirmed primary thyroid cancer.
- Patients who are ≥16 years of age at the time of diagnosis.

Exclusion criteria

- Patients diagnosed earlier than 1st September 2017.

The ANZTCR uses an *opt-out* recruitment process. Patients can opt-out of the registry at any time by emailing or calling the ANZTCR.

Recruitment can only begin after authorisation has been granted by the site's research ethics and governance office:

Phase 1 All patients diagnosed with thyroid cancer, based on histological confirmation (provided approximately 1-2 weeks post-diagnosis) are eligible to participate. The treating surgeon (or designated staff member) enters minimal patient details into the ANZTCR REDCap Database (ANZTCR-RCD) including the thyroid cancer diagnosis and patient disclosure.

Phase 2 The ANZTCR Coordinating Centre identifies new patients in the registry and provides information about the registry via a mail-out. The mail-out includes the ANZTCR Participant Introductory Letter and the ANZTCR Participant Explanatory Statement. Participation is assumed if the patient does not contact the ANZTCR within two weeks of the date of the mail-out.

Phase 3 The surgeon then enters participant diagnosis, surgical, pathology and treatment data into the registry database at approximately 90 days post-surgery to coincide with postoperative follow-up.

Recruitment of patients diagnosed with non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)

Patients diagnosed with NIFTP are included in the registry via a waiver of consent due to the potential for the terminology used around this diagnosis to vary.

DATA ELEMENTS

A consensus set of CQIs were developed for the early management of thyroid cancer using a modified-Delphi approach, informed by international thyroid cancer guidelines and relevant literature (Appendix H).

The ANZTCR minimum data set includes variables relating to the quality indicators, variables required for patient identification and contact, and other variables of particular relevance to early thyroid cancer management, based on the standard care provided (see Appendix C).

DATA COLLECTION PROCESSES

Data is collected and entered in the ANZTCR-RCD using two methods:

1. Direct data entry into the ANZTCR-RCD by surgeons (or their staff e.g., data manager). The ANZTCR-RCD provides a secure online connection to the registry database (primary method of data collection).
2. Data extracts from unit, institution and multi-institution databases held by participating surgeons or electronic medical records where data mapping indicates high levels of data item matching.

Data Importing

In 2020, the ANZTCR implemented the automated extraction and import of data from the Royal North Shore Hospital, Endocrine Surgical Unit's Database, the Alfred Monash University Endocrine Surgery Database and Chris O'Brien Lifehouse Endocrine Surgery Database into the ANZTCR-RCD. This process can also be undertaken at other sites who have closely aligned datasets or existing thyroid cancer or endocrine surgery databases. The benefits of setting up a direct import include reduced time spent on data entry, increased ease of contributing to the ANZTCR and the establishment of a data source for in-house analysis.

There are three ways to set-up data importing at a site:

1. **Using a copy of the ANZTCR-RCD:**
   A copy of the ANZTCR-RCD may be used at the site and custom fields may be added, as long as the original fields remain unedited.
2. **Using a copy of a thyroid disease database:**
   A copy of a thyroid disease database, like that from the Royal North Shore Hospital Endocrine Surgical Unit's Database, or like the Alfred's, may be used at the site. The database contains all the fields required for the ANZTCR.
3. **Undertaking data mapping to use a site's current database:**
   A site's current database can be mapped to the ANZTCR-RCD to determine if the names of the fields need to be changed and/ or added to allow for importing. To do this the site database must be in REDCap.

REPORTING

As the ANZTCR continues to expand its coverage and recruitment of patients it will be able to report CQI outcomes back to sites. A risk-adjustment process will be established to ensure that these benchmarked reports are adjusted for differences in casemix at different sites. Sufficient caseload is required before these reports can be generated, with a minimum patient volume per site to be determined.

Annual Reports

Aggregate outcomes and benchmarked funnel plots in relation to the CQIs have been included in this report.

Site Benchmarked Reports

In 2023 the ANZTCR has produced its inaugural benchmarked reports of CQIs to sites and participating clinicians with a sufficient cohort of recruited patients.

PATIENT-REPORTED MEASURES

In 2021, the ANZTCR commenced the electronic collection of patient-reported outcomes (PROs) and patient-reported experiences (PREs) as we are interested in knowing about the health and well-being of people diagnosed with thyroid cancer. The ANZTCR would like to understand what factors are important to their quality of life so they can help improve the care they receive from their surgeons and hospitals.

Process of Collecting PRMs

Eligible registry participants will be invited to participate in patient-reported outcome and experience questionnaires (patient-reported measures – PRMs) via text message or email. An invitation to complete the PRMs questionnaire will be sent at predetermined intervals following diagnosis, 3-, 6-, 12-months and then annually for five years, or until the participant opts-out or passes away.

Inclusion Criteria

- Patients participating in the ANZTCR

Exclusion Criteria

- Interpreter required (non-English speaking)
- Registry participants that have opted-out of PRMs
- Insufficient contact information

PRMs Questionnaire Content

Patient-reported data that measures patient outcomes, including quality of life, and patient experiences will be collected by providing the validated European Organisation for Research and Treatment of Cancer (EORTC) general quality of life questionnaire (QLQ-C30) and the thyroid cancer-specific module (THY34) to eligible registry participants.

In addition to measuring patient outcomes and experiences, participants may be asked if they wish to provide feedback on the process of collecting patient-reported data and the content of the questionnaires. The reason for this will be to periodically gather feedback from participants about registry processes and content to ensure participant acceptability and feasibility. The instructions for this patient evaluation clearly indicate that it is optional, states how many additional questions are included and the expected length of time required to complete it.

PRMs Reporting & Feedback

Patient Feedback

Upon completion of the questionnaire participants will receive links to patient advocacy and support websites, such as the Australian Thyroid Foundation, Cancer Australia and Cancer Council Australia. A ‘Thank you Postcard’ will be sent to all registry participants who are completing patient-reported data collection annually. This postcard will also contain the contact details for the Australia Thyroid Foundation, a consumer advocacy group.

Clinician & Hospital Reports

Patient-reported data collected from participants may be shared as aggregate data with ANZTCR participating clinicians and sites involved in their care via benchmarked reports. At this stage, no individual level, or identifiable data will be shared with any ANZTCR participating clinicians and sites. In the future, the ANZTCR will explore options for reporting these results to clinicians in real-time. Participants will be notified of this at the time of completing the questionnaire and can request that this does not occur.

CLINICIAN ENGAGEMENT

Surgeons are informed about the registry through ANZES and other sources including the ANZTCR newsletter. Principal and associate investigators at each hospital are ambassadors for the registry and further promote participation at their site.

Contributing Clinician Agreement forms are distributed to surgeons to invite them to participate in the registry. This is a once-only process for clinicians and notes the intent of the surgeon to participate in the registry and enter data on all patients for whom they are listed as the diagnosing or treating clinician in participating hospitals and private practice.

The ANZTCR annually acknowledges surgeons who participate in the registry in a number of ways:

CME Audit Points

The ANZTCR is recognised by the Royal Australasian College of Surgeons (RACS) as a Continuing Medical Education (CME) audit activity that aims to improve the quality of patient care. Contributing surgeons receive annual CME credit points in Surgical Audit and Australian and New Zealand Audits of Surgical Mortality.

Valued Contributor Logo

A valued contributor logo is provided to contributing surgeons to recognise their valued contribution to the registry. Surgeons are able to use the logo at their own discretion i.e. on their email signature, important documents and letters, and website.

Database Reports

The ANZTCR-RCD allows surgeons to run patient-level and aggregate data reports in real-time. Resources are provided to contributing surgeons with instructions on how to run these reports

Annual Clinician Specific Benchmarked Reports

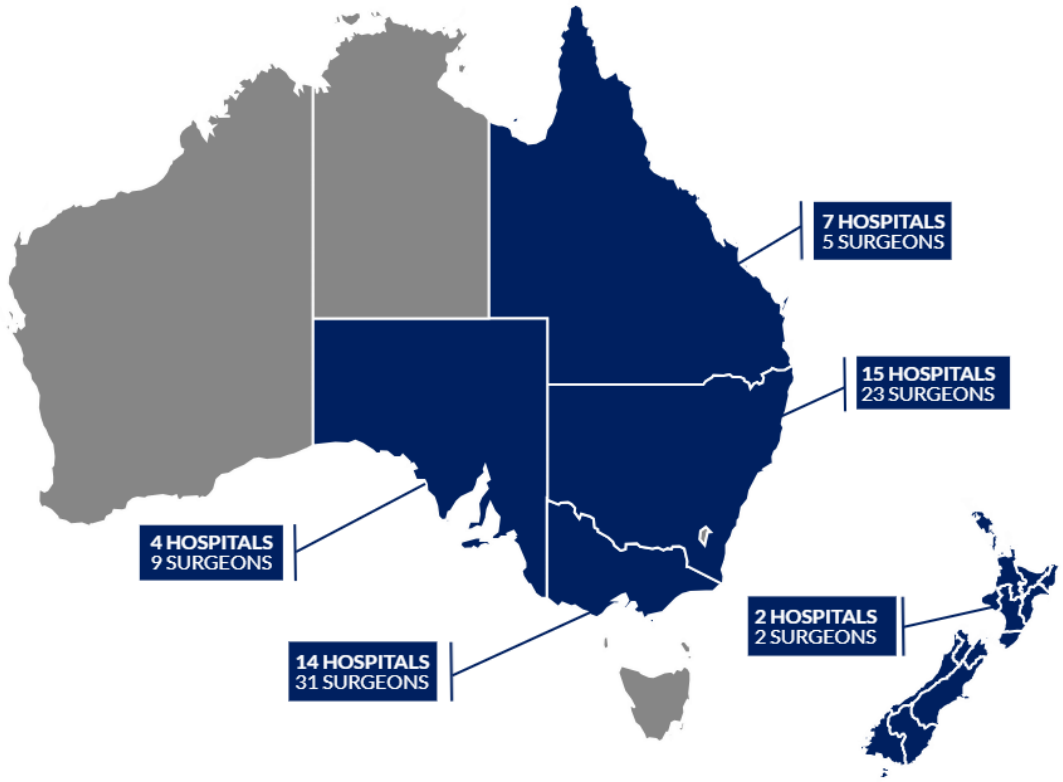
The ANZTCR has begun producing clinician specific benchmarked reports that allow for individual clinicians to be compared against the Clinical Quality Indicators. These reports contain all of the individual clinicians participating patients from their participating sites, in one report.

SUMMARY OF THE REGISTRY DATA

SITE PARTICIPATION

As of December 31 2022, 42* sites had obtained governance approval. There were 22 public and 20 private health services/ hospital sites across Australia and New Zealand participating in the ANZTCR. Figure 1 illustrates the expansion of the registry across Australia since it commenced data collection in early 2018.

FIGURE 1 NUMBER OF HOSPITAL SITES AND SURGEONS PER STATE CONTRIBUTING TO THE REGISTRY

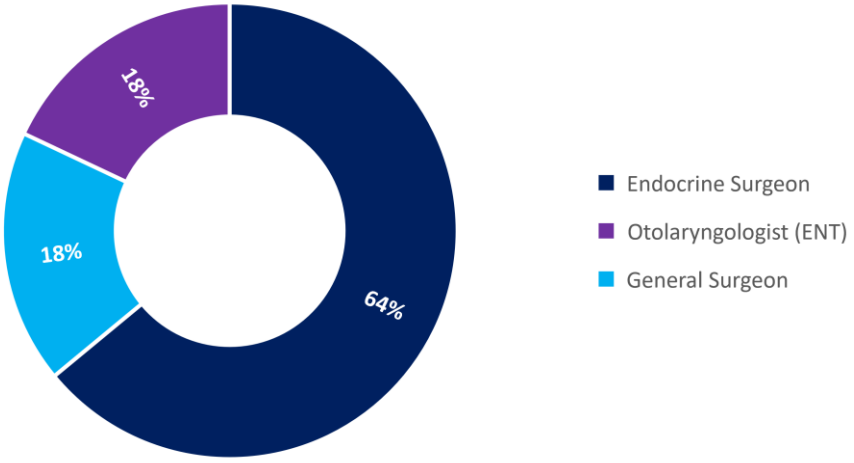


*Victorian sites are counted at the health service level

SURGEON PARTICIPATION

Surgery for thyroid cancer is performed by surgeons from different specialities including endocrine surgery, general surgery and Ear-Nose-Throat (ENT) surgery (otolaryngology). The registry aims to include all surgeons at a participating site that operate on patients with thyroid cancer. Figure 2 displays the speciality area of the 75 surgeons currently contributing to the ANZTCR.

FIGURE 2 AREA OF SURGEON EXPERTISE



REGISTRY PARTICIPATION

The data presented in this report pertains to patient events from 25 September 2017 to 31 December 2022.The ANZTCR obtained ethics approval in September 2017, and the ANZTCR-RCD was launched late January 2018. There may be some delay between the patient being entered on the database and the patient receiving their invitation letter.

A total of 2613 patients have been invited to participate in the registry since January 2018. Of the 2613 patients invited, 133 (5.1%) have chosen to opt-out and 56 (2.1%) partially opted-out, where their clinical data will be collected but they will not be contacted for patient-reported measures or other research. As at 31 December 2022, the ANZTCR confirmed the participation of 2480 thyroid cancer patients and their data.

Table 1 demonstrates patient participation in the ANZTCR from 1 January 2018 to 31 December 2022. The registry has an opt-out rate of 5.1%.

TABLE 1 PATIENT PARTICIPATION IN THE REGISTRY FROM 1 JANUARY 2018 TO 31 DECEMBER 2022

Participation Status	Frequency	%
Invited	2613	100
Complete Opt-Out	133	5.1
Participating*	2480	94.9

*57 partial opt-outs.

Figure 3 illustrates the steady growth of registry participants from across Australia since its commencement in January 2018.

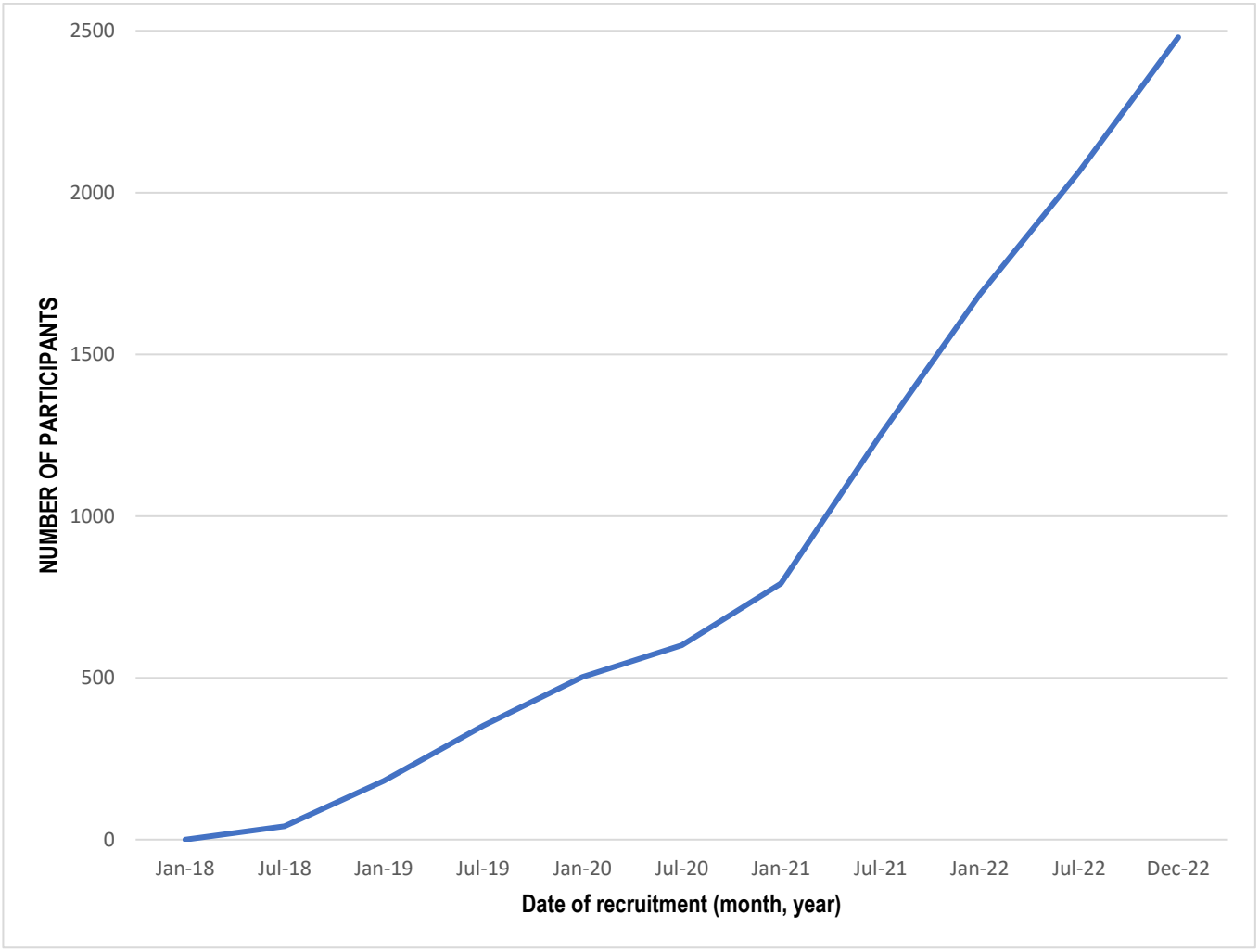


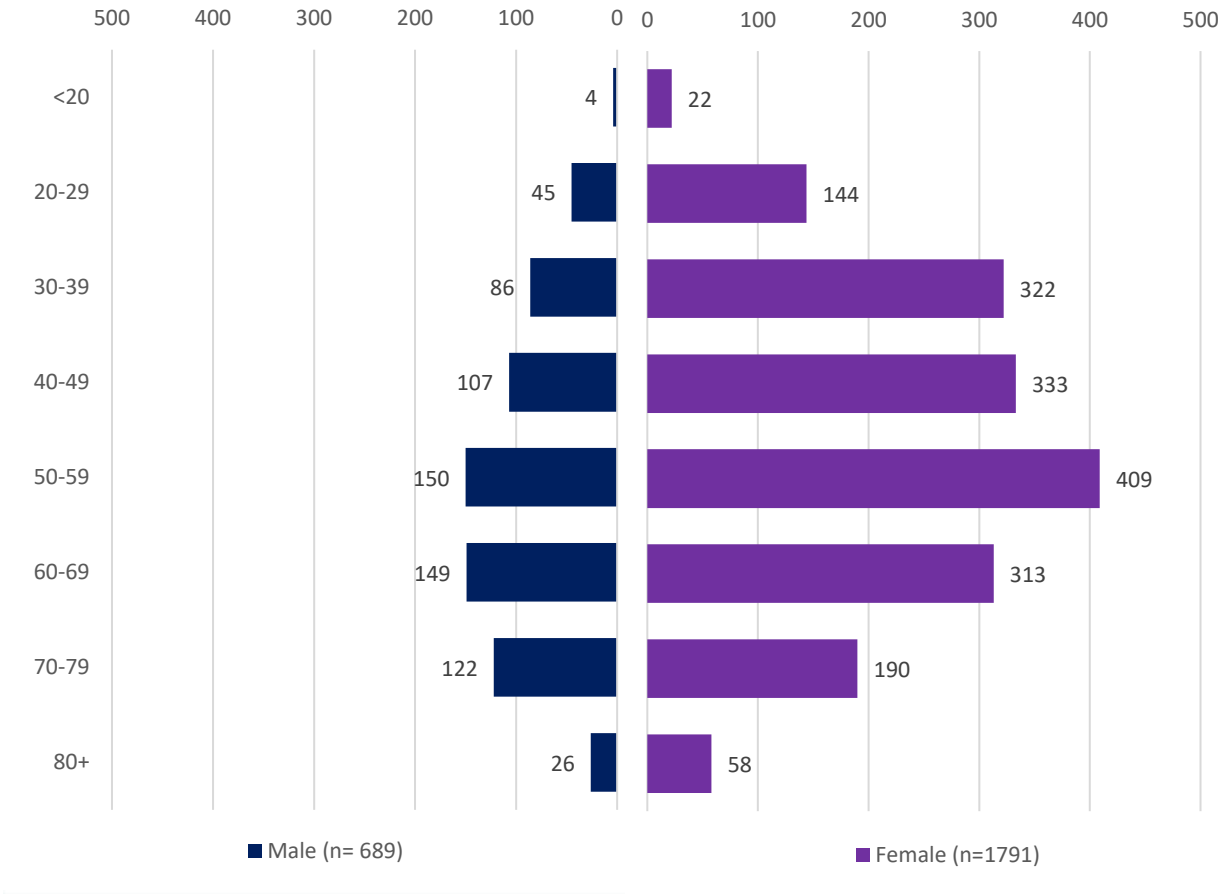
FIGURE 3 ACCUMULATION RATES OF PARTICIPANTS IN THE REGISTRY FROM JANUARY 2018-2022 (n=2480)

Participant Characteristics

As of 31 December 2022, there were 1791 (72%) females and 689 (28%) males participating in the registry who had been diagnosed with thyroid cancer.

