NATIONAL CLINICAL GUIDELINES

THE DIAGNOSIS & MANAGEMENT OF HYPERTHYROIDISM IN ADULTS

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المبادئ الإرشادية السريرية لدولة قطر
NATIONAL CLINICAL GUIDELINES FOR QATAR

وزارة الصحـــــة العامـــــة
Ministry of Public Health
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Version History

Version	Status	Date	Editor	Description
1.0	Initial Version	14th December 2016	Guidelines Team	Published version.
2.0	Updated Version	28th July 2019	Guidelines Team	Updated Published Version.

Citation

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Ministry of Public Health Qatar. National Clinical Guideline: The Diagnosis and Management of Hyperthyroidism in Adults (2019).

Abbreviations

The abbreviations used in this guideline are as follows:

ATD	Anti-thyroid drug therapy
Anti-TPO-Ab	Anti-thyroid peroxidase antibodies
Anti-TRAb	Anti-TSH-receptor antibodies
CBC	Complete blood count
CT	Computed tomography
DEXA	Dual-energy x-ray absorptiometry scan
ECG	Electrocardiogram
FT3	Free tri-iodothyronine
FT4	Free thyroxine
ICU	Intensive care unit
NSAIDs	Non-steroidal anti-inflammatory drugs
T3	Tri-iodothyronine
T4	Thyroxine (tetra-iodothyronine)
TFTs	Thyroid function tests
TSH	Thyroid-stimulating hormone

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1 Information About This Guideline

1.1 Objective and Purpose of the Guideline

The purpose of this guideline is to define the appropriate diagnosis and management of hyperthyroidism in adults. The objective is to reduce inappropriate investigation, prescribing and referral of patients presenting to provider organisations in Qatar. It is intended that the guideline will be used primarily by physicians in primary care and outpatient settings.

1.2 Scope of the Guideline

This guideline covers the following aspects of care:

- Causes and clinical features of hyperthyroidism, including:
  - Graves' disease.
  - Toxic multinodular goitre.
  - Toxic adenoma.
  - Thyroiditis.
- Clinical assessment of hyperthyroidism.
- Use of thyroid function tests (TFTs) for diagnosis.
- Management of hyperthyroidism.
- Covers adults age 18 years and older in primary and secondary care settings.

Aspects of care not covered in this guideline are:

- Assessment and management of thyroid disorders in children and pregnant women.
- Management of secondary hyperthyroidism.
- Management of thyroid cancer.

1.3 Editorial Approach

This guideline document has been developed and issued by the Ministry of Public Health of Qatar (MOPH), through a process which aligns with international best practice in guideline development and localisation. The guideline will be reviewed on a regular basis and updated to incorporate comments and feedback from stakeholders across Qatar.

The editorial methodology, used to develop this guideline, has involved the following critical steps:

- Extensive literature search for well reputed published evidence relating to the topic.
- Critical appraisal of the literature.
- Development of a draft summary guideline.
- Review of the summary guideline with a Guideline Development Group, comprised of practising healthcare professionals, subject matter experts and patient representatives, from across Qatar.
- Independent review of the guideline by the National Clinical Guidelines & Pathways Committee, appointed by the MOPH, from amongst stakeholder organisations across Qatar.

Whilst the MOPH has sponsored the development of the guideline, the MOPH has not influenced the specific recommendations made within it.

1.4 Sources of Evidence

The professional literature published in the English language has been systematically queried using specially developed, customised, and tested search strings. Search strategies are developed to allow efficient yet comprehensive analysis of relevant publications for a given topic and to maximise retrieval of articles with certain desired characteristics pertinent to a guideline.

For each guideline, all retrieved publications have been individually reviewed by a clinical editor and assessed in terms of quality, utility, and relevance. Preference is given to publications that:

1. Are designed with rigorous scientific methodology.
2. Are published in higher-quality journals (i.e. journals that are read and cited most often within their field).
3. Address an aspect of specific importance to the guideline in question.

Further information about the literature search and appraisal process is included in the appendix.

1.5 Evidence Grading and Recommendations

Recommendations made within this guideline are supported by evidence from the medical literature and where possible the most authoritative sources have been used in the development of this guideline. In order to provide insight into the evidence basis for each recommendation, the following evidence hierarchy has been used to grade the level of authoritativeness of the evidence used, where recommendations have been made within this guideline.

Where the recommendations of international guidelines have been adopted, the evidence grading is assigned to the underlying evidence used by the international guideline. Where more than one source has been cited, the evidence grading relates to the highest level of evidence cited:

- **Level 1 (L1):**
  - Meta-analyses.
  - Randomised controlled trials with meta-analysis.
  - Randomised controlled trials.
  - Systematic reviews.

- **Level 2 (L2):**
  - Observational studies, examples include:
    - Cohort studies with statistical adjustment for potential confounders.
    - Cohort studies without adjustment.
    - Case series with historical or literature controls.
    - Uncontrolled case series.
  - Statements in published articles or textbooks.

- **Level 3 (L3):**
  - Expert opinion.
  - Unpublished data, examples include:
    - Large database analyses.
    - Written protocols or outcomes reports from large practices.

In order to give additional insight into the reasoning underlying certain recommendations and the strength of recommendation, the following recommendation grading has been used, where recommendations are made:

- **Recommendation Grade A (RGA):** Evidence demonstrates at least moderate certainty of at least moderate net benefit.
- **Recommendation Grade B (RGB):** Evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended.
- **Recommendation Grade C (RGC):** Evidence demonstrates potential harm that outweighs benefit; additional research is recommended.
- **Recommendation of the GDG (R-GDG):** Recommended best practice on the basis of the clinical experience of the Guideline Development Group members.

1.6 Guideline Development Group Members

The following table lists members of the Guideline Development Group (GDG) nominated by their respective organisations and the Clinical Governance Group. The GDG members have reviewed and provided feedback on the draft guideline relating to the topic. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

Guideline Development Group members		
Name	**Title**	**Organisation**
Dr Ahmad Mostafah Abdel Wahhab	Senior Specialist Family Medicine & Trainer	Primary Health Care Corp
Dr Haidar Albustanji	Consultant Endocrinology	Ministry of Interior Clinics
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Dr Mohamed Salem Nasralla Saleh	Specialist Family Medicine	Primary Health Care Corp
Dr Mahmoud Zirie	Senior Consultant Endocrinology	Hamad Medical Corp

1.7 National Clinical Guidelines & Pathways Committee Members

The following table lists members of the National Clinical Guidelines & Pathways Committee (NCGPC), appointed by the MOPH. The NCGPC members have reviewed and provided their feedback and approval of the guideline document. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

National Clinical Guidelines & Pathways Committee (NCGPC) Members		
Name	**Title**	**Organisation**
Ms Huda Amer Al-Katheeri	Chair of the NCGPC, Director of Strategic Planning & Performance Department	Ministry of Public Health
Shk Dr Mohammed Hamad J. Al Thani	Co-Chair of the NCGPC, Director of Public Health	Ministry of Public Health
Prof Anthony Akobeng	Chair Clinical Practice Guidelines Committee	Sidra Medicine
Dr Maryam Ibrahim Al-Heidous	Registration coordinator, QCHP	Ministry of Public Health
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Dr Chris Kenny	Executive Director Clinical and Service Development, Office of the Chief Medical Officer	Hamad Medical Corporation
Dr Egon Toft	VP and Dean of College of Medicine	College of Medicine, Qatar University