The median age for patients at diagnosis was 53 (IQR 40-64) years old, with a difference in the median age between males (57, IQR 43-68) and females (52, IQR 38-63). Figure 4 demonstrates the sex and age of participants in the registry who have been diagnosed with thyroid cancer since September 2017.

FIGURE 4 PARTICIPANTS' AGE DISTRIBUTION AT TIME OF DIAGNOSIS STRATIFIED BY SEX (n=2480)



Participants' Residence by State

Of the 2480 patients participating in the registry, 1499 (60.4%) were residing in New South Wales at the time of recruitment, 570 (22.9%) in Victoria, 311 (12.5%) in Queensland, 79 (3.2%) in South Australia, 2 (0.1) in Tasmania, 2 (0.08%) in Northern Territory, 14 (0.6%) in the Australian Capital Territory, and 4 (0.1%) in New Zealand.

Table 2 highlights the frequency and percentage of patient participation in the registry across jurisdictions within Australia based on residence at time of recruitment.

TABLE 2 PATIENT PARTICIPATION IN THE REGISTRY BY JURISDICTION* (n=2480)

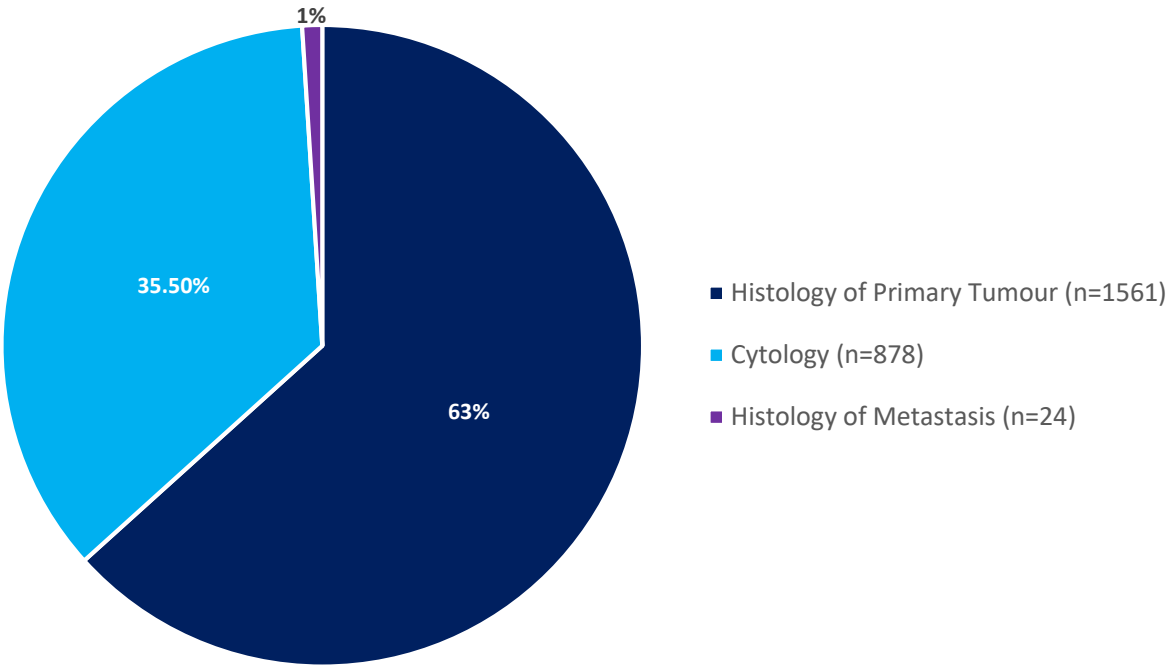
State/Country	Frequency	%
New South Wales	1499	60.4
Victoria	570	22.9
Queensland	311	12.5
South Australia	79	3.1
Australian Capital Territory	14	0.6
New Zealand	4	0.2
Tasmania	2	0.1
Northern Territory	2	0.1
Total	**2480**	**100**

*Based on participant residential postcodes.

Method of Diagnosis

Of the 2480 participants, 1561 (63.0%) were diagnosed with primary thyroid cancer based on histology of primary tumour, 878 (35.5%) based on cytology, 24 (1.0%) based on histology of metastasis and 17 were marked as unknown. Figure 5 demonstrates the method of diagnosis for participants recruited to the registry.

FIGURE 5 METHOD OF DIAGNOSIS OF PRIMARY THYROID CANCER (n=1684*)



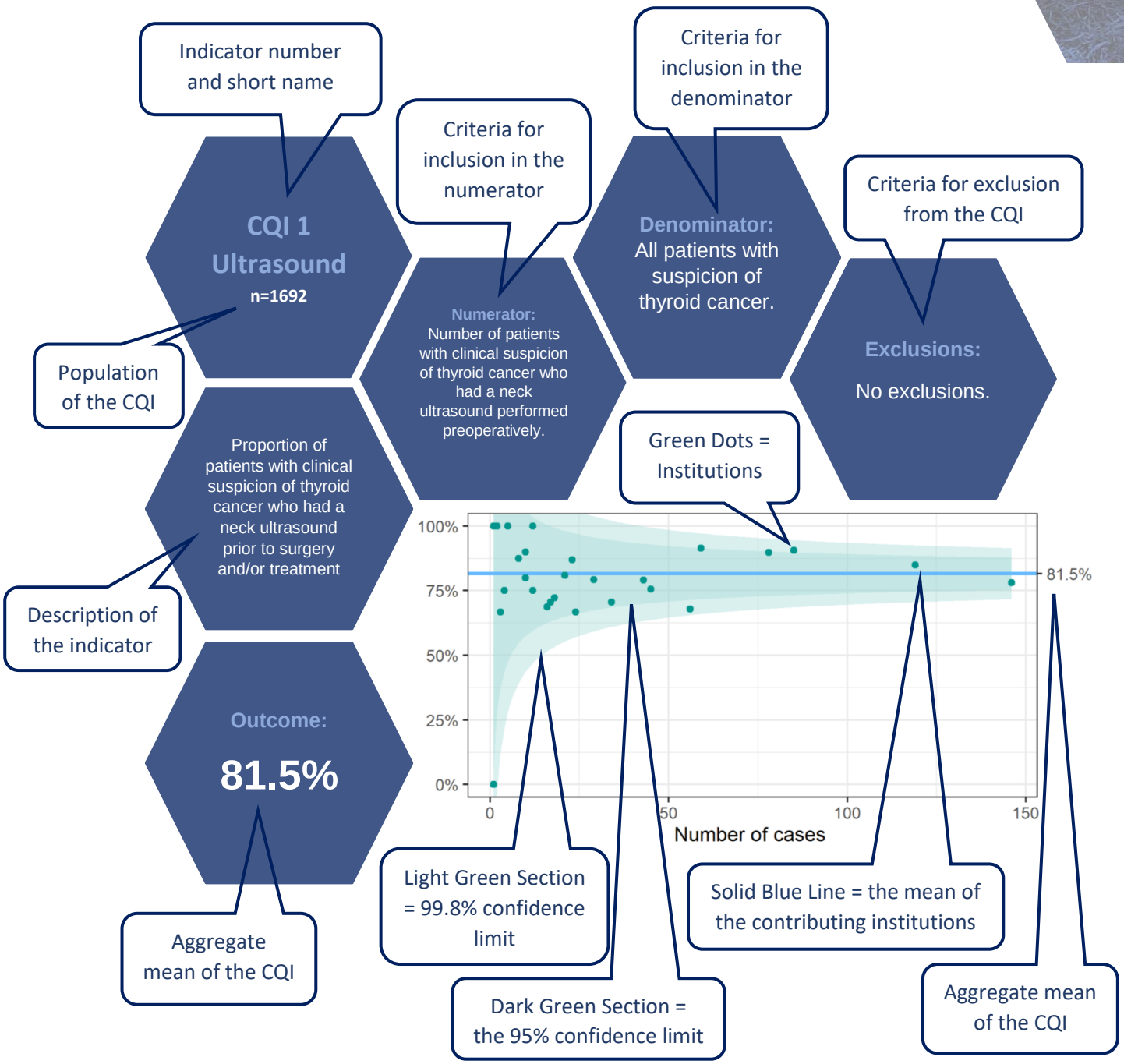
Footnote: Excludes 17 patients with an unknown basis of diagnosis

FOLLOW-UP DATA COMPLETION

Participating surgeons enter follow-up data for their patients participating in the registry at 90-days post-diagnosis. Of the 2480 participants, 2480 exceeded the 90-day post-diagnosis period and are eligible for follow-up data collection. From this point forward, this report presents data on the patients for which follow-up data has been completed, please see sample sizes reported for each individual data item.

PREOPERATIVE	**CQI 1**	All patients with suspicion of thyroid cancer should have a neck ultrasound (US) prior to initiation of treatment.	98.5%
	CQI 2	All patients with suspicion of thyroid cancer that present with clinically and/or radiologically suspicious lymph nodes should undergo a biopsy to confirm malignancy before the initiation of treatment.	97.6%
	CQI 3	All patients with suspicion of thyroid cancer that present with (subjective or objective) evidence of voice abnormality should undergo a laryngeal examination prior to initiation of treatment.	80%
SURGICAL	**CQI 4**	All patients with differentiated thyroid cancer who have a tumour size >4 cm or advanced disease (extrathyroidal extension and/or metastatic disease) should undergo a total thyroidectomy (one- or two-stage including completion thyroidectomy).	81.5%
	CQI 5	All patients with thyroid cancer undergoing surgery who have cytological or core biopsy proven lateral lymph node involvement should have a therapeutic compartmental lateral neck lymph node dissection.	98.6%
SURGICAL COMPLICATIONS	**CQI 6**	Proportion of patients with thyroid cancer who presented with recurrent laryngeal nerve (RLN) palsy that has not resolved within three months following thyroidectomy.	4.05%
	CQI 7	Patients with thyroid cancer who present with persisting hypoparathyroidism at six months following thyroidectomy	3.8%
	CQI 8	Patients with thyroid cancer who underwent a thyroidectomy and had postoperative haemorrhage within 48 hours requiring return to theatre.	0.7%
STAGING & TREATMENT PLANNING	**CQI 9**	All patients with thyroid cancer should have staging recorded postoperatively, using the tumour, node, metastasis (TNM) staging system.	71.2%
	CQI 10	All patients with thyroid cancer should be presented at a tumour-specific multidisciplinary team meeting.	60.7%
POST-SURGICAL TREATMENT	**CQI 11**	All patients undergoing surgery for differentiated thyroid cancer should have serum thyroglobulin (Tg) recorded postoperatively.	72.6%
	CQI 12	All patients with high risk differentiated thyroid cancer who had a total thyroidectomy should undergo radioactive iodine (RAI) remnant ablation.	100%

HOW TO INTERPRET FUNNEL PLOTS



The data contained in this document was extracted from the ANZTCR on 02 August 2023 and pertains to data that relates to patient events from 25 September 2017 to 31 December 2022. As the registry does not capture data in real time, there may be a lag period between the occurrence of an event and its capture in the registry's database, ANZTCR REDCap Database (ANZTCR-RCD).

The ANZTCR has implemented the use of funnel plots to demonstrate the variation in the outcomes of the CQIs. Funnel plots are used to identify the presence of variation within the indicators, but not to identify the cause of the variation. The variation that can be identified through the use of funnel plots may be due to the process or procedure not being completed, or that the data was not easily available at the time of recording amongst other possibilities. Further investigation is required to determine the causation of the variation that has been identified through this report.

PREOPERATIVE DETAILS CAPTURED BY THE REGISTRY

Previous Medical History

At the time of diagnosis, 894 out of 2257 (39.6%) patients presented with a specified comorbidity, of these 159 (17.8%) were obese, 72 (8.0%) were current smokers, and 199 (22.2%) had been diagnosed with cancer other than thyroid cancer. Only 65 (2.9%) out of 2257 participants had previously been exposed to upper body radiation. 87 of 2257 (3.8%) participants had previous thyroid surgery.

Table 3 displays participants' previous medical history at diagnosis.

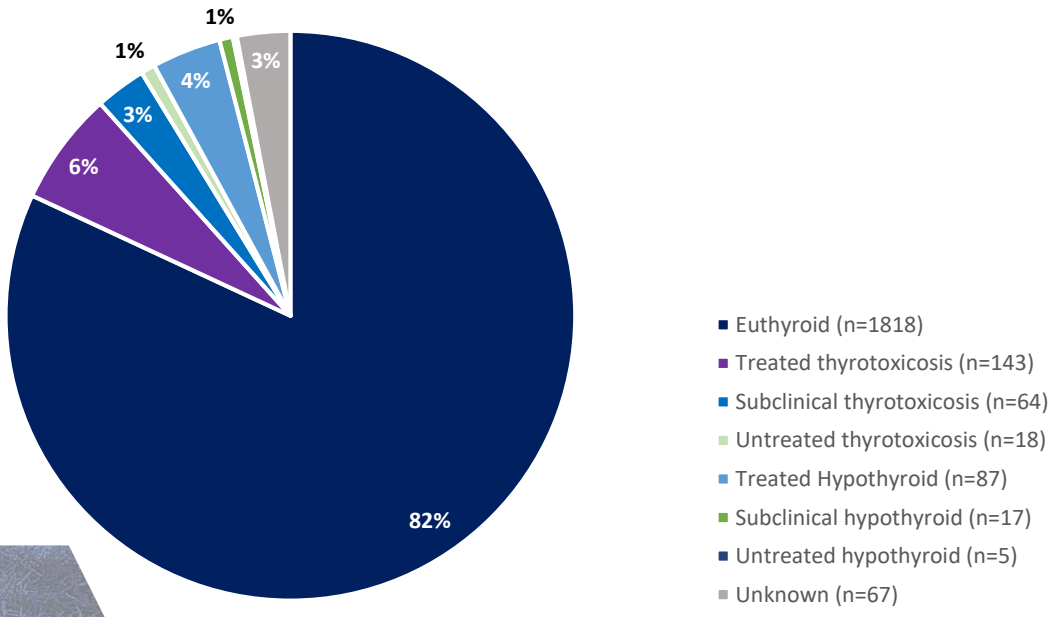
TABLE 3 PREVIOUS MEDICAL HISTORY (n=2257)

Variable	Total (n)	Response	Frequency (%)	
Specified comorbidity at diagnosis	2257	Yes	894	(39.61)
		No	317	(14.05)
		Unknown	1046	(46.34)
If yes, comorbidity type*	894	Obesity	159	(17.79)
		Smoking	72	(8.05)
		Other cancer	199	(22.26)
		Other	730	(81.66)
Upper body radiation exposure	2257	Yes	65	(2.88)
		No	2073	(91.85)
		Unknown	119	(5.27)
Previous thyroid surgery	2257	Yes	87	(3.85)
		No	2089	(92.56)
		Unknown	81	(3.59)

*Multiple responses allowed, row percentages of total shown.

A patient's thyroid function is assessed at their first presentation to a surgeon prior to diagnosis. Of the 2257 participants with complete data, 1818 (80.5%) presented with a normal functioning thyroid gland (euthyroid), 143 had treated thyrotoxicosis (6.3%), 87 had treated hypothyroidism (3.9%), 64 had subclinical thyrotoxicosis (2.8%), 18 had untreated thyrotoxicosis (0.8%) and 17 had subclinical hypothyroidism (0.8%) (Figure 6).

FIGURE 6 THYROID FUNCTION AT FIRST PRESENTATION (N=1560)

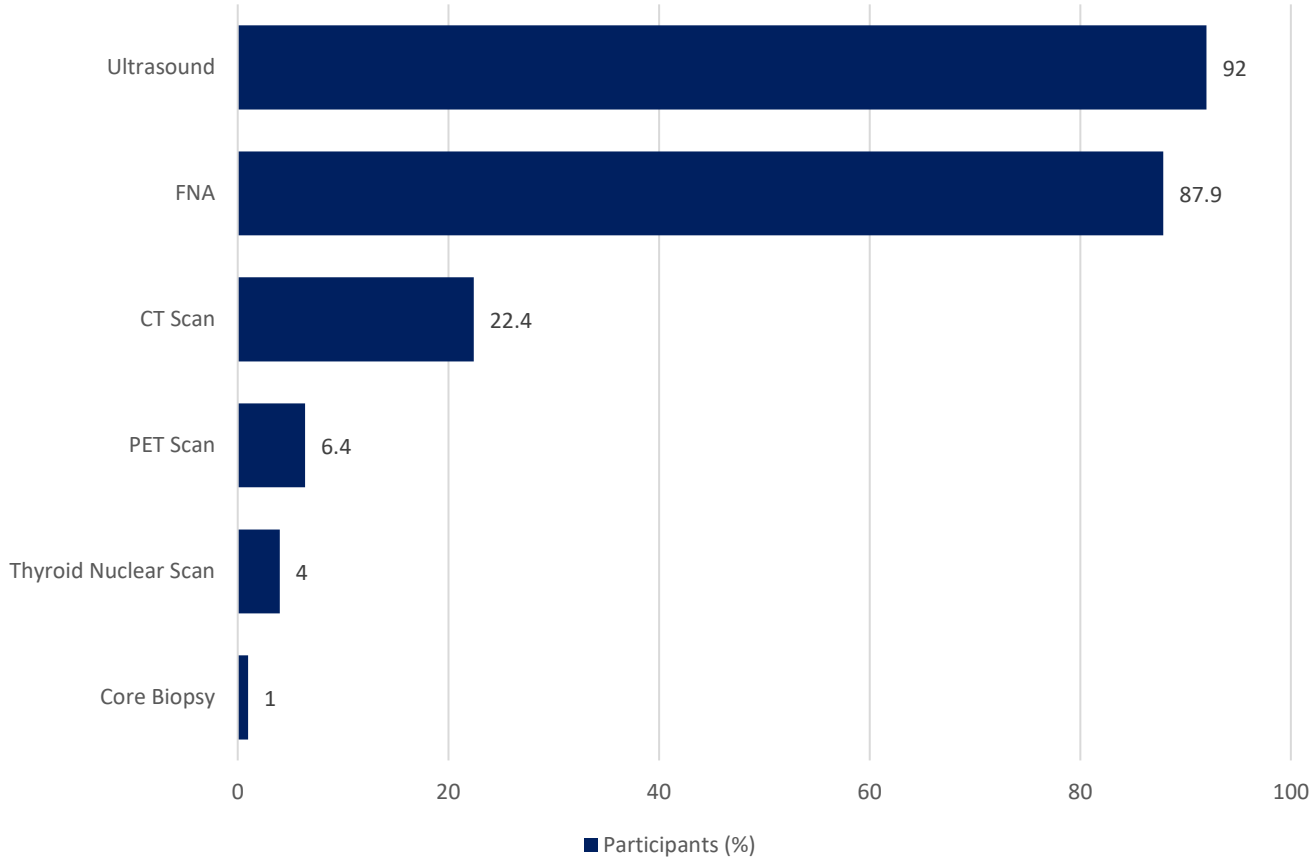


Diagnostic Tests

A total of 2077 out of 2257 participants (92.0%) had an ultrasound prior to diagnosis. Suspicious lymph nodes were present on ultrasound for 268 out of 2077 participants (12.9%). Of the 2257 participants with fine needle aspiration (FNA) information recorded, 1984 (87.9%) underwent a FNA biopsy, of these 1546 (77.9%) had one site biopsied, 300 (15.1%) had two sites, 47 (2.4%) had three sites and 30 (1.5%) with an unknown number of sites biopsied. Of the 2257 participants with core biopsy information recorded, 23 underwent a core biopsy, of these 22 (95.6%) had one site biopsied and one (4.6%) had two sites biopsied.

Figure 7 displays the type of preoperative tests conducted and the percentage of patients who underwent each test.