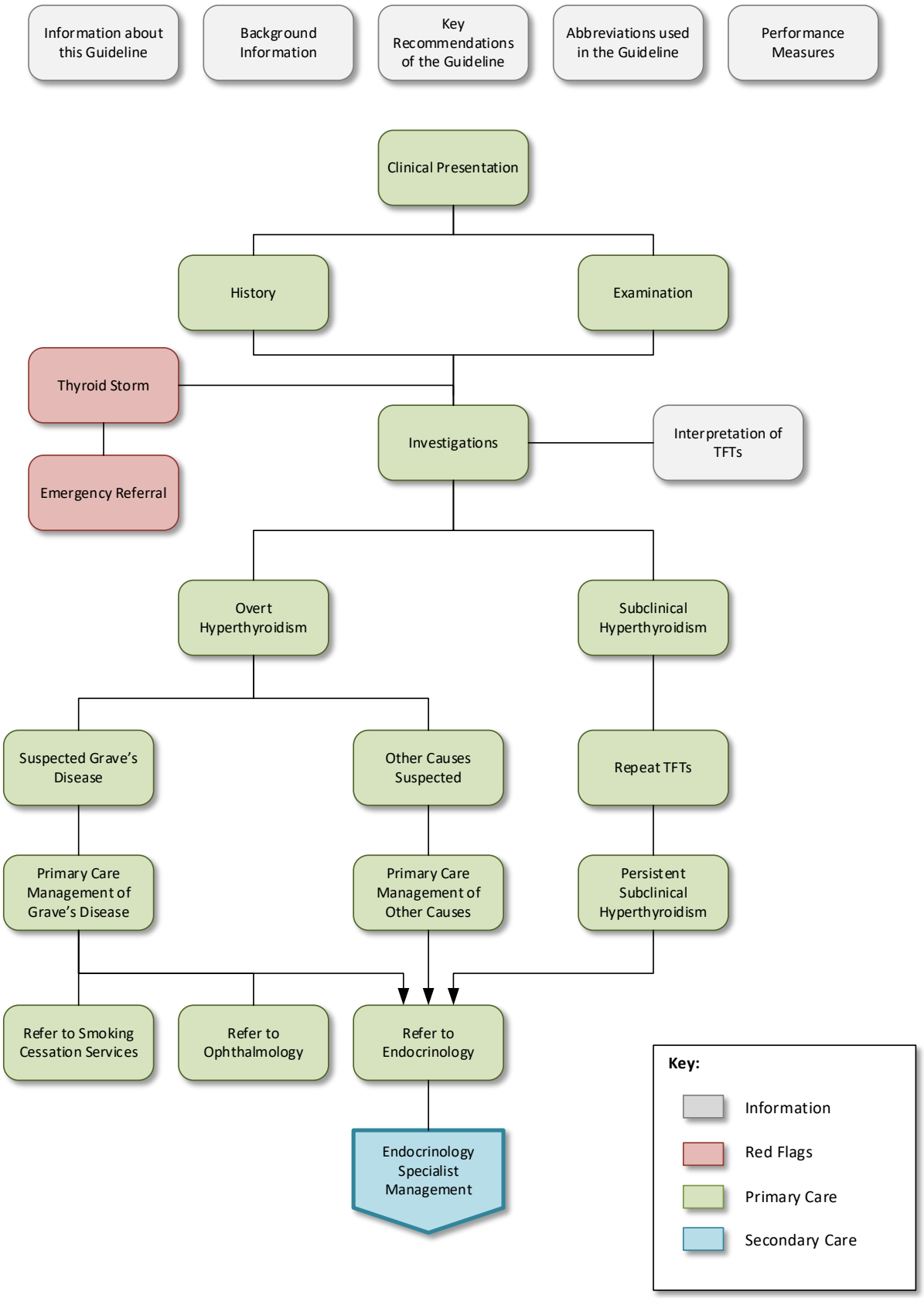
1.8 Responsibilities of Healthcare Professionals