FIGURE 7 PREOPERATIVE TESTS



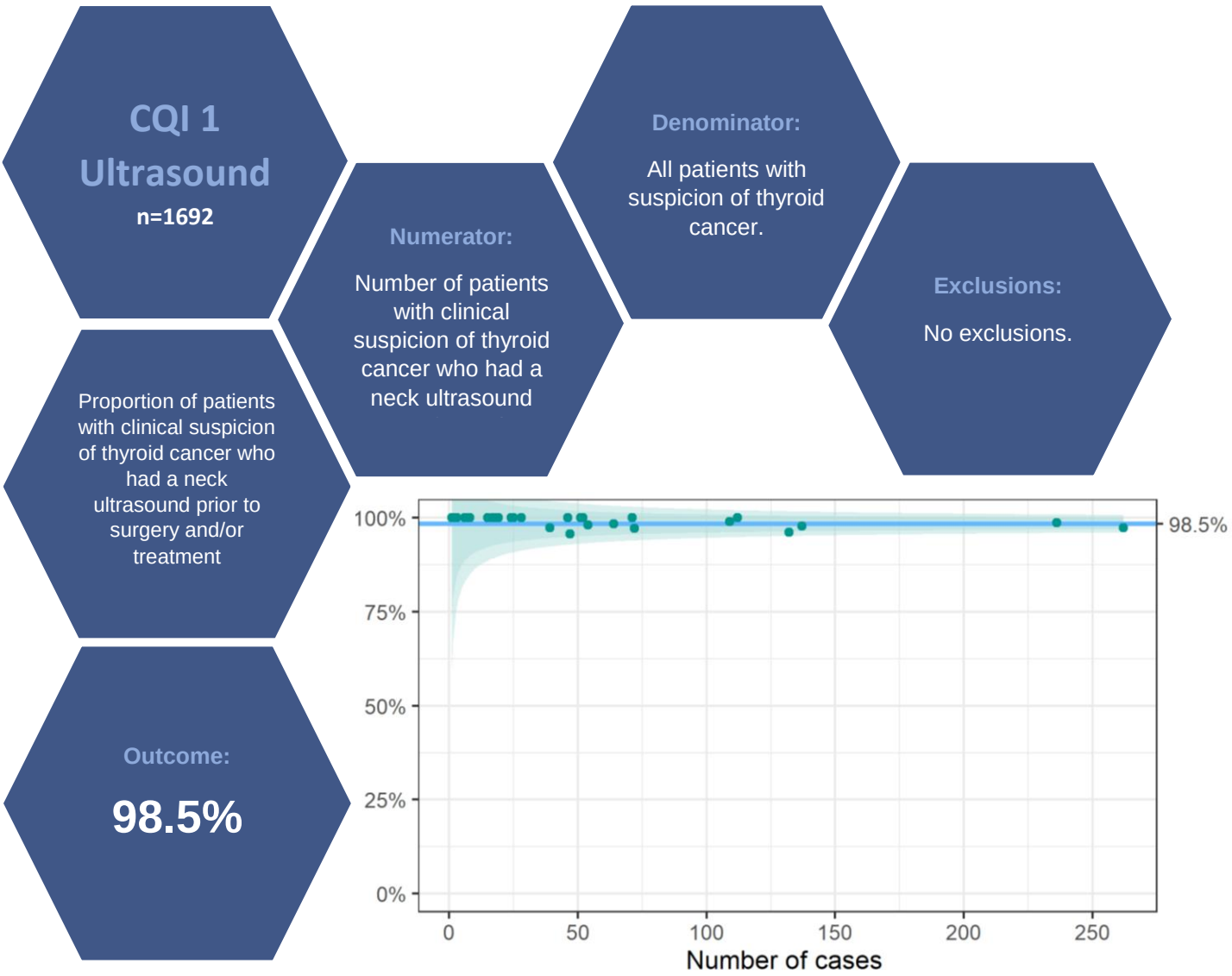


FIGURE 7 CQI 1: ULTRASOUND

Preoperative neck ultrasound aids in the identification of suspicious lymph nodes and assists with decision making about which nodules to perform FNA on consistently increasing the yield of diagnostic FNA cytology[4]. Of the 1706* participants with complete data who had suspicion of thyroid cancer, 1666 (97.7%) underwent an ultrasound of the neck prior to any treatment. Table 4 demonstrates the calculation for this indicator.

TABLE 4 ULTRASOUND OF PRIMARY SITE (CQI1)

Variable	Total (n)	Response	Frequency (%)	
Ultrasound at primary site	1692*	Yes	1666	(98.5)
		No	26	(1.5)
		Unknown	55	

*55 participants were unknown and not included in the CQI calculation

Preoperative FNA or core biopsy cytology confirms malignancy and informs the management of patients with thyroid cancer to ensure appropriate treatment is delivered[4]. Of the 2267 participants with complete data, 292 (12.8%) had suspected malignancy and presented with clinical and/or radiological suspicious lymph nodes. Of these 288 (4 unknown), 281 (97.6%) went on to have a FNA or core biopsy to confirm malignancy prior to any treatment. Table 5 provides an overview of the calculations for this indicator.

TABLE 5 FNA OR CB TO CONFIRM MALIGNANCY (CQI2)

Variable	Total (n)	Response	Frequency (%)	
Clinically and/or radiologically suspicious lymph nodes and suspected malignancy	2267	Yes	292	(12.8)
		No	1975	(86.8)
		Unknown	9	(0.4)
If yes, FNA or Core Biopsy to confirm malignancy	288*	Yes	281	(97.6)
		No	7	(2.4)
		Unknown	2	

*Two participants were unknown and not included in the CQI calculation

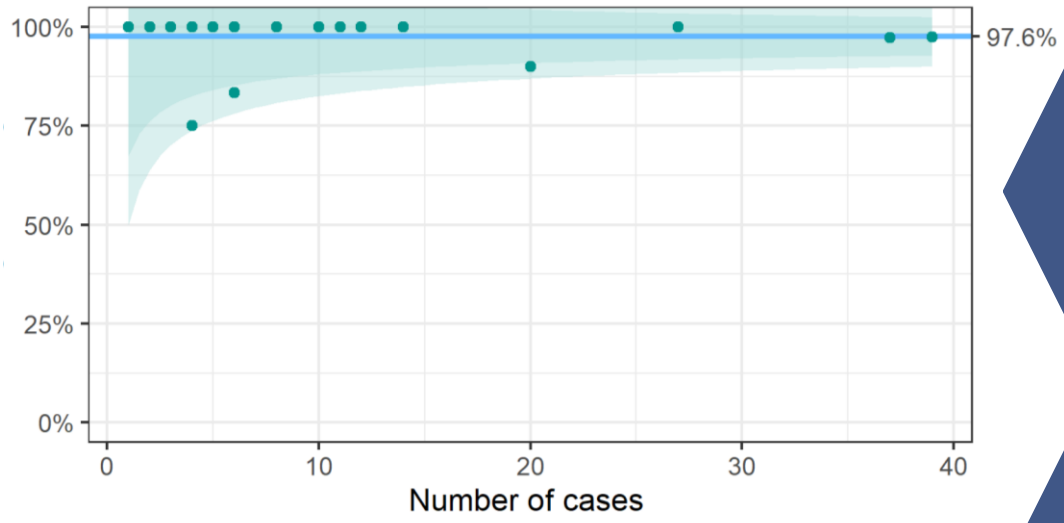


FIGURE 8 CQI 2: FINE NEEDLE ASPIRATION OR CORE BIOSPY

CQI 2
Fine Needle Aspiration (FNA) or Core

Proportion of patients with clinically and/or radiologically suspicious lymph nodes that underwent a biopsy

Exclusions:
Patients who did not have suspected malignancy.

Denominator:
All patients with clinically and/or radiologically suspicious lymph nodes.

Numerator:
Number of patients with suspicious lymph nodes who underwent a biopsy.

Outcome:
97.6%

Voice Assessment

Voice alteration is an important complication of thyroid surgery affecting patients' quality of life. Preoperative voice assessment provides a necessary baseline reference and is important for planning the extent of surgery and perioperative airway management.[4] It may also lead to the identification of preoperative vocal cord paralysis or paresis, providing evidence of invasive thyroid malignancy[4].

Of the 2317 participants with complete data, 64 (2.76%) had evidence of subjective or objective voice abnormality prior to diagnosis. Of these, a laryngeal exam was performed prior to any treatment for 40 (80.0%) out of 50 (14 unknown) participants, with 28 (70%) returning a normal result, three (7.5%) indicating right palsy, six (15%) left palsy and three (7.5%) other.

TABLE 6 PREOPERATIVE VOICE ASSESSMENT (CQI3)

Variable	Total (n)	Response	Frequency (%)
Evidence of subjective or objective voice abnormality	2317	Yes	64 (2.8)
		No	2003 (86.4)
		Unknown	250 (10.8)
If yes, laryngeal exam	50*	Yes	40 (80.0)
		No	10 (20.0)
		Unknown	14

*14 participants were unknown and not included in the CQI calculation

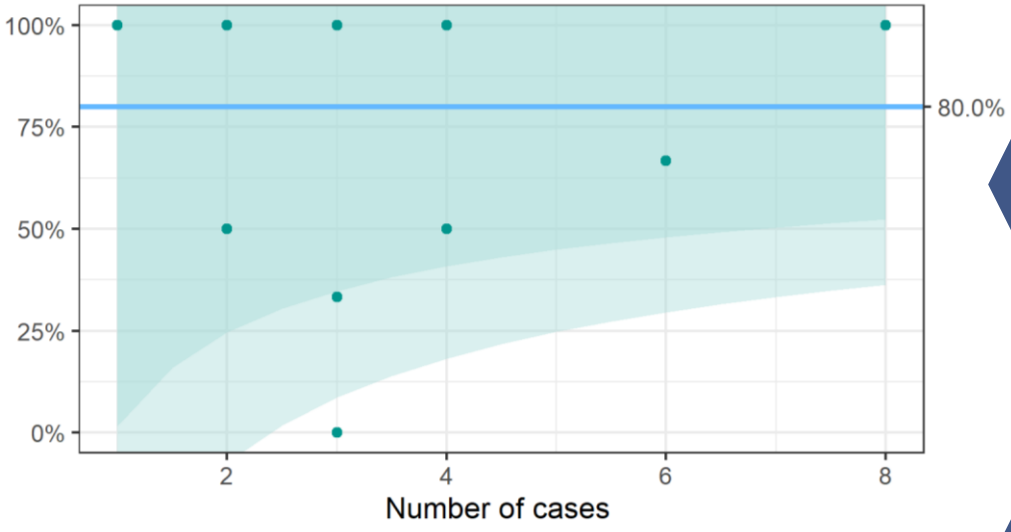


FIGURE 9 CQI 3: VOICE ASSESSMENT

PROCEDURES CAPTURED BY THE REGISTRY

Primary procedure

Of the 2252 participants with initial procedure information, 1190 had a total thyroidectomy (52.8%), 935 (41.5%) a hemithyroidectomy, 23 (1.0%) an isthmusectomy, 18 (0.8%) a nodulectomy, 24 (1.1%) a completion thyroidectomy, 4 (0.2%) a redo-thyroidectomy unilateral, 5 (0.2%) a sub-total thyroidectomy and 39 (1.7%) another procedure type not listed.

Figure 8 outlines the type of procedure initially performed on patients in the registry.

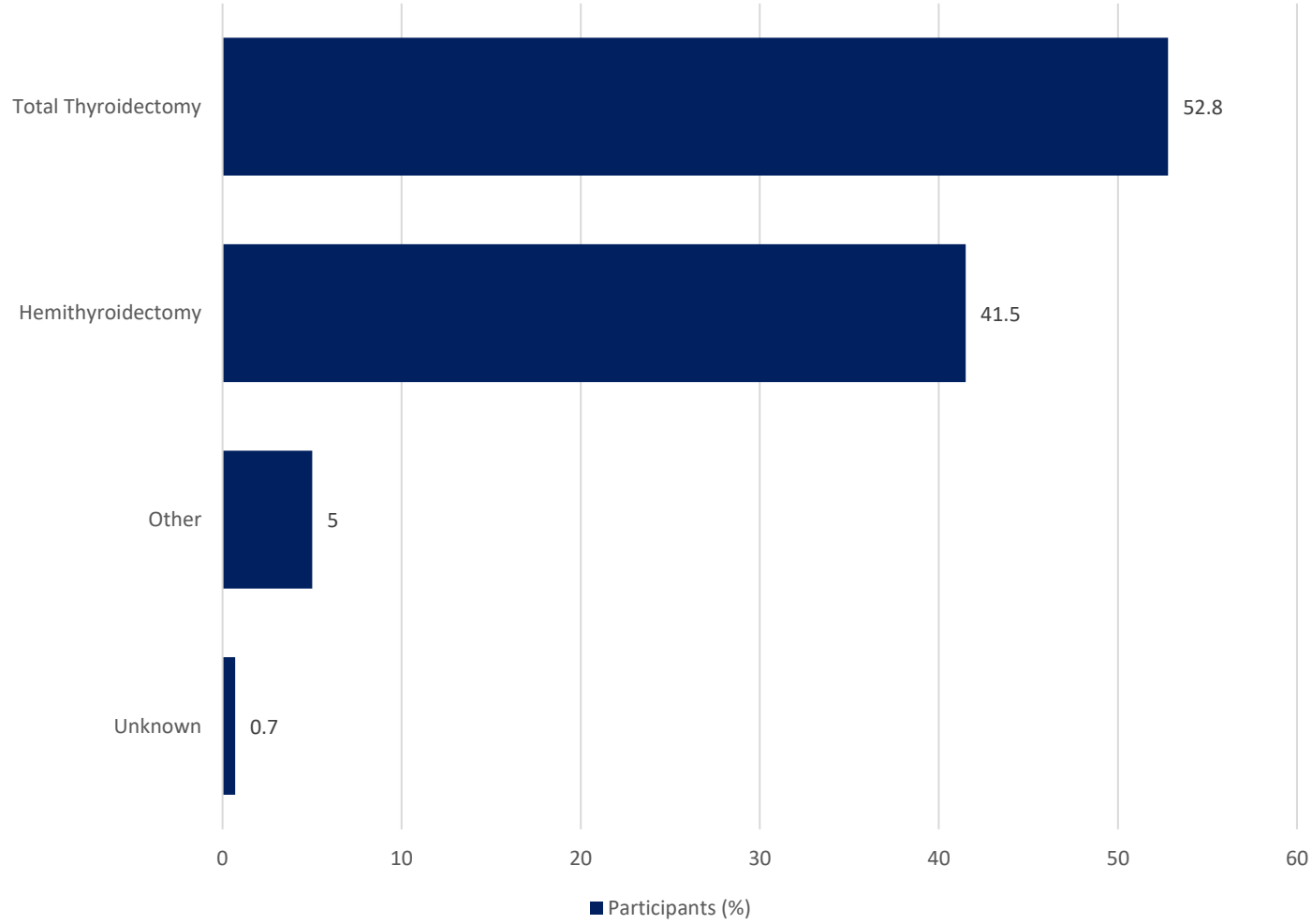


FIGURE 10 TYPE OF INITIAL PROCEDURE (N=2252)

Of the 2252 participants with a recorded initial procedure, the main reason for surgery was malignancy (41.3%) followed by risk of malignancy (37.3%) and compression (12.2%). Other reasons for surgery that have been recorded include non-toxic single nodular goitre (4.3%), Graves' disease (3.9%), retrosternal goitre (3.3%), growth (3.2%), toxic multinodular goitre (3.1%), non-toxic multinodular goitre (3.1%), toxic single nodular goitre (0.8%) and other (4.4%)

TABLE 7 REASONS FOR INITIAL PROCEDURE (N=2252)

Reason for Procedure*	Frequency	%
Malignancy	930	41.3
Risk of malignancy	840	37.3
Compression	275	12.2
Other	99	4.4
Graves' disease	88	3.9
Retrosternal goitre	74	3.3
MNG toxic	69	3.1
Growth	73	3.2
MNG nontoxic	69	3.1
Single nodule nontoxic	97	4.3
Single nodule toxic	19	0.8
Unknown	6	0.3

*Multiple responses were allowed for this data item, row percentages of total shown.

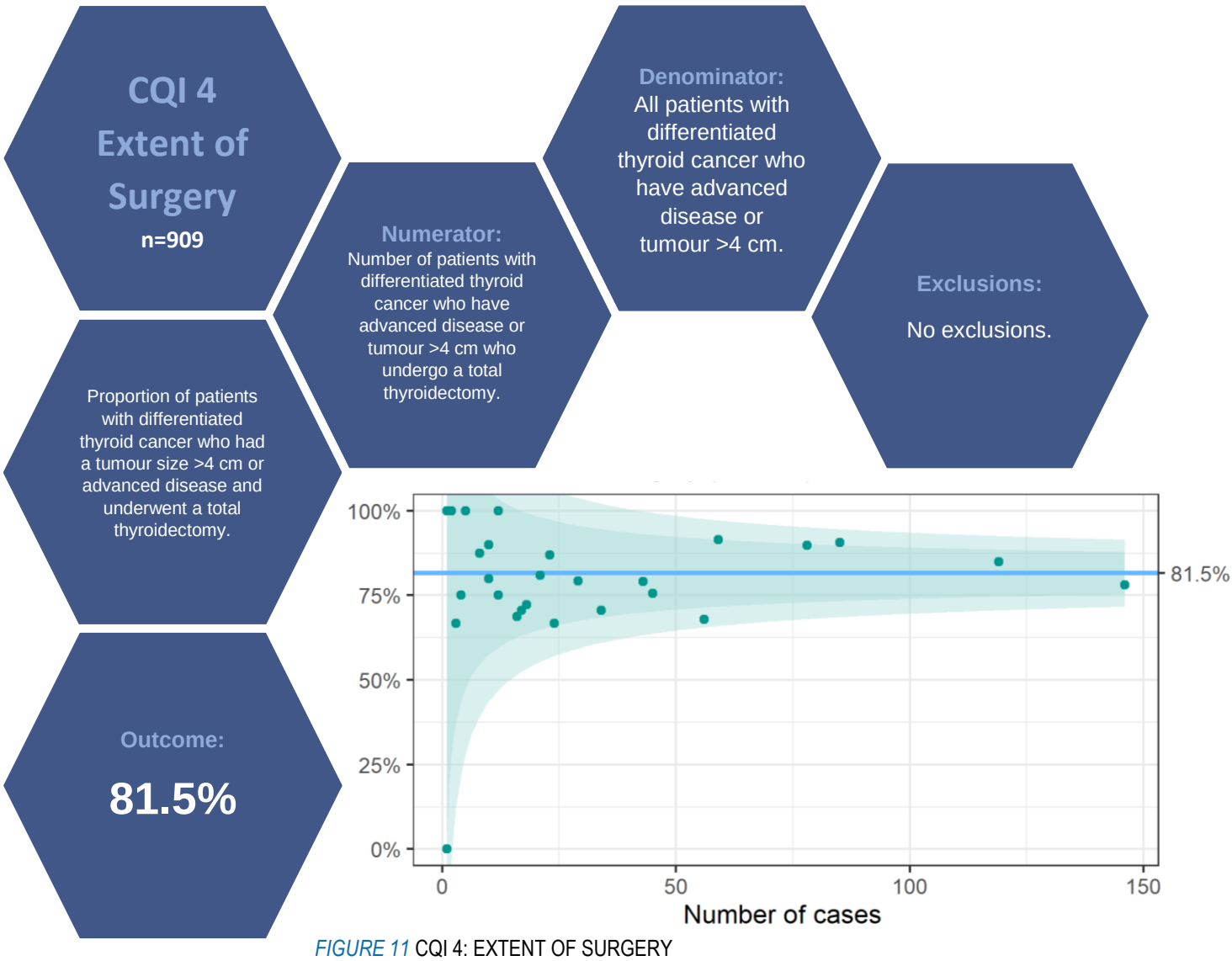


FIGURE 11 CQI 4: EXTENT OF SURGERY

Extent of initial thyroid surgery can impact disease-specific survival for patients with advanced disease of primary thyroid carcinoma that is greater than 4 cm, as a total (or near-total) thyroidectomy is necessary for the provision of radioactive iodine therapy postoperatively[4]. Of the 2246 participants with surgical information recorded, 909 (39.0%) had advanced differentiated thyroid cancer or a tumour size greater than 4 cm. Of the 904* where details of thyroid surgery were recorded, 737 (81.5%) had a total (or near-total) thyroidectomy.

TABLE 8 TOTAL (OR NEAR-TOTAL) THYROIDECTOMY FOR PATIENTS WITH ADVANCED DISEASE (CQI4)

Variable	Total (n)	Response	Frequency (%)
Differentiated thyroid cancer with advanced disease or tumour >4 cm	2246	Yes	909 (40.5)
		No	1335 (59.4)
		Unknown	2 (0.1)
If yes, total (or near total) thyroidectomy (CQI4)	904*	Yes	737 (81.5)
		No	167 (18.5)
		Unknown	5

*Five participants were unknown and were not included in the CQI calculation

Subsequent procedure(s)

Of the 2252 participants with complete procedure data, 407 participants (18.1%) recorded a subsequent procedure. The main subsequent procedure was a completion thyroidectomy (75.4%).

TABLE 9 SUBSEQUENT PROCEDURE TYPE (N=401)

Variable	Frequency	(%)
Total thyroidectomy	17	(4.2)
Hemithyroidectomy	31	(7.6)
Completion Thyroidectomy	307	(76.4)
Other	45	(11.1)
Nodulectomy	1	(0.2)
Unknown	6	(1.5)

Lymph node dissection

Of the 2252 participants with initial procedure data, 2128 had known lymph node dissection information.