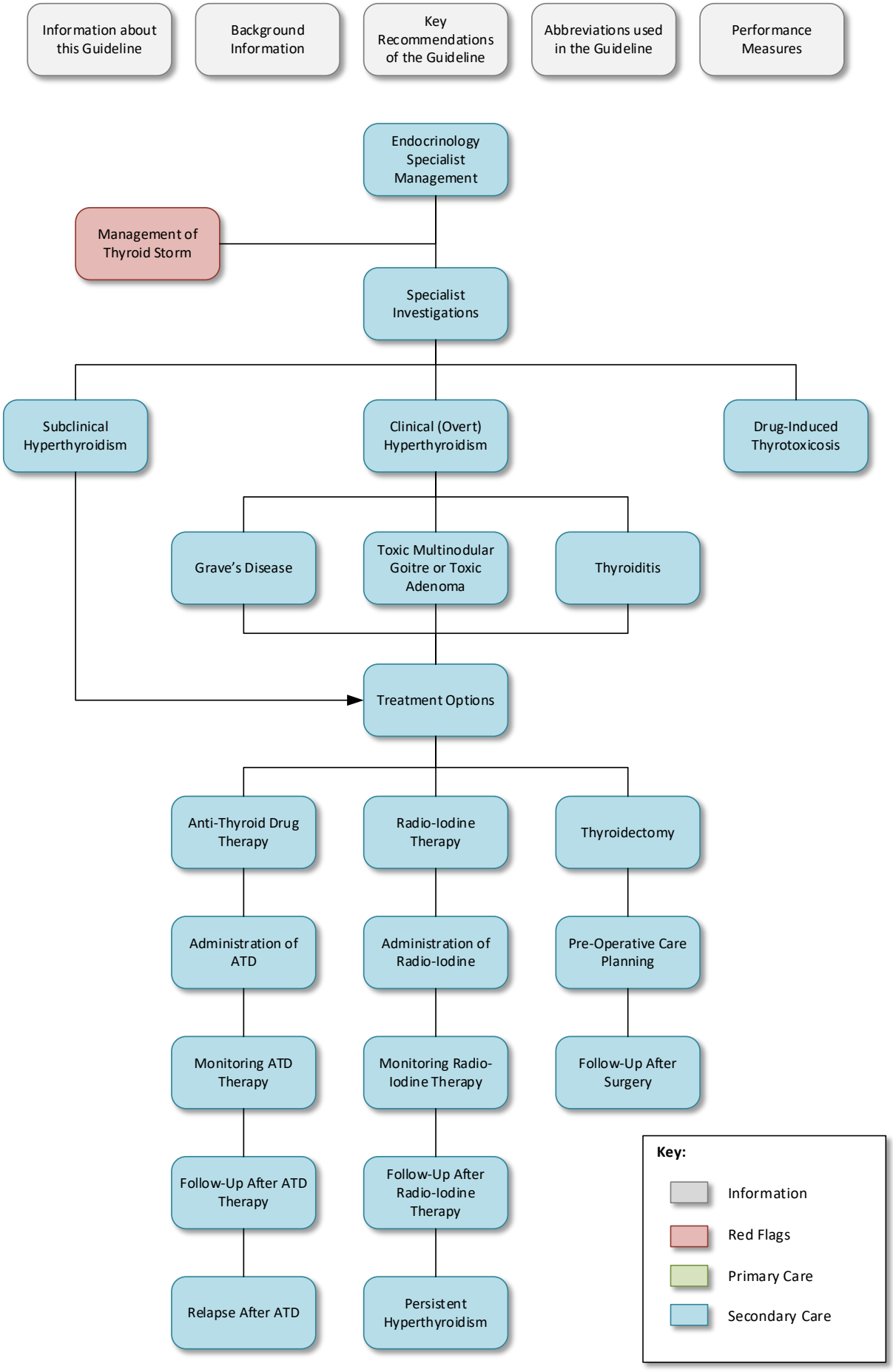
This guideline has been issued by the MOPH to define how care should be provided in Qatar. It is based upon a comprehensive assessment of the evidence as well as its applicability to the national context of Qatar. Healthcare professionals are expected to take this guidance into account when exercising their clinical judgement in the care of patients presenting to them.

The guidance does not override individual professional responsibility to take decisions which are appropriate to the circumstances of the patient concerned. Such decisions should be made in consultation with the patient, their guardians, or carers and should consider the individual risks and benefits of any intervention that is contemplated in the patient's care.

2 Hyperthyroidism Pathway

Click on a box below to see the relevant page of the Pathway.

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3 Key Recommendations of the Guideline

The key recommendations of this guideline are as follows:

Investigations (*Section 8*):

- Symptomatic patients should have TSH and FT4 checked. If FT4 is normal, then check FT3 [1].
- Targeted testing for hyperthyroidism, with TSH, is recommended in specific patient groups [1,2][**L2, RGA**].

Referral to Specialist Care (*Section 10.4*):

- Refer all patients with confirmed clinical (overt) hyperthyroidism to an endocrine specialist [**R-GDG**].
- Persistent subclinical hyperthyroidism should prompt referral to an endocrine specialist [2][**L2, RGA**].
- For patients whose dominant clinical features are due to Graves' eye disease, refer directly to a specialised ophthalmology unit or joint thyroid eye clinic [3].

Subclinical hyperthyroidism (*Section 11.1*):

- Treatment of subclinical hyperthyroidism should be considered in elderly patients and those at risk of complications of hyperthyroidism [2,4,5][**L2**].
- Treatment of subclinical hyperthyroidism is NOT generally recommended:
    - For young, asymptomatic patients with low but detectable TSH, although these patients should be monitored [5][**L2, RGB**].

Anti-Thyroid Drug Therapy (*Section 11.5*):

- When using anti-thyroid drugs as the primary treatment for Graves' disease, continue carbimazole for 12-18 months then taper or discontinue if TSH is normal [2,4][**L1, RGA**].
- Long term therapy (>18 months) may be appropriate in patients in whom definitive treatment is contraindicated, where regular monitoring is possible, and in those who prefer this option [4,6–8].
- Specific features of anti-thyroid drug therapy during pregnancy should be carefully reviewed before the initiation of the treatment [4][**L1, RGA**].

Radioactive Iodine Therapy (*Section 11.6*):

- Is an acceptable treatment option in Graves' disease and is the preferred treatment in toxic multinodular goitre or toxic adenoma [2,3][**L2**].

Thyroidectomy (*Section 11.7*):

- The surgeon performing the procedure should be thoroughly trained and have an active practice in thyroid surgery [4]**[L1, RGA]**.
- Following inadequate surgery for toxic multinodular goitre or toxic adenoma with persistent or recurrent hyperthyroidism, radioactive iodine therapy should be used for retreatment [2][**L2, RGA**].

4 Background Information

4.1 Definition and Classification

Hyperthyroidism:

- Occurs when an excess of thyroid hormones is produced by an overactive thyroid gland [2].
- May be classified as either:
    - **Primary hyperthyroidism:**
        - Occurs when thyrotoxicosis is caused by an abnormality of the thyroid gland and maybe classified as either:
            - Clinical (overt) hyperthyroidism.
            - Subclinical hyperthyroidism.
    - **Secondary hyperthyroidism:**
        - Occurs when thyrotoxicosis is caused by abnormal stimulation of a normal thyroid gland, e.g. by a TSH-secreting pituitary tumour.

Thyrotoxicosis:

- Refers to a clinical state that results from inappropriately high thyroid hormone action in tissues, regardless of the source of the excess thyroid hormone.
- Thyrotoxicosis can be induced by drugs, e.g. amiodarone.

4.2 Aetiology

Primary hyperthyroidism may be caused by [1,9]:

- Graves' disease.
- Toxic multinodular goitre.
- Toxic adenoma.
- Thyroiditis.