A total of 1119 out of 2128 (52.6%) participants had a lymph node dissection (data missing for 18 participants). Of these, where it was known, it was therapeutic in 239 (21.4%), and prophylactic in 746 (66.7%). Of the 935 participants who had an initial hemithyroidectomy, 338 (15.0%) had a lymph node dissection.

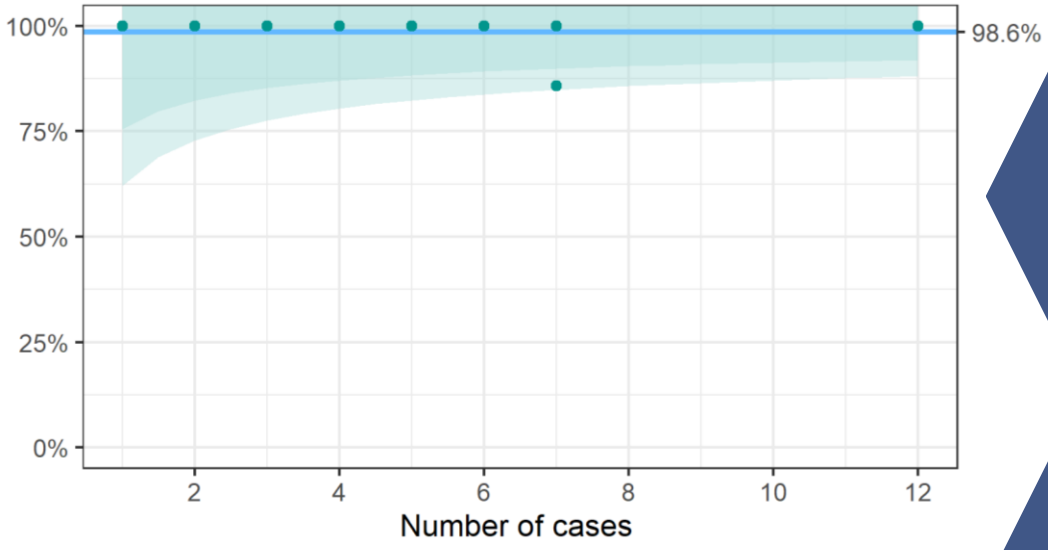


FIGURE 12 CQI 5: LATERAL LYMPH NODE DISSECTION

CQI 5
Lateral Lymph Node Dissection
n=71

Proportion of patients with thyroid cancer who undergo surgery with therapeutic compartmental lateral neck lymph node dissection due to cytological proven lateral lymph node involvement.

Numerator:
Number of patients with thyroid cancer with cytological proven lateral lymph node involvement who had a therapeutic compartmental lateral neck lymph node dissection.

Denominator:
All patients with thyroid cancer with cytological or core biopsy proven lateral lymph node involvement who had surgery.

Exclusions:
No exclusions.

Outcome:
98.6%

TABLE 10 LYMPH NODE DISSECTION BY INITIAL PROCEDURE TYPE (N=2128*)

Procedure Type	Yes, N (%)		No, N (%)	
Total-thyroidectomy	736	(64.6)	404	(35.4)
Hemithyroidectomy	338	(38.8)	533	(61.2)
Isthmusectomy	6	(26.1)	17	(73.9)
Redo-thyroidectomy	2	(66.7)	1	(33.3)
Completion	1	(5.0)	19	(95.0)
Nodulectomy	4	(23.5)	13	(76.5)
Subtotal-thyroidectomy	3	(60.0)	2	(40.0)
Other	26	(68.4)	12	(31.6)
Unknown	3	(27.3)	8	(72.7)
Total	**1119**	**(52.6)**	**1009**	**(47.4)**

*18 with initial procedure data with unknown lymph node dissection

Compartmental lymph node dissection can reduce the risk of recurrence and, potentially, mortality for patients where nodal disease is evident[4]. A lymph node dissection was performed in 1119 out of 2128 participants (52.6%), with 239 (21.4%) of these being classified as a therapeutic lymph node dissection.

TABLE 11 THERAPEUTIC LYMPH NODE DISSECTION (CQI5)

Variable	Total (n)	Response	Frequency (%)	
Suspicious Lymph Nodes	2317	Yes	315	(13.60)
		No	1878	(81.0)
		Unknown	124	(5.4)
Cytology Conducted	315	Yes	92	(29.2)
		No	204	(64.8)
		Unknown	19	(6.0)
Clinical lymph node involvement confirmed cytologically	92	Yes	79	(85.9)
		No	12	(13.0)
		Unknown	1	(1.1)
If yes, lateral lymph node dissection	79	Yes	72	(91.1)
		No	7	(8.9)
		Unknown	0	(0.0)
If Yes, Therapeutic Intent	71*	Yes	70	(98.6)
		No	1	(1.4)
		Unknown	1	

*One participant was unknown and were not included in the CQI calculation

Pathology

Of the 2252 participants with complete pathology information, 1848 (82.1%) had papillary carcinoma, 186 (8.3%) follicular cell carcinoma, 88 (3.9%) hürthle cell carcinoma, 53 (2.4%) medullary carcinoma, 20 (0.9%) poorly differentiated carcinoma and four (0.2%) lymphoma (Figure 9).

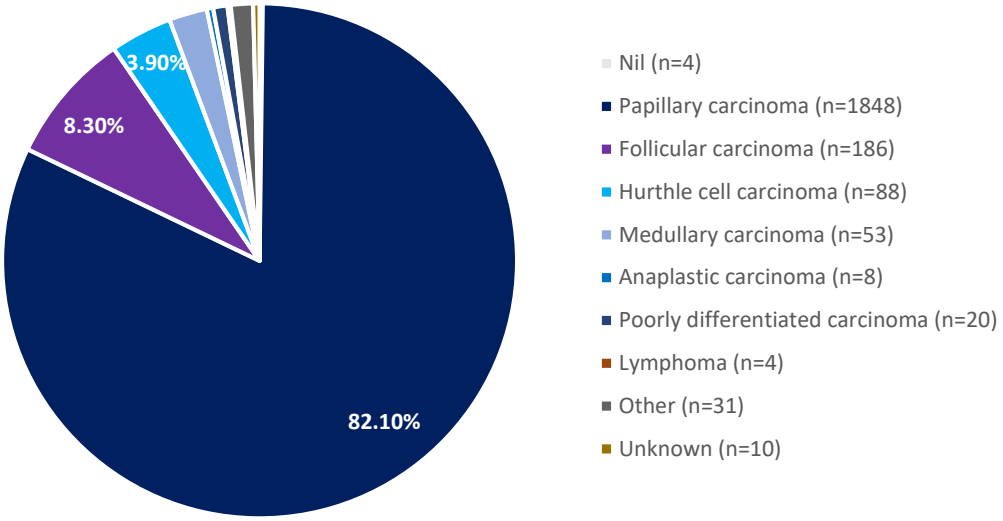


FIGURE 13 PATHOLOGY OF PRIMARY TUMOUR (N=2252)

An incidental finding of cancer was observed for 627 out of 2252 (27.8%) of participants in the registry undergoing an initial procedure, see Table 12 for additional pathology features.

TABLE 12 ADDITIONAL PATHOLOGY FEATURES

Variable	Total (n)	Response	Frequency (%)
Incidental findings of cancer	2252	Yes	627 (27.8)
		No	1404 (62.3)
		Unknown	221 (9.9)
Histological margin status	2252	Residual tumour cannot be assessed (RX)	12 (0.5)
		No residual tumour (R0)	1831 (81.3)
		Microscopic residual tumour (R1)	286 (12.7)
		Unknown	123 (5.5)
Residual tumour at surgery	2252	Residual tumour cannot be assessed (RX)	128 (5.68)
		No residual tumour (R0)	1807 (80.24)
		Macroscopic residual tumour (R2)	56 (2.49)
		Unknown	261 (11.59)
Multifocal cancer	2252	Yes	674 (29.9)
		No	1352 (60.0)
		Unknown	226 (10.1)
Lymphovascular invasion	2252	Yes	563 (25.0)
		No	1551 (68.9)
		Unknown	138 (6.1)
Extrathyroidal extension	2252	Sternothyroid muscle	319 (14.2)
		Subcutaneous soft tissues	51 (2.3)
		Prevertebral fascia	6 (0.3)
		No	1625 (72.2)
		Unknown	251 (11.0)

Of the 2252 participants with complete data, 674 (29.93%) were reported to have multifocal cancer with the site of the multifocality reported in the right lobe for 200 (29.7%) participants, in the left lobe for 135 (20.0%) participants, in both lobes for 335 (49.7%) participants and unknown in six (0.9%) participants. Extrathyroidal extension and lymphovascular invasion were observed in 376 (16.7%) and 563 (25.0%) of the 2252 participants, respectively. Microscopic residual tumour (R1) was pathologically identified in 286 out of 2252 (12.7%) participants and macroscopic residual tumour (R2) reported for 56 out of 1555 (2.5%) participants.

Metastatic Disease

Lymph node metastases were reported in 676 out of 2252 (30.0%) participants undergoing initial procedure, and distant metastases were reported in 26 out of 2252 (1.2%) participants. A single distant metastasis was reported in 19 participants, three in the bone, 13 in the lung and three not specified, two distant metastases were reported in five participants, four with one in the bone and in the lung and the other with one in the bone and the other not specified, and three distant metastases were reported in two participants, in the bone, lung and liver.

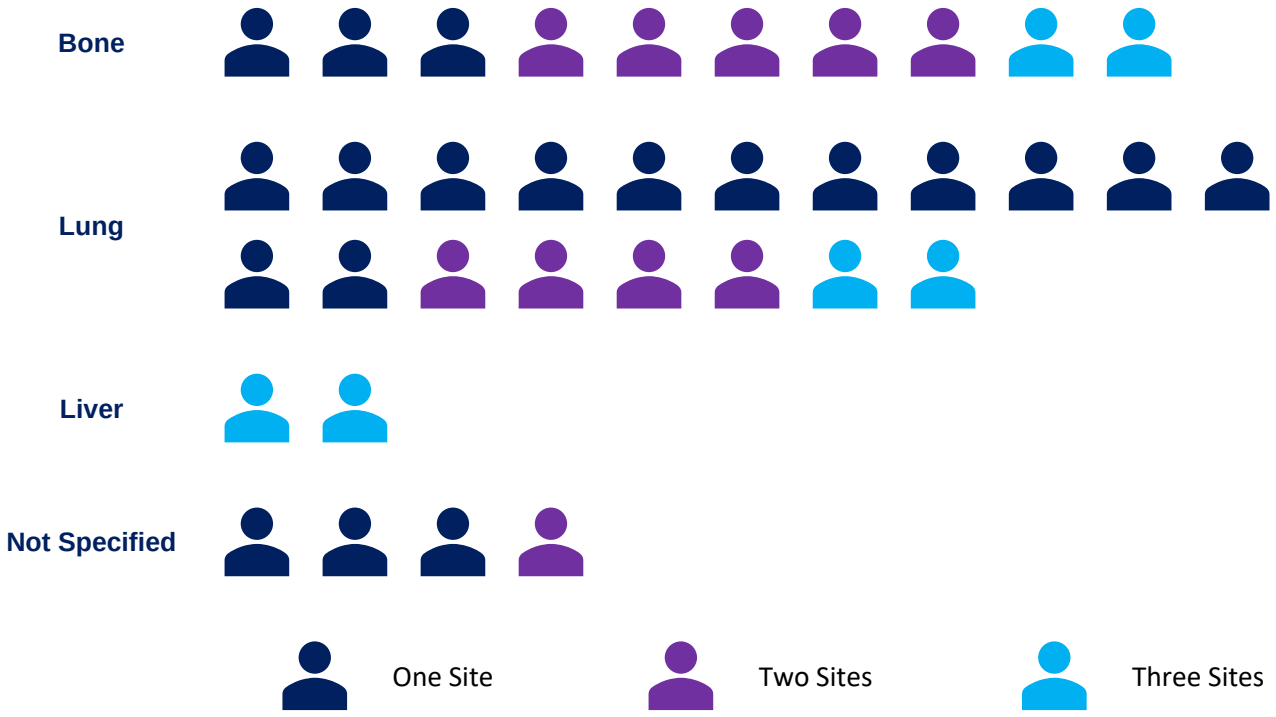


FIGURE 14 SITES OF METSTATIC DISEASE (n=26)

Recurrent Laryngeal Nerve

During surgery, the recurrent laryngeal nerve (RLN) on the right remained intact for 1770/1783 (99.3%) participants, was damaged in ten (0.5%) participants and was sacrificed to clear tumour in three (0.2%) participants. The RLN on the left remained intact for 1616/1632 (99.0%) participants, was damaged in 11 (0.7%) participant and sacrificed to clear tumour in five (0.3%) participants. During the initial procedure for 2252 participants, 1718 (76.3%) had nerve integrity monitoring used, with a loss of signal reported for the left RLN in 46 participant procedures (2.7%), in the right RLN for 45 procedures (2.6%) and in both for one procedure (data unknown for 10 participants).

TABLE 13 RLN MONITORING DURING INITIAL PROCEDURE

Variable	Total (n)	Response	Frequency (%)	
RLN Right	1783*	Intact	1770	(99.3)
		Damaged	10	(0.5)
		Sacrificed	3	(0.2)
RLN Left	1632^	Intact	1616	(99.0)
		Damaged	11	(0.7)
		Sacrificed	5	(0.3)
Nerve integrity monitoring used	2252	Yes	1718	(76.3)
		No	408	(18.1)
		Unknown	126	(5.6)

*19 patients not seen, 337 not applicable and 43 unknown.
^30 patients not seen, 450 not applicable and 43 unknown.

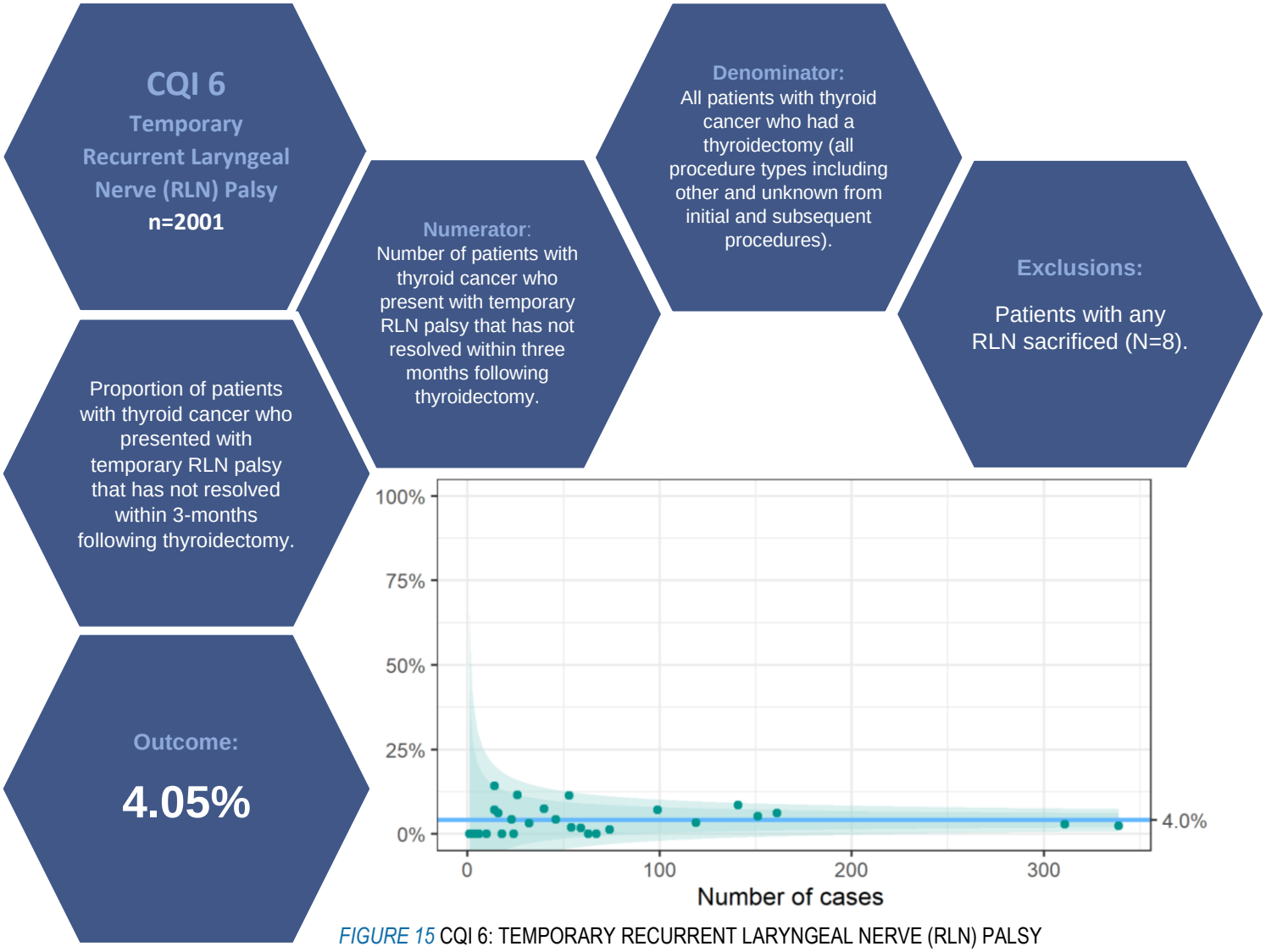


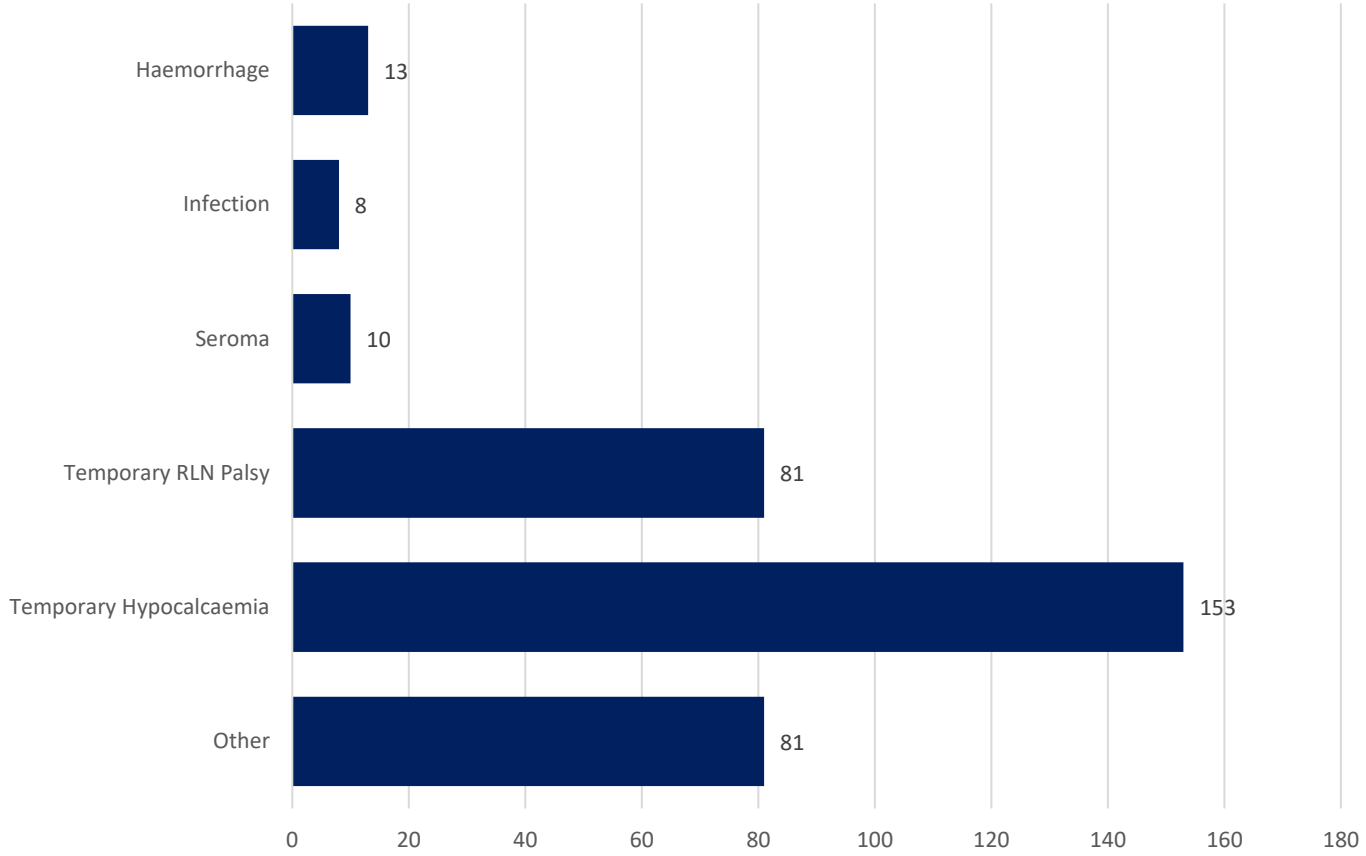
FIGURE 15 CQI 6: TEMPORARY RECURRENT LARYNGEAL NERVE (RLN) PALSY

#The denominator for this indicator is different in-text for RLN Palsy as it excludes those with RLN sacrificed.

Complications from Surgery

Complications were recorded in a small number of patients at 90-days following the initial procedure. Complications included temporary hypocalcaemia (6.8%*), temporary RLN palsy (3.6%*), haemorrhage (return to theatre within 48 hours) (0.6%*), infection (0.4%), and seroma (0.4%) (Figure 16).

FIGURE 16 SURGICAL COMPLICATIONS FOLLOWING INITIAL PROCEDURE (N=2252)



*Surgical complications in figure 16 are calculated on the ANZTCR population which differs from the calculations of CQI 6, 7 & 8

The rates of these complications are similar to those reported in the literature. The mean incidence of temporary RLN palsy for all thyroid surgery is 9.8% in the literature, while our rate in patients with cancer only was lower at 3.6%[5].

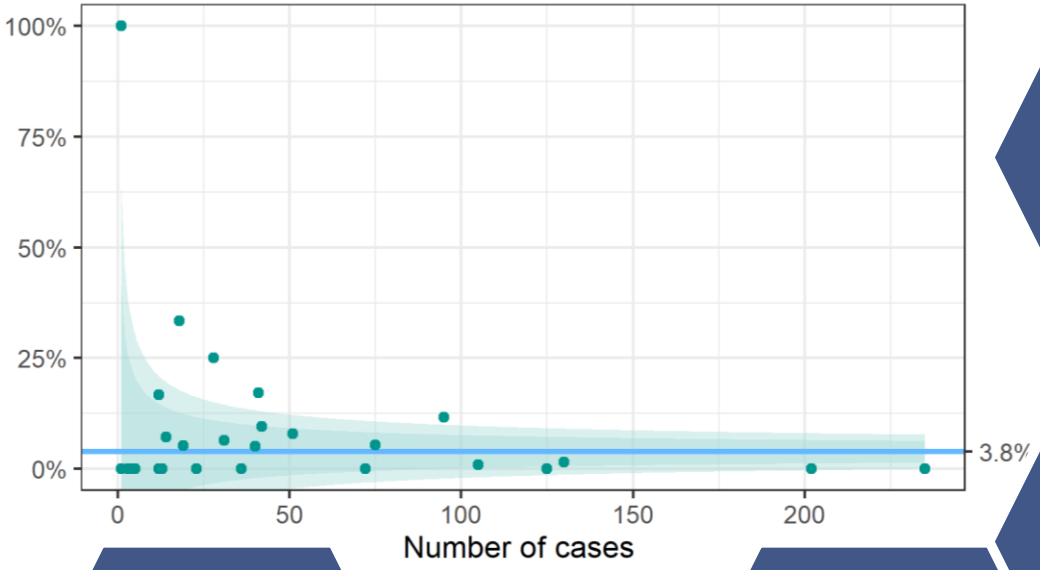
The literature has shown that temporary hypoparathyroidism, resulting in hypocalcaemia, occurs in approximately 19-38% of patients undergoing total thyroidectomy, while our rate in patients with cancer only was lower at 3.8%[6].

TABLE 14 SURGICAL COMPLICATIONS FOLLOWING PROCEDURE (CQI6, 7, 8)

Variable	Total	Response	Frequency (%)
Temporary RLN palsy (CQI6)	2001*	Yes	81 (4.05)
		No	1920 (96.6)
		Unknown	1
Temporary Hypoparathyroidism (Hypocalcaemia) (CQI 7)	1463'	Yes	56 (3.8)
		No	1407 (96.2)
		Unknown	71
Haemorrhage requiring return to theatre (CQI8)	2228^	Yes	15 (0.7)
		No	2213 (99.3)
		Unknown	23

*One participant was unknown and were not included in the CQI calculation
'71 participants were unknown and were not included in the CQI calculation
^23 participants were unknown and were not included in the CQI calculation

FIGURE 17 CQI 7: TEMPORARY HYPOPARATHYROIDISM (HYPOCALCAEMIA)



CQI 7
Temporary Hypoparathyroidism (Hypocalcaemia)
n=1463

Proportion of patients with thyroid cancer who present with persisting hypoparathyroidism at 3 months following thyroidectomy.

Numerator:
Number of patients with thyroid cancer who present with hypoparathyroidism at 3-months post-thyroidectomy.

Outcome:
3.8%

Denominator:
All patients with thyroid cancer who had a total or completion thyroidectomy.

Exclusions:
No exclusions.

CQI 8
Haemorrhage Requiring Return to Theatre
n=2228

Numerator:
Number of patients with thyroid cancer who have postoperative haemorrhage within 48-hours requiring return to theatre following thyroidectomy.

Denominator:
All patients with thyroid cancer who had a thyroidectomy (all procedure types including other and unknown).

Exclusions:
No exclusions.

Proportion of patients with thyroid cancer who underwent a thyroidectomy and had postoperative haemorrhage within 48 hours requiring return to theatre following thyroidectomy.

Outcome:
0.7%

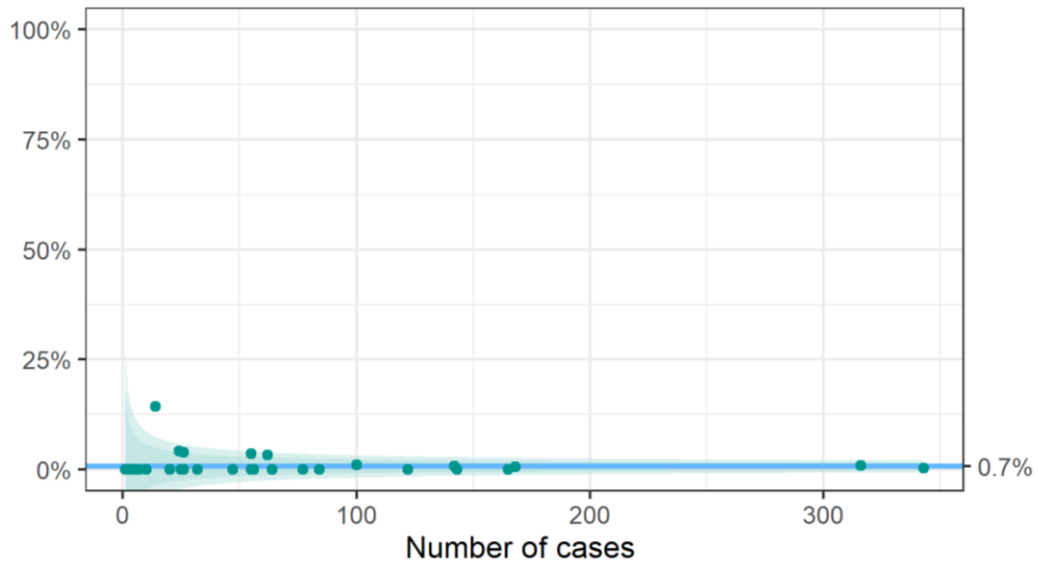


FIGURE 18 CQI 8: HAEMORRHAGE REQUIRING RETURN TO THEATRE

Hemorrhage has been reported to occur in approximately 0.6-2.9% of patients undergoing thyroid surgery. The rates of postoperative hemorrhage that has been reported in our previous annual reports has consistently been on the lower aspect of this approximated range, with our reported rate being 0.7%[8].

TABLE 15 POSTOPERATIVE HAEMORRHAGE (CQI 8) RATES PREVIOUSLY REPORTED

Year	Rate (%)
2019	0.2
2020	0.3
2021	0.3
2022	0.7

POSTOPERATIVE DETAILS CAPTURED BY THE REGISTRY

Staging & Treatment Planning

Staging to describe extent of disease progression for thyroid cancer patients uses the American Joint Committee on Cancer (AJCC) TNM Cancer Staging Manual, Eighth Edition[8].

Postoperative TNM staging for thyroid cancer, as for other cancer types, is used to provide prognostic information, enable risk-stratified description of patients, and for research purposes[4]. Of the 2221 participants with staging details recorded, 1582 (71.2%) had complete TNM staging recorded.

For participants with differentiated thyroid cancer for whom TNM staging was available (N=1373), patients were stratified by risk of structural disease recurrence according to the American Thyroid Association (ATA) guidelines[4], with 920 (67.0%) patients being classified as low risk, 409 (29.8%) as intermediate risk and 44 (3.2%) as high risk of disease recurrence.

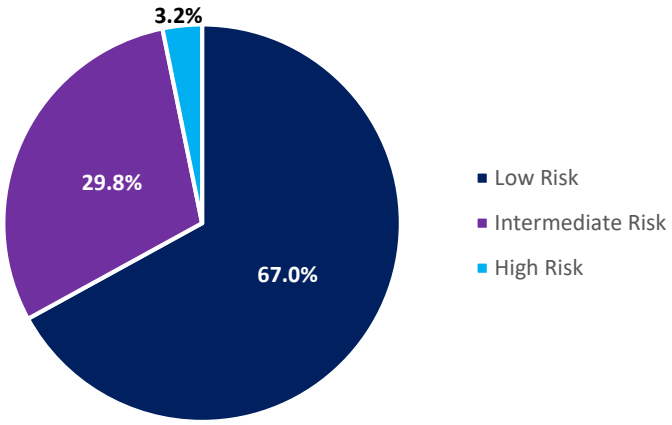


FIGURE 19 ATA RISK STRATIFICATION (N=973)

TABLE 16 TNM STAGING RECORDED (CQI9)

Variable	Total (n)	Response	Frequency (%)
TNM staging recorded	2221*	Yes	1582 (71.2)
		No	639 (28.8)
		Unknown	1

*One participants were unknown and were not included in the CQI calculation

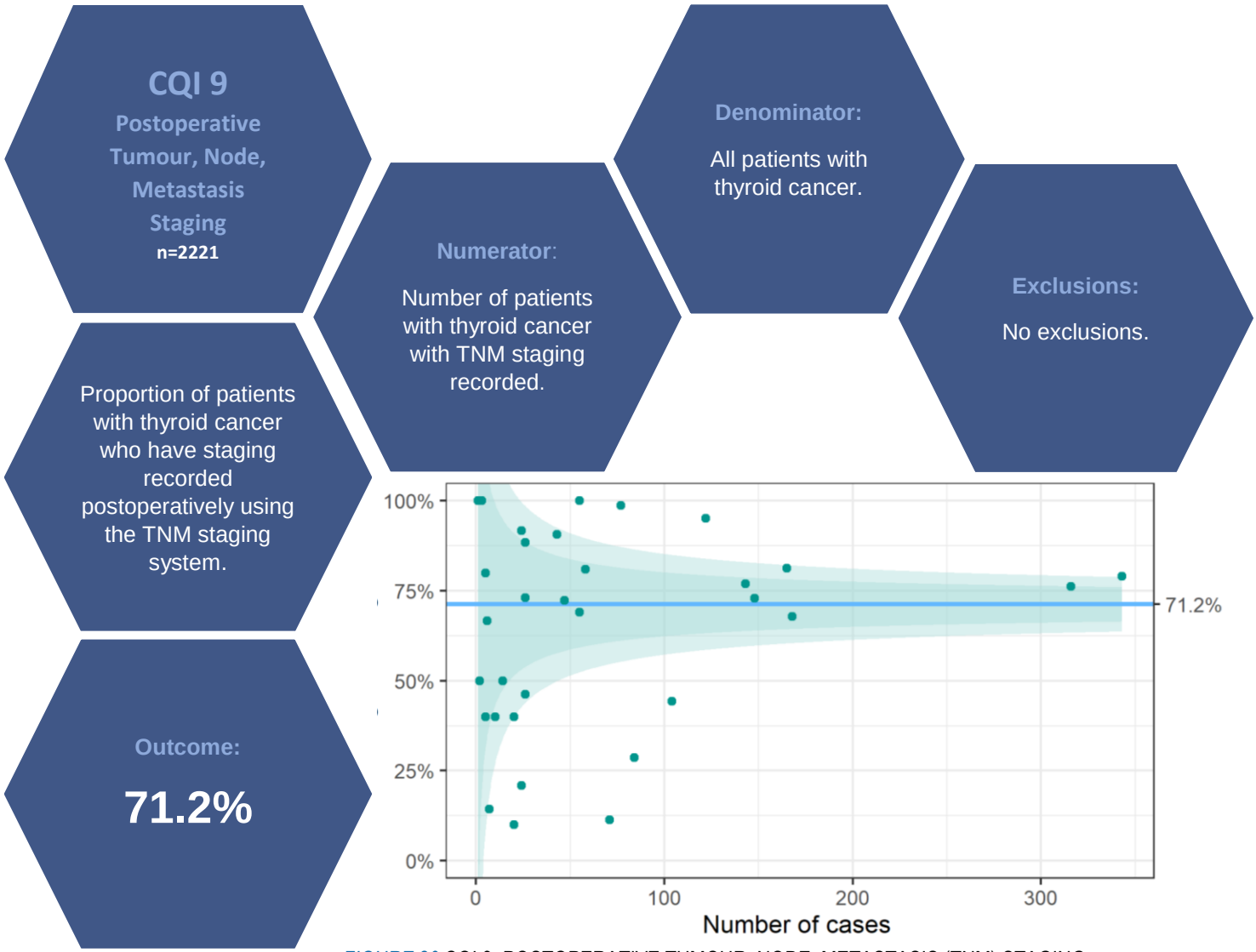


FIGURE 20 CQI 9: POSTOPERATIVE TUMOUR, NODE, METASTASIS (TNM) STAGING

Evidence suggests that patients with cancer managed by an MDT have a better outcome[4]. As a result of this, tumour-specific MDT meetings are regularly held within each site or health service. Of the 1337* participants with complete data and tumour size greater than 1 cm, 811 (60.7%) were presented at a thyroid cancer specific MDT meeting.

*259 unknown responses were not included in the calculation

TABLE 17 PRESENTATION AT MDT MEETING (CQI10)

Variable	Total (n)	Response	Frequency (%)	
Patients with tumour size <1 cm, or staged as N1a, N1b or M1	2238	Yes	1596	(71.3)
		No	544	(24.1)
		Unknown	98	(4.4)
If yes, Presented at MDT	1337*	Yes	811	(60.7)
		No	526	(39.3)
		Unknown	259	

*259 participants were unknown and were not included in the CQI calculation

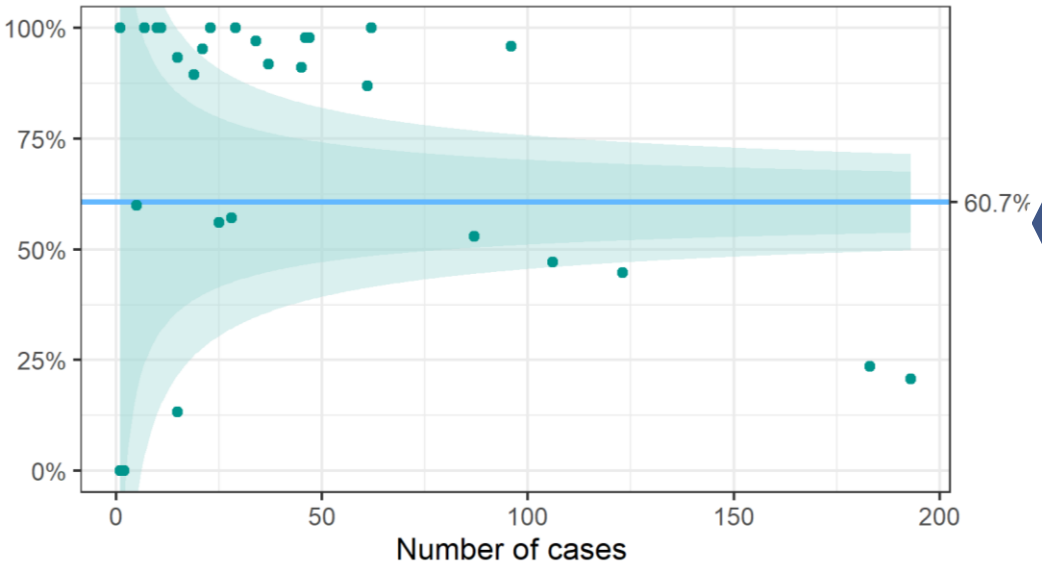


FIGURE 21 CQI 10: MULTI-DISCIPLIARY TEAM (MDT) MEETING

CQI 10
Multi-disciplinary Team (MDT) Meeting
n=1337

Proportion of patients with thyroid cancer who were presented at a tumour-specific MDT meeting.

Exclusions:
Patients with tumour size >1 cm (unless N1a, N1b or M1 staged).

Numerator:
Number of patients with thyroid cancer reviewed at a MDT meeting.

Denominator:
All patients with thyroid cancer.

Outcome:
60.7%

Supplementation & Therapy

In the early postoperative period, 1256 out of 2223 (56.5%) were receiving supplementation with calcium and 272 out of 2223 (12.2%) receiving supplementation with activated vitamin D (Table 18).

TABLE 18 POSTOPERATIVE SUPPLEMENTATION & THERAPY

Variable	Total (n)	Response	Frequency (%)	
Supplementation with calcium	2223	Yes	1256	(56.5)
		No	876	(39.4)
		Unknown	91	(4.1)
Supplementation with vitamin D	2223	Yes	272	(12.2)
		No	1853	(83.4)
		Unknown	98	(4.4)

Postoperative Treatment

Postoperative thyroglobulin (Tg) was recorded for 1106 out of 2070 (53.4%) participants. Of the 2070 participants with complete data, 718 (34.7%) had radioactive iodine (RAI) remnant ablation (RRA) following surgery. The main reasons for not having RRA were that the participant was classified as low risk according to the ATA risk stratification (72.3%) or that the participant had a micropapillary thyroid cancer (<20mm) (62.1%). For more details see Table 19 below.

TABLE 19 POSTOPERATIVE TREATMENT DETAILS

Variable	Total (n)	Response	Frequency (%)	
Postoperative Tg recorded	2070	Yes	1106	(53.4)
		No	687	(33.2)
		Unknown	277	(13.4)
RRA following thyroid surgery	2070	Yes	718	(34.7)
		No	1152	(55.7)
		Unknown	200	(9.7)
If no, reason for no RRA*	1152	PTC ≤10mm	545	(47.3)
		PTC 11-20mm	170	(14.8)
		Hemithyroidectomy only	143	(12.4)
		MTC	5	(0.4)
		ATC	2	(0.2)
		Patient age	12	(1.0)
		Low risk	833	(72.3)
		Comorbidities	26	(2.3)
		Patient declined	29	(2.5)
		Other	69	(6.0)
		Unknown	9	(0.8)

*Multiple responses were allowed, row percentages of total shown.

Research has shown that the recording serum Tg levels postoperatively, prior to RAI therapy, can assist in assessing persistent disease and the probability of recurrent disease[4]. Of the 1225* participants with differentiated thyroid cancer who underwent a total thyroidectomy, 1225 (72.6%) had serum Tg recorded postoperatively. This figure may be low as the ANZTCR is a surgeon-based registry and surgeons may not be able to access this information, or it may not be available at 90-days post-diagnosis.

Research has shown that the recording serum Tg levels postoperatively, prior to RAI therapy, can assist in assessing persistent disease and the probability of recurrent disease[4]. Of the 825* participants with differentiated thyroid cancer who underwent a total thyroidectomy, 610 (73.9%) had serum Tg recorded postoperatively. This figure may be low as the ANZTCR relies on busy clinicians to collect data, and this data may be very difficult to quickly access at the time and place the clinician enters the data.

TABLE 20 SERUM THYROIGLOBULIN (CQI11)

Variable	Total (n)	Response	Frequency (%)	
Total/completion thyroidectomy and not medullary/ anaplastic thyroid cancer	2088	Yes	1338	(64.1)
		No	711	(34.0)
		Unknown	39	(1.9)
If yes, serum Tg reported	1225*	Yes	889	(72.6)
		No	336	(27.4)
		Unknown	113	

*113 participants were unknown and were not included in the CQI calculation.