Secondary hyperthyroidism may be caused by [1,9]:

- TSH-secreting pituitary tumour.
- Chorionic gonadotrophin-secreting tumours.

Other causes of thyrotoxicosis may include [1,9]:

- Ingestion of excess thyroid hormone (factitious thyrotoxicosis).
- Gestational thyrotoxicosis.
- Medications (e.g., amiodarone, iodine).
- Other causes of thyroid destruction, e.g.:
    - External irradiation.
    - Infarction of an adenoma.

4.3 Prevalence

Data on the incidence and prevalence of hyperthyroidism in Qatar is presently lacking. In the USA, the prevalence of hyperthyroidism is 1.2-1.6%, of which clinical (overt) hyperthyroidism is 0.5-0.6% and subclinical hyperthyroidism is 0.7-1.0% [2,4].

Graves' disease is the most prevalent cause of hyperthyroidism in iodine-replete areas. It occurs more often in women with the peak incidence in patients aged 30–60 years [4].

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4.4 Complications

Possible complications of hyperthyroidism include [2,4,5,10]:

- Atrial fibrillation – risk increases with decreasing levels of TSH.
- Graves' orbitopathy (ophthalmopathy) in patients with Graves' disease.
    - In 30% of cases, subclinical Graves' disease can progress to clinical (overt) hyperthyroidism in 3 years [4].
- Increased risk of coronary heart disease mortality.
- Congestive cardiac failure.
- Osteoporosis and fractures.
- Pretibial myxoedema.
- Thyroid storm.

4.5 Higher Risk Groups

- Groups at higher risk of developing hyperthyroidism include [4,9,11]: Graves' disease:
    - Women.
    - Individuals with a family history of thyroid disease.
    - Individuals with a family or personal history of autoimmune disease.
    - Smokers.
    - Individuals with a high dietary iodine intake.

Toxic multinodular goitre or toxic thyroid nodule:

- Age over 50 years.
- Patients living in areas of low iodine intake.

5 Clinical Presentation

5.1 Thyrotoxicosis

Thyrotoxicosis can present with the following symptoms [9,11]:

- Palpitations.
- Hyperactivity, irritability, altered mood.
- Fatigue, weakness.
- Diarrhoea, steatorrhoea.
- Heat intolerance, increased sweating.
- Weight loss with increased appetite.
- Infertility, oligomenorrhoea, amenorrhoea.
- Polyuria.
- Reduced libido.
- In people with diabetes: deterioration in diabetic control and hyperglycaemia.

Signs of thyrotoxicosis can include [2,9,11]:

- Warm, moist skin; palmar erythema.
- Tremor.
- Eye manifestations (e.g., exophthalmos, ophthalmoplegia, eyelid retraction or lid lag).
- Thyroid enlargement (although the thyroid may be normal in size).
- A bruit over the thyroid gland in Graves' disease.
- Sinus tachycardia, atrial fibrillation.
- Diffuse alopecia.
- Muscle wasting and weakness, proximal myopathy, hyperreflexia.
- Rarely:
    - Onycholysis, pruritus, urticaria, diffuse pigmentation.
    - Gynaecomastia in men.
    - Pretibial myxoedema.
    - Chorea.
    - Periodic paralysis.
    - Psychosis.
    - Impaired consciousness.

NB: Elderly patients may present with few classical signs [5].

5.2 Thyroid Storm

Thyroid storm (thyrotoxic crisis) is a **medical emergency** that should be managed in an intensive care unit (ICU) setting [2,4,12][**L2, RGA**] (see *Section 11.4*). It is characterised by an extreme hypermetabolic state with a with a high mortality rate (over 10%) [12].

It may occur in patients with untreated or poorly treated hyperthyroidism after [2,12–14]:

- Surgery.
- Trauma.
- Childbirth.
- Infection.
- Myocardial infarction.
- Diabetic ketoacidosis.