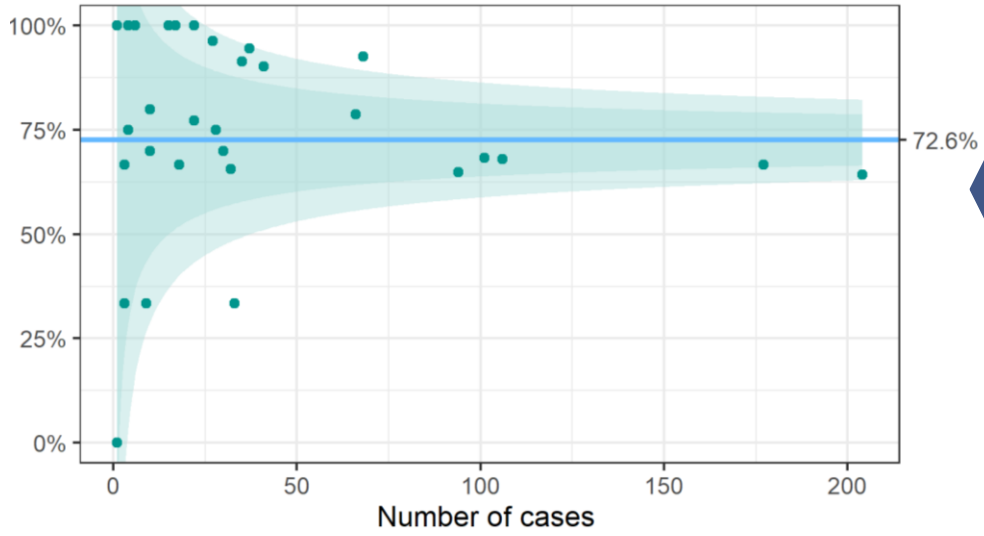


FIGURE 22 CQI 11: SERUM THYROGLOBULIN (Tg)

CQI 11
Serum Thyroglobulin (Tg)
n=1225

Proportion of patients with differentiated thyroid cancer that underwent a total (or completion) thyroidectomy and have serum Tg recorded postoperatively.

Numerator:
Number of patients that underwent total thyroidectomy for differentiated thyroid cancer and had serum Tg recorded postoperatively.

Exclusions:
No Exclusions.

Denominator:
All patients with differentiated thyroid cancer that underwent a total thyroidectomy.

Outcome:
72.6%

TABLE 21 RADIOACTIVE IODINE (CQI12)

Variable	Total (n)	Response	Frequency (%)	
High-risk differentiated thyroid cancer and a total/completion thyroidectomy	2088	Yes	30	(1.4)
		No	2058	(98.6)
		Unknown	0	(0.0)
If yes, RAI	30	Yes	30	(100.0)
		No	0	(0.0)
		Unknown	0	(0.0)

The postoperative administration of RAI after total (or completion) thyroidectomy can facilitate the detection of recurrent disease, treat persistent disease in high risk patients and improve disease-specific and disease-free survival[4]. Currently in the registry there are only 30 participants who were diagnosed with high-risk differentiated thyroid cancer and underwent a total or completion thyroidectomy, with all 30 of these participants receiving RRA therapy postoperatively. For more details please see Table 21.

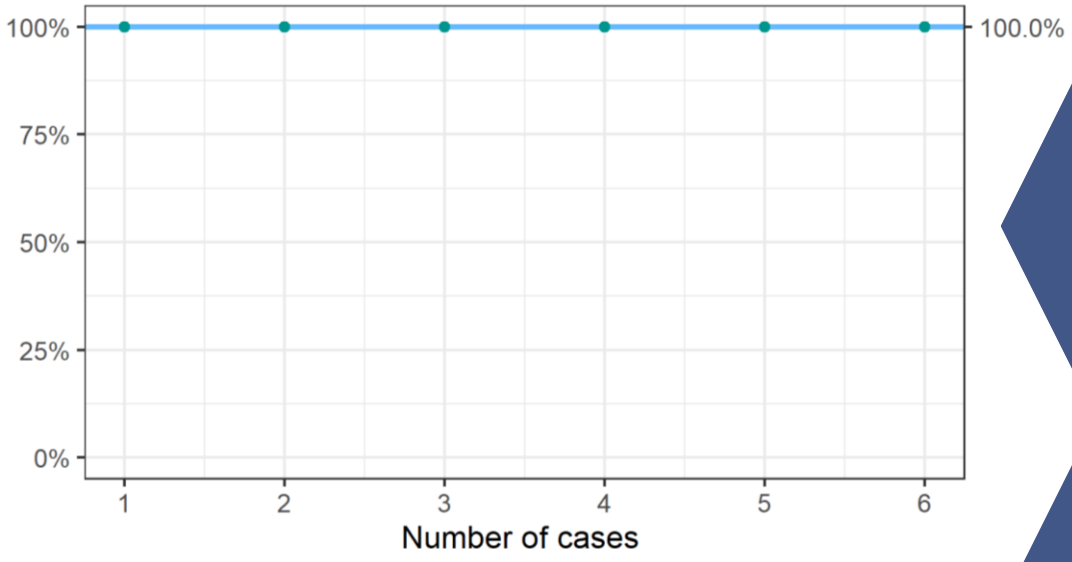


FIGURE 23 CQI 12: RADIOACTIVE IODINE (RAI)

CQI 12 Radioactive Iodine (RAI)
n=30

Proportion of patients with high-risk differentiated thyroid cancer that underwent RAI remnant ablation (RRA) following a total (or completion) thyroidectomy.

Exclusions: Patients with differentiated thyroid cancer who are classified as low and/or intermediate risk according to the ATA risk stratification.

Denominator: All patients with high-risk differentiated thyroid cancer that had total thyroidectomy.

Numerator: Number of patients with high-risk differentiated thyroid cancer that underwent a total (or near total) thyroidectomy and received RRA.

Outcome:
100%

PATIENT-REPORTED MEASURES (PRMs)

With the long-term survival of thyroid cancer rated as one of the highest for all cancers in Australia, the importance of understanding long-term outcomes and the impact on patients is paramount. Patient-reported measures can either be categorised by patient-reported outcome measures (PROMs) or patient-reported experience measures (PREMs). In July 2021, the ANZTCR launched the collections of PROMs up to twelve months post diagnosis, with extending the capture to five years post diagnosis in July 2022.

INCLUSION CRITERIA

All participants that have been recruited into the ANZTCR are eligible to receive an invitation to complete a PROMs questionnaire. Participants are excluded from receiving an invitation if they have partially opted out of the ANZTCR, require an interpreter, or have not provided an active email or mobile phone number.

Inclusion Criteria

- Patients participating in the ANZTCR

Exclusion Criteria

- Interpreter required (non-English speaking)
- Registry participants that have opted-out of PRMs
- Insufficient contact information

RESPONSE RATE

As at December 31st 2022, there were 2480 participants registered in the ANZTCR from 42 sites across NSW, QLD, VIC, SA and New Zealand. Of the 2480 participants, 1909 were eligible participants to receive the questionnaire for at least one of the time points, three, six, twelve months, two, three, four and five years post-diagnosis. Of the remaining 571 participants, 286 were not eligible for a PROMs invitation, with 57 partially opted out, 229 with insufficient contact information and 41 participants requiring an interpreter. The remaining 244 participants had not moved into an eligible timeframe to receive an invitation.

TABLE 22 RESPONSE RATE OF PATIENT-REPORTED MEASURES

Timepoints	Eligible Participants (N=1909)*	Participants (N=848)*	
3 months	359	166	(46.2)
6 months	702	304	(43.3)
12 months	909	355	(39.1)
2 years	440	148	(33.6)
3 years	324	127	(39.2)
4 years	288	88	(30.6)
5 years	69	16	(23.2)

*Participants received multiple invitations for different timepoints

Of the 1909 eligible participants, 359 were at 3-months, 702 were at 6-months, 909 were at 12-months, 440 were at two years, 324 were at three years, 228 were at four years, and 69 were at five years (see Table 22).

Overall, a total of 848 (44.4%) participants completed the PRMs, 166 out of 359 (46.2%) at three months, 304 out of 702 (43.3%) at six months, 355 out of 909 (39.1%) at twelve months, 148 out of 440 (33.6%) at two years, 127 out of 324 (39.2%) at three years, 88 out of 288 (30.6%) at four year, and 16 out of 66 (23.2%) at five years (Table 22).

PARTICIPANT CHARACTERISTICS

Of the 848 participants, 637 were female (75.1%) and 211 (24.9%) were male. The most common surgery undertaken was a total thyroidectomy at 434 (51.2%), followed by a partial or hemithyroidectomy at 319 participants (37.6%). The majority of the participants had papillary thyroid cancer (665, 78.4%), followed by follicular thyroid cancer (n=70, 7.7%) Hurthle cell carcinoma (24, 2.8%) and medullary thyroid cancer (n=21, 2.5%)

TABLE 23 PATIENT-REPORTED MEASURES PARTICIPANT CHARACTERISTICS

Characteristic	Category	Total	n (%)
Sex (N=848)	Male	211	(24.9)
	Female	637	(75.1)
State/Country of Residence (N=848)	VIC	162	(19.1)
	NSW	536	(63.2)
	QLD	119	(14.0)
	SA	22	(2.6)
	TAS	2	(0.2)
	NT	2	(0.2)
	ACT	3	(0.4)
	New Zealand	2	(0.2)
Cancer Type (N=848)	Papillary carcinoma	665	(78.4)
	Follicular carcinoma	70	(8.3)
	Hurthle cell carcinoma	24	(2.8)
	Medullary carcinoma	21	(2.5)
	Anaplastic Carcinoma	0	(0.0)
	Poorly differentiated carcinoma	8	(0.9)
	Lymphoma	1	(0.1)
	Other	55	(6.5)
Cancer Stage (N=848)	Low risk	359	(42.3)
	Intermediate risk	152	(17.9)
	High risk	16	(1.9)
Type of Surgery (N=848)	Total thyroidectomy	434	(51.2)
	Partial/hemi-thyroidectomy	319	(37.6)
	Nodulectomy	7	(0.8)
	Sub-total thyroidectomy	3	(0.4)
	Isthmusectomy	12	(1.4)
	Redo thyroidectomy	1	(0.1)
	Completion thyroidectomy	10	(1.2)
	Other	62	(7.3)
Radioactive Iodine (RAI) administered (N=848)	Yes	259	(29.6)
	No	411	(70.4)
	Unknown	15	(1.8)
Lymph node (LN) dissection (N=848)	Yes	417	(49.2)
	No	322	(39.2)
	Unknown	99	(11.6)

QUESTIONNAIRES

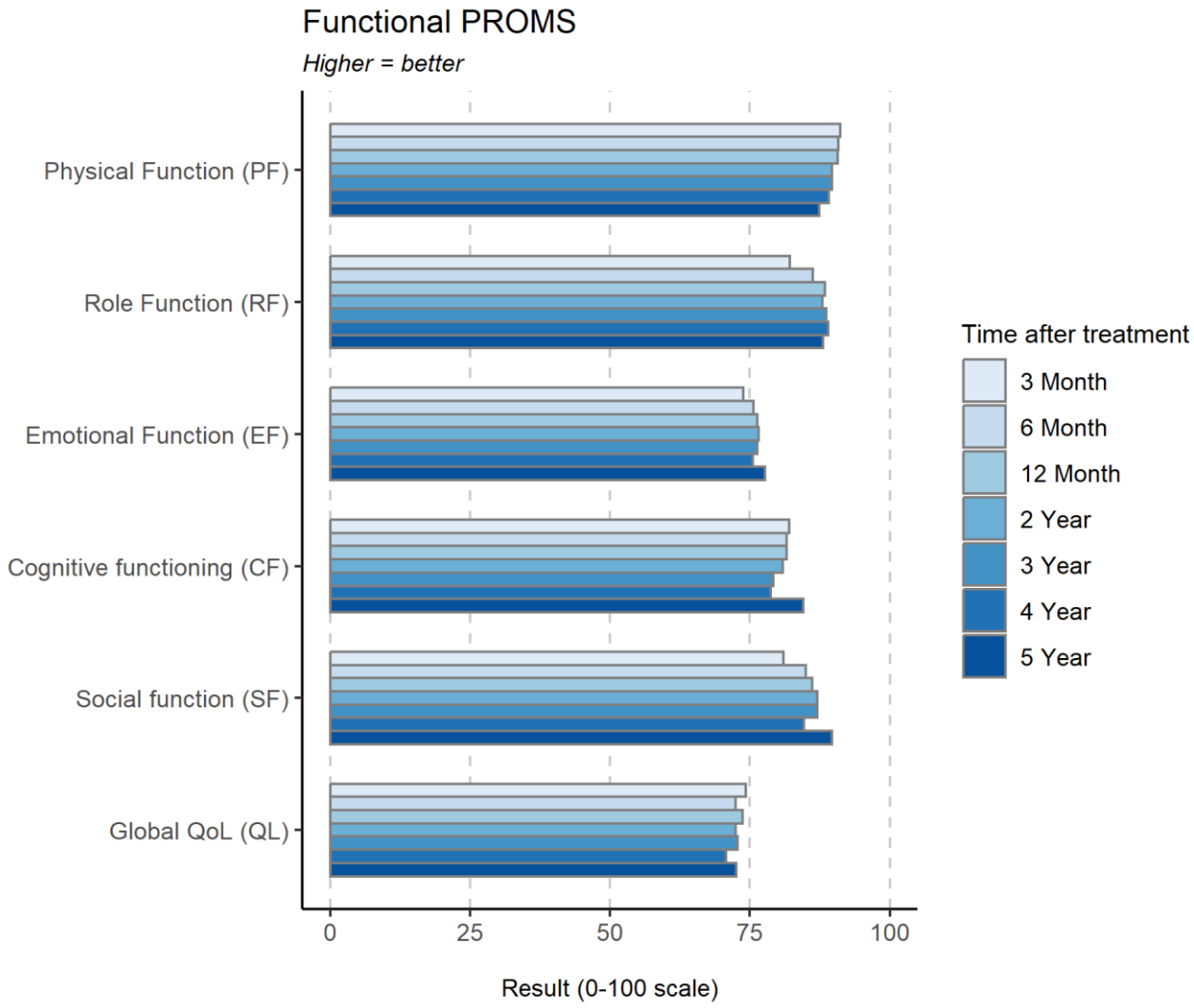
The ANZTCR has implemented a combination of two questionnaires to measure the post-surgical quality of life of thyroid cancer patients. We have chosen to implement a combination of two surveys, the EORTC QLQ-C30 and the thyroid cancer specific addition, the THY34.

QUALITY OF LIFE

Participants were asked to select from a Likert scale from 1 to 4, where 1 was 'not at all, and 4 was 'very much'. All of the scores range from 0-100. For functioning domains, a score closer to 100 suggests higher functioning, whereas a high score for the symptom domain represents higher level of symptom burden.

The overall quality of life (QOL) was generally good with scores ranging between 70 and 75 out of 100. The median scores at each timepoint are 74.3 (±20.3) at three months, 72.5 (±20.3) at six months, 73.7 (±19.9) at twelve months, 72.5 (±18.7) at two years, 72.8 (±20.2) at three years, 70.7 (±22.6) at four years, and 72.6 (±21.4) at five years.

FUNCTIONAL MEASURES



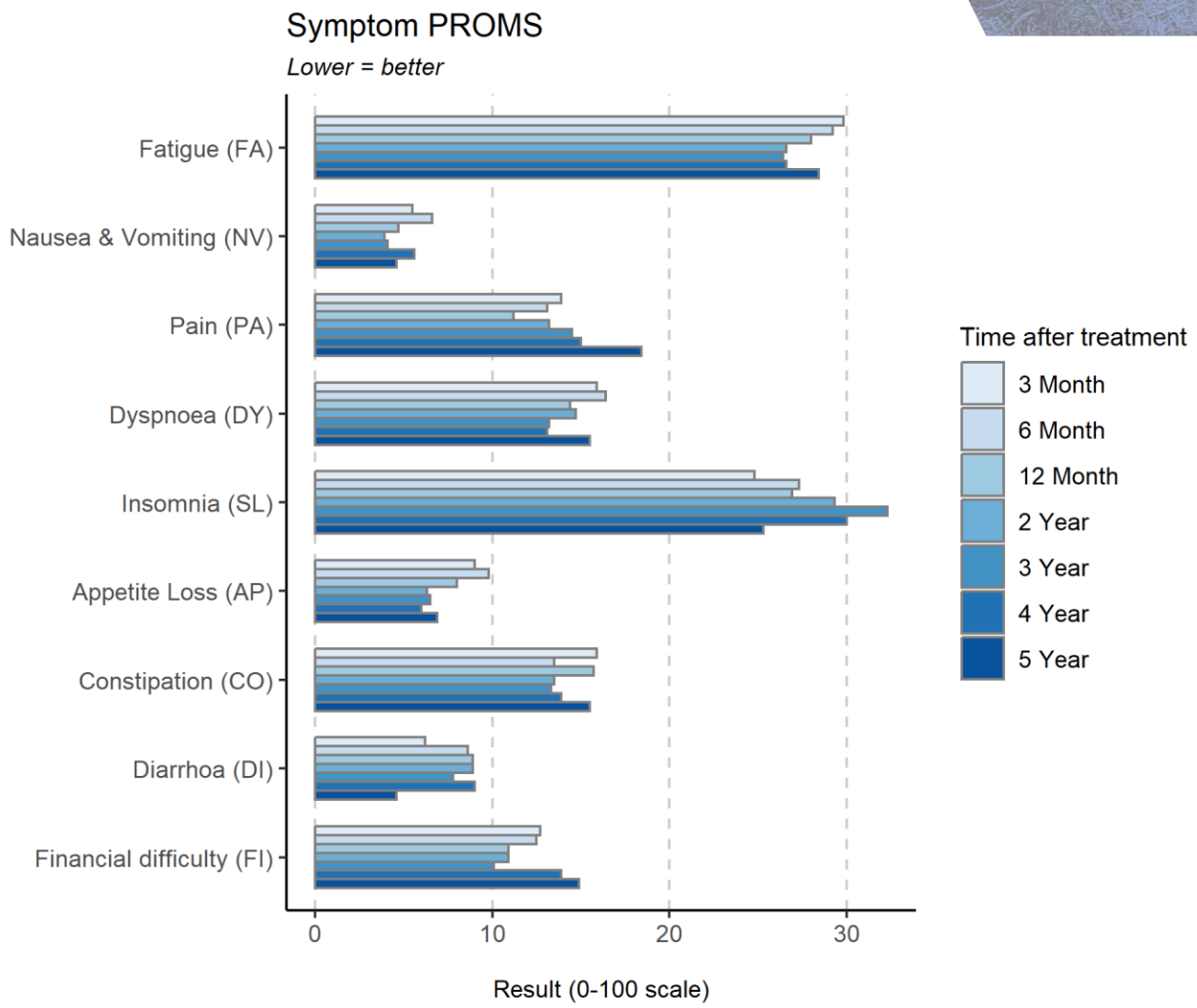
**Higher scores indicate better results*

FIGURE 24 ANZTCR PRMs: EORTC QLQC-30: FUNCTIONAL MEASURES

The functional measures aim to assess the impact that treatment has on the patient's ability to perform routine daily tasks. The functional measures include physical function, role function, emotional function, cognitive function and social function.

Overall, scores for functioning were high, with the highest functioning scores being physical functioning, role functioning, and social functioning. The lowest functioning scales were emotional functioning and cognitive functioning.

SYMPTOM MEASURES



**Lower scores indicate better results*

FIGURE 25 ANZTCR PRMs: EORTC QLQC-30: SYMPTOM MEASURES

The symptom measures aim to assess the impact that effects of the treatment have on the patient's day to day life. The symptom measures include fatigue, nausea & vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulty.

Scores for the symptom scales were generally low indicating low symptom burden in these participants. The symptom scales that had the highest overall scores, indicating greater burden to participants were fatigue and insomnia. The lowest symptom scales, indicating a lower burden to participants were nausea & vomiting, appetite loss, diarrhoea, pain, dyspnoea, constipation and financial difficulty.

THYROID SPECIFIC QUALITY OF LIFE MEASURES

The THY34 aims to specifically target measures that relate directly to thyroid cancer treatment and surgery. The measures include fatigue, discomfort around the head & neck, voice concerns, hair problems, swallowing, dry mouth, altered temperature tolerance, body image concerns, restlessness, shoulder functioning, fear, joint pain, tingling or numbness, cramps, concern about important others, impact on job or education and social support.

The EORTC-QLQ-C30 and THY34 scores as well as the distribution of the mean and standard deviation of the functioning and symptom domains are shown in appendix I.

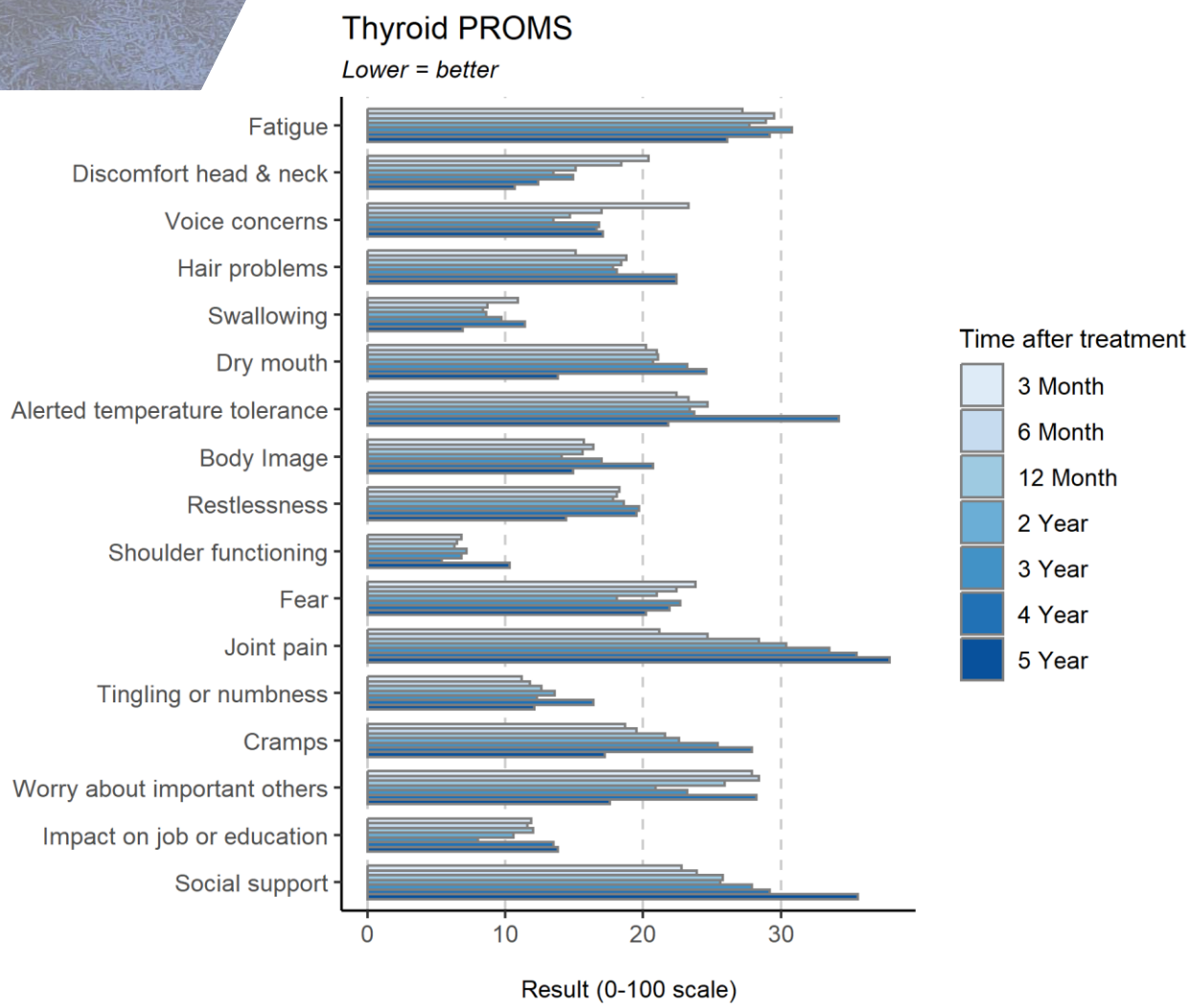


FIGURE 26 ANZTCR PRMs: EORTC THY-34: FUNCTION & SYMPTOM MEASURES

EVALUATION SURVEY

Of the 848 participants who completed the PRMs, 666 participants completed the evaluation survey giving a response rate of 78.5%. With the evaluation survey collected at every timepoint, from the 666 participants, there was a total of 801 survey responses.

Responses to the survey were generally positive, see Table 24 below. Across all timepoints, the overwhelming response was that participants found the PRMs “very easy” (88.5%) to complete and the instructions “very easy” (93.4%) to follow. Similarly, 735 (91.8%) responses found the length of the questionnaire to be appropriate and overall, participants were either satisfied (403, 50.3%) or very satisfied (222, 27.7%) with the questionnaire.

The vast majority stated they would prefer to complete the questionnaire online rather than over the phone or via hardcopy (739 or 92% of responses). In terms of how frequently the participants would want to complete the questionnaire, responses were quite varied. In the timepoints closer to surgery, responses indicated the wish for more frequent questionnaires, with 47 responses (43.1%) at three months post-surgery selecting every three months. The further away from the surgery date the participant is, the more infrequent they would prefer the questionnaires, with a six months frequency at six months post-surgery (81, 49.4%) and then yearly from twelve months (114, 40.9%), two years (85, 65.7%), three years (78, 65.5%), four years (60, 69.8%) and five years (20, 83.3%) post-surgery.

A sizable proportion of the participants (561, 70.0%) would be happy for their responses to the PRMs to be provided to their doctors, with 169 (21.1%) not wanting their responses to be shared with their doctors and 62 (7.7%) unsure.

Of the participants who would be happy to provide their PRM responses to their doctors,308 (54.9%) would like their responses provided to their general practitioner, surgeon, and endocrinologist with 78 (13.9%) wanting their responses provided to their endocrinologist only, 111 (19.8%) GP only and 53 (9.4%) surgeon only (see Table 24).

TABLE 24 PATIENT-REPORTED MEASURES PARTICIPANT EVALUATION SURVEY

PRM Evaluation Question	Responses	3 Month N=109		6 Month N=164		12 Month N=279		2 Year N=129		3 Year N=119		4 Year N=86		5 Year N=24		Total N=801	
		N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
How easy was it to complete the questionnaire?	Very Easy	100	(91.7)	144	(87.8)	249	(89.2)	114	(88.4)	107	(89.9)	73	(84.9)	22	(91.7)	709	(88.5)
	Somewhat Easy	6	(5.5)	14	(8.5)	23	(8.2)	10	(7.8)	8	(6.7)	10	(11.6)	1	(4.2)	66	(8.2)
	Neither Easy nor Hard	2	(1.8)	4	(2.4)	3	(1.1)	2	(1.6)	4	(3.4)	2	(2.3)	1	(4.2)	16	(2.0)
	Somewhat Difficult	1	(0.9)	1	(0.6)	2	(0.7)	1	(0.8)	0	(0.0)	0	(0.0)	0	(0.0)	4	(0.5)
	Very Difficult	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Were the instructions provided easy to follow?	Very Easy	101	(92.7)	144	(87.8)	253	(90.7)	117	(90.7)	140	(87.4)	74	(86.0)	20	(83.3)	748	(93.4)
	Somewhat Easy	8	(7.3)	16	(9.8)	21	(7.5)	7	(5.4)	10	(8.4)	8	(9.3)	3	(12.5)	65	(8.1)
	Neither Easy nor Hard	0	(2.5)	3	(1.8)	2	(0.7)	3	(2.3)	2	(1.7)	4	(4.7)	1	(4.2)	15	(1.9)
	Somewhat Difficult	0	(0.0)	0	(0.0)	2	(0.7)	1	(0.8)	2	(1.7)	0	(0.0)	0	(0.0)	5	(0.6)
	Very Difficult	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
How would you rate the length of the questionnaire?	Too Short	0	(0.0)	7	(4.3)	7	(2.5)	3	(2.3)	2	(1.7)	3	(3.5)	1	(4.2)	23	(2.9)
	About Right	105	(96.3)	151	(92.1)	252	(90.3)	120	(93.0)	114	(95.8)	77	(89.5)	21	(87.5)	735	(91.8)
	Too Long	3	(2.8)	2	(1.2)	9	(3.2)	2	(1.6)	2	(1.7)	3	(3.5)	1	(4.2)	19	(2.4)
	Unsure	1	(0.9)	4	(2.4)	7	(2.5)	2	(1.6)	1	(0.8)	3	(3.5)	1	(4.2)	18	(2.2)
How often would you prefer to complete the questionnaire?	Every month	11	(10.1)	18	(11.0)	15	(5.4)	0	(0.0)	1	(0.8)	1	(1.2)	0	(0.0)	35	(4.4)
	Every 3 month	47	(43.1)	39	(23.8)	53	(19.0)	11	(8.5)	8	(6.7)	4	(4.7)	0	(0.0)	115	(14.4)
	Every 6 month	27	(24.8)	81	(49.4)	86	(30.8)	28	(21.7)	28	(23.5)	16	(18.6)	3	(12.5)	242	(30.2)
	Yearly	21	(19.3)	25	(15.2)	114	(40.9)	85	(65.7)	78	(65.5)	60	(69.8)	20	(83.3)	382	(47.7)
	Other	3	(2.8)	1	(0.6)	8	(2.9)	1	(0.8)	3	(2.5)	4	(4.7)	0	(0.0)	17	(2.1)
How would you prefer to complete the questionnaire?	Online	102	(93.6)	150	(91.5)	255	(91.4)	121	(93.8)	111	(93.3)	82	(95.3)	20	(83.3)	739	(92.3)
	Telephone	1	(0.9)	2	(1.2)	4	(1.4)	2	(1.6)	0	(0.0)	0	(0.0)	0	(0.0)	8	(1.0)
	Hardcopy	1	(0.9)	6	(3.7)	6	(2.2)	2	(1.6)	2	(1.7)	0	(0.0)	1	(4.2)	17	(2.1)
	No preference	5	(4.6)	5	(3.0)	11	(3.9)	3	(2.3)	5	(4.2)	4	(4.7)	3	(12.5)	31	(3.9)
How would you feel about providing the responses to doctors in the future?	Yes	81	(74.3)	125	(76.2)	194	(69.5)	91	(70.5)	82	(68.9)	54	(62.8)	15	(62.5)	561	(70.0)
	Unsure	5	(4.6)	9	(5.5)	25	(9.0)	10	(7.8)	5	(4.2)	12	(14.0)	1	(4.2)	62	(7.7)
	No	23	(21.1)	30	(18.3)	57	(20.4)	27	(20.9)	29	(24.4)	19	(22.1)	7	(29.2)	169	(21.1)
If Yes, who would you like to receive the responses to your questionnaire?	GP	14	(17.3)	25	(20.0)	28	(14.4)	22	(24.2)	19	(23.2)	11	(20.4)	6	(40.0)	111	(19.8)
	Surgeon	9	(11.1)	18	(14.4)	19	(9.8)	4	(4.4)	9	(11.0)	2	(3.7)	1	(6.7)	53	(9.4)
	Endocrinologist	10	(12.3)	11	(8.8)	29	(14.9)	19	(20.9)	10	(12.2)	8	(14.8)	1	(6.7)	78	(13.9)
	All of the above	47	(58.0)	70	(56.0)	113	(58.2)	43	(47.3)	43	(52.4)	33	(61.1)	6	(40.0)	308	(54.9)
Overall, how would you rate your satisfaction with the questionnaire?	Very dissatisfied	2	(1.8)	7	(4.3)	13	(4.7)	1	(0.8)	4	(3.4)	1	(1.2)	0	(0.0)	26	(3.2)
	Dissatisfied	1	(0.9)	1	(0.6)	2	(0.7)	2	(1.6)	1	(0.8)	2	(2.3)	0	(0.0)	8	(1.0)
	Neutral	15	(13.8)	27	(16.5)	47	(16.8)	18	(14.0)	25	(21.0)	15	(17.4)	4	(16.7)	136	(17.0)
	Satisfied	60	(55.0)	83	(50.6)	142	(50.9)	59	(45.7)	60	(50.4)	45	(52.3)	14	(58.3)	403	(50.3)
	Very Satisfied	31	(28.4)	43	(26.2)	74	(26.5)	48	(37.2)	29	(24.4)	23	(26.7)	5	(20.8)	222	(27.7)

ASSOCIATED STUDIES

IMPACT OF DELAYED TREATMENT DUE TO COVID-19

Project Lead(s): A/Professor Anthony Glover, Dr Brooke Nickel, Dr Liane Ioannou, Bianka D'souza

Aims

The overall aim of this research is to provide an Australian-based perspective on the impact of COVID-19 on the diagnosis and treatment of patients with thyroid cancer in Australia. This will be addressed using a two-phase approach. Phase I will focus on the qualitative interviewing of patients who experienced delayed diagnosis or treatment due to COVID-19. Phase II will quantitatively explore the impact of COVID-19 on patterns of treatment for patients diagnosed with thyroid cancer. It is hypothesised that diagnosis and both surgical and postsurgical treatment will be significantly delayed due to COVID-19 and that, subsequently, these delays will negatively impact on patients with thyroid cancer in Australia. This research may provide an insight into the impact of diagnosis and treatment delays on patients with thyroid cancer. The findings of this research may also improve our understanding of how delayed thyroid cancer treatments can be clinically managed in the future.

Methods

Phase I

Semi-structured interviews were conducted with people diagnosed with thyroid cancer who experienced delayed diagnosis or treatment during COVID-19. The data was analysed using the thematic framework analysis, and reported using the Consolidated Criteria for Reporting Qualitative Research (COREQ).

Phase II

A data access request was submitted to the ANZTCR steering committee to allow access to de-identified registry data for analysis. Data was extracted from the ANZTCR for all participants over the age 18 years who were not diagnosed with NIFT-P from 2017-2020. The data was analysed using a Chi-squared test, with a Benjamini-Hochberg procedure, and a Wilcoxon rank-sum (Mann-Whitney) test for the statistical analysis.

Conclusions

This research indicates an increased burden of anxiety on patients with thyroid cancer who experienced delayed diagnosis and/or treatment during COVID-19, however further research is required to assess the clinical impact of possible disease progression to patients impacted by COVID-19 delays.

Output

- A manuscript on the qualitative study (Phase I) is under review at the Journal of American Medical Association (JAMA) Otolaryngology.
- A manuscript on the quantitative study (Phase II) is currently in preparation.
- A manuscript will be prepared for a systematic review on the impact of delayed treatment for patients with thyroid cancer.

THYROID CANCER HAS SIMILAR RATES OF PRESENTATION FOR SYMPTOMATIC AND ADVANCED DISEASE FOR MEN AND WOMEN: ANALYSIS FROM THE ANZTCR

Project Lead(s): Tong CW, Bhimani N, Ioannou L, Serpell J, Glover AR

Purpose

Thyroid cancer has a higher rate of diagnosis in women than men. However, not much is known regarding the percentage of symptomatic detection versus incidental detection. U.S. data from The Surveillance, Epidemiology, and End Results (SEER) showed that the ratio of detection of subclinical thyroid cancer on autopsy approaches 1:1 in women to men, and that aggressive subtypes of thyroid cancer is also similar between both genders. In this project we sought to examine the relationship of thyroid cancer diagnosis by presentation and stage between women and men.

Methodology

Data from Australian & New Zealand Thyroid Cancer Registry (ANZTCR) from 2017-2022 was analysed.

Results

In this study, there were 1799 participants with confirmed thyroid cancer on pathology, 27% (480) were males and 73% (1319) were females. Symptomatic presentation of differentiated thyroid cancers was similar between genders with 20% of males and 25% of females with thyroid cancer presenting with thyroid related symptoms (P=0.07), while 43% males and 40% females were asymptomatic (P=0.169). There were equal numbers of medullary, anaplastic cancers and PDTC in both men and women. Furthermore, 62% of incidental tumours are found to be small (<20mm), 58% in males compared to 64% females (P<0.001).

Conclusion

These findings show that symptomatic detection and advanced thyroid cancers have a more equal sex distribution challenging the belief that women are more likely to develop thyroid cancer. Further research to understand causes of increased diagnosis in women are important to understand and improve patterns of care for thyroid cancer patients.

Output

- Presented as oral abstract at RACS ASC,
- Manuscript reviewed by *Lancet Regional Health Western Pacific*
- In revision for submission to *World Journal Surgery*

RURAL-URBAN DISPARITIES IN THYROID CANCER STAGING AT PRESENTATION: INSIGHTS FROM AN AUSTRALIAN CONTEXT

Project Lead(s): Zihao Yang, Chai Tong, Nazim Bhimani, Christine O'Neill, Christine Lai, Jonathan Serpell, Anthony Glover

Background

Thyroid cancer has seen the largest increases in the incidence of any cancer in Australia over the last several decades. Rural patients are known to have reduced access to healthcare and may have different thyroid cancer presentation rates. We examined the relationship between thyroid cancer diagnosis and patient rurality.

Design, patients, measurements

Data from the Australia and New Zealand Thyroid Cancer Registry (ANZTCR) from 2017-2022 were analysed, stratifying patient postcodes into rurality groups using the Australian Statistical Geography Standard (ASGS). The American Thyroid Association (ATA) guidelines defined risk categories and treatment adequacy. Statistical analysis assessed demographic, clinical, and management differences.

Results

Among 1,766 patients included, 70.6% were metropolitan (metro), and 29.4% were non-metropolitan (non-metro). Non-metro patients were older at diagnosis (median 56.0 vs. 51.0 years), presented with more advanced T stage (Stage II-IV, 41.9% vs. 34.9%, p=0.005), cancers larger than 4cm (14.3% vs. 10.3%, p=0.016), and advanced AJCC stage (Stage II-IV, 18.6% vs. 14.6%, p=0.038). Diagnostic differences included more CT and PET scans in non-metro patients and more fine-needle aspirations in metro patients. No significant differences in treatment adequacy were observed when defined by ATA guidelines.

Conclusion

Non-metropolitan patients in the registry present with more advanced thyroid cancer, possibly due to differences in healthcare access. There was no different in treatment adequacy for patients treated in registry centres. Further research should assess long-term survival outcomes and influencing factors. Understanding the impact on patient outcomes and addressing healthcare access barriers can optimize thyroid cancer care in diverse geographic regions.

Output

- Presented as oral abstract at NSW Cancer Conference
- Manuscript currently been finalised for submission to *Clinical Endo*

ACADEMIC OUTPUTS

PUBLICATIONS

Ioannou, L., Serpell, J., Dean, J., Bendinelli, C., Gough, J., Lisewski, D., Miller, J., Meyer-Rochow, W., Sidhu, S., Topliss, D., Walters, D., Zalcberg, J., Ahern, S. Development of a Bi-National Thyroid Cancer Clinical Quality Registry: A Protocol Paper. *BMJ Open*; 9: bmjopen-2018-023723. Doi: 10.1136/bmjopen-2018-023723

PRESENTATIONS

Ioannou, L., Serpell, J., Bendinelli, C., Walters, D., Gough, J., Lisewski, D., Meyer-Rochow, W., Miller, J., Topliss, D., Fleming, B., Farrell, S., Kid, A., Kollias, J., Sywak, M., Aniss, A., Fenton, L., Ghusn, D., Harper, S., Popadich, A., Stringer, K., Watters, D., Ahern, S. Development of a Core Set of Clinical Indicators to Measure Quality of Care for Early Thyroid Cancer Management: A Modified-Delphi Approach. Royal Australian College of Surgeons (RACS) 88th Annual Scientific Congress (ASC), Bangkok, Thailand (6-10 May 2019) (Oral Presentation).

Ioannou, L., Serpell, J., Bendinelli, C., Walters, D., Gough, J., Lisewski, D., Meyer-Rochow, W., Miller, J., Topliss, D., Fleming, B., Farrell, S., Kiu, A., Kollias, J., Sywak, M., Aniss, A., Fenton, L., Ghusn, D., Harper, S., Popadich, A., Stringer, K., Watters, D., Ahern, S. Development of a Core Set of Clinical Indicators to Measure Quality of Care for Thyroid Cancer: A Modified-Delphi Approach. A verbal presentation at the Victorian Integrated Cancer Services (VICS) Conference, Melbourne, Australia (8-10 May 2019) (Oral Presentation).

Serpell, J., Ioannou, L., Greenhill, E., Bendinelli, C., Walters, D., Gough, J., Lisewski, D., Meyer-Rochow, W., Miller, J., Topliss, D., Fleming, B., Farrell, S., Kiu, A., Kollias, J., Sywak, M., Aniss, A., Fenton, L., Ghusn, D., Harper, S., Popadich, A., Stringer, K., Watters, D., Ahern, S. Development of the Australian and New Zealand Thyroid Cancer Registry. A verbal presentation at the 8th Multidisciplinary Update on Thyroid and Parathyroid Surgery, Noosa, Australia (14-16 November 2019) (Oral Presentation).

Ioannou, L., Serpell, J., Bendinelli, C., Walters, D., Gough, J., Lisewski, D., Meyer-Rochow, W., Miller, J., Topliss, D., Fleming, B., Farrell, S., Kiu, A., Kollias, J., Sywak, M., Aniss, A., Fenton, L., Ghusn, D., Harper, S., Popadich, A., Stringer, K., Watters, D., Ahern, S. Development of a Core Set of Clinical Indicators to Measure Quality of Care for Thyroid Cancer: A Modified-Delphi Approach. 88th Annual Meeting of the American Thyroid Association (ATA), Washington D.C., United States (3-7 October 2018) (Oral Presentation).

Ioannou, L., Serpell, J., Dean, J., Bendinelli, C., Gough, J., Lisewski, D., Miller, J., Meyer-Rochow, W., Sidhu, S., Topliss, D., Walters, D., Zalcberg, J., Ahern, S. Development of a Bi-National Thyroid Cancer Clinical Quality Registry. Alfred Health Research Week, Melbourne, Australia (June 2018) (Poster Presentation).