- Radioactive iodine therapy (rarely).
- Exposure to excess iodine.

Triggering conditions could be inappropriate hormone ingestion and drugs such as [12]:

- Amiodarone.
- Sorafenib.
- Ipilimumab.

Typical features include [4,12]:

- Encephalopathy: anxiety, emotional lability, restlessness, agitation, confusion, delirium, frank psychosis, and coma.
- Cardiac manifestations: sinus tachycardia, atrial arrhythmias, and congestive heart failure.
- Systolic hypertension.
- Fever.
- Gastrointestinal symptoms: diarrhoea, nausea, vomiting, and diffuse abdominal pain.
- Hepatic failure (abnormal liver enzymes levels), jaundice.

In order to increase the accuracy of clinical diagnosis, the severity of individual manifestations can be estimated according to *Burch-Wartofsky Point Scale* (see *Table 5.2* below)[12,15]:

- ≥45 points: Thyroid storm.
- 25–44 points: Impending thyroid storm.
- <25 points: Thyroid storm is unlikely.

Variables	Points
Thermoregulatory Dysfunction	
37.2–37.7 °C	5
37.8–38.3 °C	10
38.4–38.8 °C	15
38.9–39.3 °C	20
39.4–39.9 °C	25
≥40 °C	30
Tachycardia	
90–109 bpm	5
110–119 bpm	10
120–129 bpm	15
130–139 bpm	20
≥140 bpm	25
Atrial Fibrillation	
Absent	0
Present	10
Congestive Cardiac Failure	
Absent	0
Mild	5
Moderate	10
Severe	15
Central Nervous System Disturbance	
Absent	0
Mild	10
Moderate	20
Severe	30
Precipitating Event	
Absent	0
Present	10

Table 5.2: The Burch-Wartofsky Point Scale [15]:

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6 History

A comprehensive history should be taken, asking specifically about the following [1,2,16]:

- Compressive symptoms such as swelling, dysphagia, hoarseness.
- Rate of growth of any neck masses.
- Previous head or neck irradiation.
- Emigration from an iodine-deficient area.
- Family history of:
    - Thyroid disease.
    - Autoimmune disease.
- Medication that can cause thyrotoxicosis (see *Section 9.2.4*).

7 Examination

A thorough examination should be performed, including [2]:

- Vital signs, including:
    - Pulse rate.
    - Blood pressure.
    - Respiratory rate.
    - Body weight.
- Eye examination.
- Thyroid examination, including:
    - Size.
    - Tenderness.
    - Symmetry.
    - Nodularity.
- General physical examination, particularly including:
    - Skin and hand signs.
    - Signs of heart failure.
    - Neuromuscular examination.
    - Pretibial myxoedema.

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8 Investigations

8.1 Primary Care / Generalist Investigations

8.1.1 Investigations in Symptomatic Patients

If the patient is symptomatic [1]:

- Perform TFTs:
  - Check TSH and FT4.
  - If TSH is low (i.e. below the reference range) and FT4 is normal, then check FT3.
- Consider performing an electrocardiography (ECG) if clinically indicated.
- Consider thyroid ultrasound scanning if clinically indicated and available.

8.1.2 Targeted Testing for Hyperthyroidism

TSH should be checked at presentation in patients with the following [1,2][**L2**, **RGA**]:

- Goitre.
- Atrial fibrillation.
- Osteoporosis.
- Subfertility.
- Untreated subclinical hyperthyroidism:
  - Check TSH every 6-12 months and then follow up FT4 and FT3 if TSH is low.
- Taking amiodarone:
  - Check TSH before starting treatment, at 1st and 3rd months after starting, then every 3-6 months whilst on treatment.
  - Continue to monitor TSH up to 12 months after treatment has stopped.
- Taking lithium:
  - Check TSH before starting treatment, then every 6-12 months whilst on treatment.
- Turner's Syndrome or Down's Syndrome:
  - Check TSH annually.
- All patients with a history of autoimmune thyroid disease at the first presentation during pregnancy [4].