Ioannou, L., Serpell, J., Dean, J., Bendinelli, C., Gough, J., Lisewski, D., Miller, J., Meyer-Rochow, W., Sidhu, S., Topliss, D., Walters, D., Zalcberg, J., Ahern, S. Development of a Bi-National Thyroid Cancer Clinical Quality Registry. Victorian Comprehensive Cancer Centre (VCCC) Postdoctoral Symposium, Melbourne, Australia (1 June 2018) (Poster Presentation).

Ioannou, L., Serpell, J., Dean, J., Bendinelli, C., Gough, J., Lisewski, D., Miller, J., Meyer-Rochow, W., Sidhu, S., Topliss, D., Walters, D., Zalcberg, J., Ahern, S. Development of a Bi-National Thyroid Cancer Clinical Quality Registry. Royal Australian College of Surgeons (RACS) Annual Scientific Congress (ASC), Sydney, Australia (7-11 May 2018) (Oral Presentation).

FUTURE DEVELOPMENTS

BASELINE PRMS

Currently, the ANZTCR is unable to collect PRMs at baseline (i.e., time of diagnosis and/or surgery) as patients are entered into the registry at a later timepoint. Due to the nature of thyroid cancer, with the majority being diagnosed following surgery this can be a very stressful time for patients and assessing their quality of life at this time point is of extreme importance. The ANZTCR will pilot a 'PRM Postcard' that can be provides to patients by their surgeons at their pre- or postoperative consultation (as close to surgery as practicable), once a thyroid cancer diagnosis has been confirmed. The 'PRM Postcard' will contain a QR code that directs the patient to the ANZTCR patient-reported questionnaire. Informed consent is implied if the patient completes the questionnaire. The first page of the questionnaire will include demographic details in order to link the patient to their registry record.

CASE ASCERTAINMENT & QUALITY ASSURANCE

To ensure that the data collected by the registry is accurate and epidemiologically sound, the ANZTCR will be undertaking quality assurance activities to ensure records are complete for all participants. Furthermore, HIS extracts from sites will be reviewed to ensure that 100% of the eligible patients from a site are being captured.

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LIST OF ABBREVIATIONS

ACSQHC	Australian Commission on Safety and Quality in Health Care
ANZES	Australian and New Zealand Endocrine Surgeons
ANZTCR	Australian and New Zealand Thyroid Cancer Registry
ANZTCR-RCD	ANZTCR REDCap Database
ASOHNS	Australian Society of Otolaryngology Head & Neck Surgery
ATA	American Thyroid Association
CME	Continuing Medical Education
CQI	Clinical Quality Indicator
CT	Computed Tomography
ENT	Ear Nose Throat
EORTC	European Organisation for Research and Treatment of Cancer
FNA	Fine Needle Aspiration
HIS	Health Information Services
HRQoL	Health-related Quality of Life
MDT	Multi-disciplinary Team
MNG	Multinodular Goitre
MTC	Medullary Thyroid Cancer
NIFT-P	Non-Invasive Follicular Thyroid Neoplasm with papillary like features
PET	Positron Emission Tomography
PRE	Patient-reported Experience
PRM	Patient-reported Measure
PRO	Patient-reported Outcome
PTC	Papillary Thyroid Cancer
QLQ-C30	Quality of Life Questionnaire
QOL	Quality of Life
RACS	Royal Australasian College of Surgeons
RAI	Radioactive Iodine
RLN	Recurrent Laryngeal Nerve
RRA	Radioactive Iodine Remnant Ablation
Tg	Thyroglobulin
THY34	Thyroid Specific Module (Quality of Life Questionnaire)
TNM	Tumour, Node, Metastasis
TSH	Thyroid Stimulating Hormone

APPENDICES

APPENDIX A: LIST OF TABLES

APPENDIX B: LIST OF FIGURES

APPENDIX C: DATA ELEMENTS CAPTURED

Recruitment

- Patient ID
- Given Name(s)
- Surname
- Date of Birth
- Sex
- Country
- Street Address
- Suburb
- State/City
- Postcode
- Contact Number
- Email Address
- Medical Record Number
- Surgeon Name
- Site of Diagnosis
- Date of Diagnosis
- Basis of Diagnosis
- Diagnosed with only a microPTC
- Diagnosed with primary NIFT-P
- Disclosure of Diagnosis to Patient
- Vital Status
- Date of Death
- Cause of Death

Preoperative

- Interpreter Required
- Aboriginal, Torres Strait Islander Status
- Maori Status
- Presence of Comorbidities
- Medication at Diagnosis
- Thyroid Function at First Presentation
- Neck Examination
- Palpable Lymph Nodes
- Previous Exposure to Radiation
- Previous Thyroid Surgery
- Preoperative Imaging
- Presence of Suspicious Lymph Nodes
- Largest Thyroid Nodule Diameter
- Fine-Needle Aspiration
- Clinical Voice Abnormality
- Preoperative Laryngeal Exam

Procedure(s)

- Date of procedure
- Procedure Type
- Indication for Procedure
- Residual Tumour
- Lymph Node Dissection
- Lymph Node Dissection Intent
- Lymph Node Dissection Levels
- Recurrent Laryngeal Nerve
- Nerve Integrity Monitor
- Primary & Secondary Pathology
- Incidental Finding of Cancer
- Largest Tumour Diameter
- Margin Status
- Multifocal Cancer
- Lymphovascular Invasion
- Extrathyroidal Extension
- Lymph Node Metastases
- Distant Metastases
- Surgical Complications

Postoperative

- Presented at MDM
- TNM Staging
- Supplementation
- Biobank Sample
- Genetic Testing

Treatment

- Postoperative Tg
- RAI Remnant Ablation (RRA)
- Other Adjuvant Therapy

Recurrent Thyroid Disease

- Recurrent Thyroid Cancer
- Date of Recurrence
- Surgeon Name
- Hospital Name
- Diagnostic Testing
- Site of Recurrence
- Treatment for Recurrent Disease

APPENDIX D: COMMITTEES & STAFF

Steering Committee Members

Professor Jonathan Serpell	Committee Chair, Endocrine Surgeon
Professor Jeremy Millar	Radiation Oncologist
Professor John Zalcberg	Head, Cancer Research Program, Monash University
Professor Susannah Ahern	Head, Clinical Outcomes data Reporting and Research Program, Monash University
Ms Madeleine Allnutt	Australian Thyroid Foundation, Consumer Advocate (outgoing)
Dr Adam Aniss	Database Manager
Dr Cino Bendinelli	Endocrine Surgeon
Dr Daron Cope	Otolaryngologist
A/Professor Anthony Glover	Endocrine Surgeon
Dr Jenny Gough	Breast and Endocrine Surgeon
Dr Simon Harper	Endocrine and General Surgeon
A/Professor James Lee	Endocrine Surgeon
A/Professor Julie Miller	ANZES Immediate Past-President, Endocrine Surgeon
Dr Win Meyer-Rochow	Endocrine and General Surgeon
Professor Andrew Scott	Nuclear Medicine Physician
Professor Stan Sidhu	Endocrine Surgeon
A/Professor Mark Sywak	Endocrine Surgeon
Professor Duncan Topliss	Endocrinologist
Dr David Walters	Breast and Endocrine Surgeon
Dr Matti Gild	Endocrinologist, Endocrine Society if Australia
Mr Glen Ramos	Australian Thyroid Foundation, Consumer Advocate

Registry Leads

Professor Jonathan Serpell, Clinical Lead
Professor Jeremy Millar, Co-academic Lead
Professor John Zalcberg, Co-academic Lead

ANZTCR Coordinating Centre, Monash University

Dr Liane Ioannou, Research Fellow
Ms Claire Bavor, Operations Manager (Jan-May 2022)
Mr Benjamin Brown, Data Manager

APPENDIX E: LIST OF PARTICIPATING SITES & CLINICIANS

Participating Sites

VIC	Alfred Health
	Austin Health
	Barwon Health
	Cabrini Health
	Eastern Health
	Epworth Healthcare
	Linacre Private Hospital
	Monash Health
	Peninsula Health
	Peninsula Private
	St Vincent's Hospital Melbourne
	St Vincent's Private Hospital Melbourne
	The Royal Melbourne Hospital
	Western Health
NSW	Baringa Private Hospital
	Campbelltown Hospital
	Chris O'Brien Lifehouse
	Dudley Private Hospital
	Hornsby Hospital
	John Hunter Hospital
	Lake Macquarie Private Hospital
	Liverpool Hospital
	Maitland Private Hospital
	Manly District Hospital (Site closed)
	Mater Hospital, North Sydney
	Newcastle Private Hospital
	Royal North Shore Hospital
	Royal North Shore Private Hospital
	Sydney Adventist Hospital
QLD	Greenslopes Private Hospital
	Logan Hospital
	North West Private Hospital
	Redland Hospital
	St Vincent's Private Hospital Northside
	Townsville Hospital
	Wesley Hospital
SA	Flinders Medical Centre
	Royal Adelaide Hospital
	St Andrew's Hospital
	The Queen Elizabeth Hospital
NZ	Waikato Hospital
	Wellington Regional Hospital

Participating Clinicians

Dr Muzib Abdul-Razak	A/Prof Hubert Low
Dr Earl Abraham	Dr Stephanie Manning
Dr Cino Bendinelli	Dr Rick Masters
Dr Janne Bingham	Dr Sally Meade
Dr Melissa Bochner	Dr David Merenstein
Dr Alvin Cham	Dr Win Meyer-Rochow
Dr Sor Way Chan	Dr Robert Millar
Dr Michael Cheng	A/Prof Julie Miller
Dr Laura Chin-Lenn	Dr Sue Moore
Dr Joanne Chionh	Dr Joanna Morgan
Prof Jonathan Clark	Dr Teresa Nano
Dr Anthony Clifford	Dr Kevin Nguyen
Dr Tim Connolly	A/Prof Chris O'Neill
Dr Daron Cope	Prof Carsten Palme
Prof Leigh Delbridge	Dr Leo Pang
A/Prof Michael Elliot	Dr Alexander Papchristos
Dr Stephen Farrell	Dr Andrew Parasyn
Dr Linda Fenton	A/Prof Robert Parkyn
Dr Bill Fleming	Dr Siva Ravindran
Dr Christina Foley	Prof Jonathan Serpell
A/Prof Anthony Glover	A/Prof Kerwin shannon
Dr Jenny Gough	Prof Stan Sidhu
Dr Simon Grodski	A/Prof Anita Skandarajah
Dr Ronald Guevara	Dr Kate Stringer
Dr Jane Harding	A/Prof Mark Sywak
Dr Simon Harper	Dr Jason Tan
Dr Eugenia Ip	Dr Robert Tasevski
Dr Tim Iseli	Dr Leong Tiong
Dr Suren Jayaweera	Dr Cyril Tsan
Dr Andrew Kiu	Dr David Walsh
Dr Jim Kollias	Dr David Walters
Dr Russel Krawitz	Prof David Watters
Dr Christine Lai	Dr Robert Whitfield
Dr Tracey Lam	Dr James Wykes
A/Prof James Lee	Dr Meei Yeung

APPENDIX F: LIST OF DATA MANAGERS

Data Managers

Dr Adam Aniss	Royal North Shore Hospital, Endocrine Surgical Unit's Database
Dr Afsaneh Koohestani	Alfred Monash University Endocrine Surgery Database
Mr Ryan Le	Alfred Monash University Endocrine Surgery Database

APPENDIX G: LIST OF ANZTCR POLICIES & PROCEDURES

ANZTCR Policies and Procedures
Protocol
Data Dictionary
Data Access & Publication Policy
Privacy Policy
ANZTCR-RCD User Manual
Conflict of Interest Statement

APPENDIX H: ANZTCR CLINICAL QUALITY INDICATORS

Preoperative

CQI1 Proportion of patients with clinical suspicion of thyroid cancer who had a neck ultrasound prior to surgery and/or treatment.

CQI2 Proportion of patients with clinically and/or radiologically suspicious lymph nodes that underwent a biopsy to confirm malignancy before the initiation of treatment.

CQI3 Proportion of patients with suspicion of thyroid cancer that present with (subjective or objective) evidence of voice abnormality who underwent a laryngeal examination prior to surgery and/or treatment.

Surgery

CQI4 Proportion of patients with differentiated thyroid cancer who had a tumour size >4 cm or advanced disease (extrathyroidal extension and/or metastatic disease) and underwent a total thyroidectomy (one- or two-stage including completion thyroidectomy).

CQI5 Proportion of patients with thyroid cancer who undergo surgery with therapeutic compartmental lateral neck lymph node dissection due to cytological proven lateral lymph node involvement.

Surgical Complications

CQI6 Proportion of patients with thyroid cancer who presented with temporary RLN palsy that has not resolved within 3-months following thyroidectomy.

CQI7 Proportion of patients with thyroid cancer who present with persisting hypoparathyroidism at 3 months following thyroidectomy, as evidence by need for ongoing calcium and/or vitamin D.

CQI8 Proportion of patients with thyroid cancer who underwent a thyroidectomy and had postoperative haemorrhage within 48 hours requiring return to theatre following thyroidectomy.

Staging & Postoperative Treatment Planning

CQI9 Proportion of patients with thyroid cancer who have staging recorded postoperatively using the tumour, node, metastasis (TNM) staging system.

CQI10 Proportion of patients with thyroid cancer who were presented at a tumour-specific MDT meeting.

Postoperative Treatment

CQI11 Proportion of patients with differentiated thyroid cancer that underwent a total (or completion) thyroidectomy and have serum Tg recorded postoperatively.

CQI12 Proportion of patients with high-risk differentiated thyroid cancer that underwent RAI remnant ablation (RRA) following a total (or completion) thyroidectomy.

APPENDIX I: ANZTCR PROMS DATA

TABLE 25 EORTC-QLQ-C30 SCORES AT 3-, 6-, 12-MONTHS, 2-, 3-, 4-, 5-YEARS

EORTC-QLQ-C30	3 months (N=161) Mean (SD±)	6 months (N=303) Mean (SD±)	12 months (N=368) Mean (SD±)	2 years (N=185) Mean (SD±)	3 years (N=155) Mean (SD±)	4 years (N=111) Mean (SD±)	5 years (N=29) Mean (SD±)
Physical functioning*	91.2(±12.9)	90.8(±14.2)	90.7(±13)	89.7(±15.2)	89.7(±14.6)	89.1(±16.1)	87.4(±17.3)
Role functioning*	82.2(±23.3)	86.2(±22.1)	88.4(±18.8)	88(±20.4)	88.6(±20.5)	89(±21.5)	88.1(±23.1)
Emotional Functioning*	73.8(±23)	75.7(±21.7)	76.3(±20.9)	76.6(±18.9)	76.3(±19.2)	75.5(±21)	77.7(±22.5)
Cognitive functioning*	82(±20)	81.6(±20.9)	81.6(±20.6)	80.9(±19.7)	79.2(±22.6)	78.7(±22.5)	84.5(±20.9)
Social functioning*	81(±25)	85(±22.7)	86.1(±20.3)	87(±19.8)	87.1(±19.8)	84.7(±24.7)	89.7(±23.3)
Fatigue#	29.8(±21.1)	29.2(±23)	28(±21)	26.6(±21.4)	26.4(±23)	26.6(±23.9)	28.4(±23.5)
Nausea/vomiting#	5.5(±11.9)	6.6(±13.5)	4.7(±10.4)	3.9(±8.6)	4.1(±10.8)	5.6(±9.7)	4.6(±10.8)
Pain#	13.9(±19.6)	13.1(±19.4)	11.2(±17.6)	13.2(±20.4)	14.5(±21.8)	15(±25.3)	18.4(±26.5)
Dyspnoea#	15.9(±22.4)	16.4(±24)	14.4(±21.6)	14.7(±22)	13.2(±19.6)	13.1(±20.3)	15.5(±27.9)
Insomnia#	24.8(±29.3)	27.3(±29.2)	26.9(±27.7)	29.3(±26.3)	32.3(±31.9)	30(±27.7)	25.3(±24.6)
Appetite loss#	9(±19)	9.8(±20)	8(±16.6)	6.3(±15.3)	6.5(±17.4)	6(±13.6)	6.9(±16.4)
Constipation#	15.9(±24.5)	13.5(±22.1)	15.7(±24.3)	13.5(±21.8)	13.3(±23)	13.9(±21.4)	15.5(±26.4)
Diarrhoea#	6.2(±14)	8.6(±17)	8.9(±17.4)	8.9(±19.1)	7.8(±18.2)	9(±20.1)	4.6(±11.7)
Financial difficulties#	12.7(±23.3)	12.5(±23.1)	10.9(±20.4)	10.9(±19.2)	10.1(±21.3)	13.9(±24.1)	14.9(±27.6)
Global Health/QOL^	74.3(±20.3)	72.5(±20.3)	73.7(±19.9)	72.5(±18.7)	72.8(±20.2)	70.7(±22.6)	72.6(±21.4)

Footnote: *Functioning scales: A higher score out of 100 indicates higher function. #Symptom scales: A higher score out of 100 represents a higher level of symptom burden; ^QOL scales: A higher score out of 100 represents better QOL.

TABLE 26 3-, 6-, 12-MONTHS, 2-, 3-, 4-, 5-YEARS

EORTC-QLQ-THY34	3 months (N=161) Mean (SD±)	6 months (N=303) Mean (SD±)	12 months (N=368) Mean (SD±)	2 years (N=185) Mean (SD±)	3 years (N=155) Mean (SD±)	4 years (N=111) Mean (SD±)	5 years (N=29) Mean (SD±)
Social support*	27.2(±23.1)	29.5(±23.2)	28.9(±24)	27.7(±23.4)	30.8(±25.2)	29.2(±26.4)	26.1(±21.5)
Fatigue#	20.4(±20)	18.4(±19.3)	15.1(±17.5)	13.5(±15.2)	14.9(±19.1)	12.4(±16.8)	10.7(±15)
Discomfort in head/neck#	23.3(±25)	17(±23.1)	14.7(±20.2)	13.5(±20.6)	16.8(±24.4)	16.6(±19.9)	17.1(±24.1)
Voice concerns#	15.1(±23.1)	18.8(±25.4)	18.4(±26.1)	17.8(±24.5)	18.1(±25.6)	22.4(±27.2)	22.4(±32.2)
Hair problems#	10.9(±17.5)	8.7(±16.8)	8.4(±16.3)	8.6(±15.7)	9.7(±17)	11.4(±18.1)	6.9(±12.2)
Swallowing#	20.2(±24.8)	21(±25.5)	21.1(±27.5)	20.7(±27.2)	23.2(±27)	24.6(±29)	13.8(±20.9)
Dry mouth#	22.4(±28.8)	23.3(±28.6)	24.7(±29.6)	23.4(±27.7)	23.7(±28.4)	34.2(±30.6)	21.8(±25.6)
Altered temperature#	15.7(±25.3)	16.4(±24.6)	15.6(±25.7)	14.1(±25)	17(±28.4)	20.7(±29.5)	14.9(±29)
Body Image#	18.3(±21.1)	18.1(±20.1)	17.8(±21.2)	18.6(±19.9)	19.7(±20.3)	19.5(±17.8)	14.4(±23.5)
Restlessness#	6.8(±20.1)	6.5(±17.3)	6.3(±17.8)	7.2(±19.3)	6.8(±18.9)	5.4(±15.3)	10.3(±20.1)
Shoulder functioning#	23.8(±20.9)	22.4(±21)	21(±19.8)	18.1(±20.1)	22.7(±23.4)	21.9(±21.6)	20.2(±23)
Fear of recurrence#	21.2(±27.1)	24.7(±27.9)	28.4(±29)	30.4(±29.1)	33.5(±30.8)	35.5(±31.7)	37.9(±33)
Joint pain#	11.2(±17)	11.8(±17.5)	12.6(±17.2)	13.6(±18.6)	12.3(±16.5)	16.4(±18.3)	12.1(±19.9)
Tingling or numbness#	18.7(±25.3)	19.5(±23.6)	21.6(±24.7)	22.6(±24.9)	25.4(±27.2)	27.9(±30.1)	17.2(±26.2)
Cramps#	27.9(±26.4)	28.4(±26.3)	25.9(±24.6)	20.9(±23.2)	23.2(±24.1)	28.2(±29.9)	17.6(±22.9)
Worry about others#	11.9(±22.5)	11.6(±22.7)	12(±24)	10.6(±23.7)	8(±20.2)	13.5(±26.9)	13.8(±24.4)
Impact on job or education#	22.8(±24.4)	23.9(±26.5)	25.8(±26.8)	25.6(±27)	27.9(±27.5)	29.2(±28)	35.6(±32.4)

Footnote: *Functioning scales: A higher score out of 100 indicates higher function. #Symptom scales: A higher score out of 100 represents a higher level of symptom burden

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