8.2 Secondary Care / Specialist Investigations

Specialist investigations may include:

- TFTs as clinically indicated [**R-GDG**].
- Complete blood count (CBC) and chemistry panel [**R-GDG**].
- Thyroid autoantibodies [1,2,4] [**L2, RGA**]:
  - Anti-thyroid peroxidase antibodies (Anti-TPO Ab):
    - A positive result is suggestive of autoimmune thyroiditis.
    - May also be useful in assessing risk of thyroid dysfunction in patients who are taking certain medications, e.g. amiodarone or lithium.
  - Anti-TSH-receptor antibodies (Anti-TRAb):
    - Specific biomarkers for Grave's disease.
- Ultrasonography is recommended [2]:
  - For patients with palpable thyroid nodules or multinodular goitres.
  - When distinguishing between subtypes of the amiodarone-induced thyrotoxicosis.

- Thyroid scintigraphy:
    - Indicated when the clinical presentation of thyrotoxicosis is not diagnostic of Graves' disease [2][**L2, RGA**].
    - Indicated for a thyroid nodule or multinodular goitre in the following settings [1,4]:
        - With a single thyroid nodule and low TSH level (i.e. below the reference range).
        - For multinodular goitres with low TSH (i.e. below the reference range).
        - In the diagnosis of ectopic thyroid tissue.
        - In subclinical hyperthyroidism to identify occult hyperfunctioning tissue.
        - To determine eligibility for radioiodine therapy.
        - To distinguish low-uptake from high-uptake thyrotoxicosis.
    - Contraindicated during pregnancy [17] [**L2, RGC**].
- ECG:
    - If clinically indicated and not already performed in primary care [**R-GDG**].
- DEXA scan:
    - If clinically indicated [**R-GDG**].

9 Diagnosis

9.1 Interpretation of TFTs

Hyperthyroidism is diagnosed on the basis of TFTs and symptoms as follows [1,2,4][**L2, RGA**]:

- Clinical (overt) hyperthyroidism is diagnosed by:
  - Low TSH levels (i.e. below the reference range).
  - Elevated FT4 and FT3 levels.
  - Symptoms of hyperthyroidism.

- Subclinical hyperthyroidism:
  - Low TSH levels (i.e. below the reference range).
  - Normal FT4 and FT3 levels
  - Clinical symptoms and signs are typically absent, mild, or non-specific.

- Thyrotoxicosis:
  - Low TSH levels (i.e. below the reference range).
  - Normal FT4 and elevated FT3.

NB:

- Low TSH levels and low FT3 levels may be caused by the presence of non-thyroidal illness [1]. The diagnosis may be evident on re-testing, once other morbidity is eliminated.
- Low TSH levels associated with thyroid pain may be caused by thyroiditis [1].
- The degree of elevation of serum FT4 and FT3 provides an indication of the severity of hyperthyroidism and should be interpreted in the context of clinical symptoms and signs to direct first-line therapy [1][**L2, RGA**].

If TSH is not low and FT4 is raised consider the possibility of [1,2]:

- Assay interference (discuss with biochemistry personnel).
- TSH-secreting pituitary adenoma.
- Familial dysalbuminaemic hyperthyroxinaemia.
- Syndrome of thyroid hormone resistance.

9.2 Distinguishing Between Causes

9.2.1 Graves' Disease

Features of Graves' disease include:

- Low TSH levels and raised FT4 and/or FT3 levels [1,2,9,10].
- The presence of Anti-TPO-Ab is suggestive of autoimmune disorders, but is not specific to Graves' disease.
- Anti-TRAb is highly sensitive and specific for Graves' disease.
- A diffuse enlarged thyroid gland is commonly palpable; and it may be possible to auscultate a bruit over the gland.
- Eye manifestations (see below).
- Pretibial myxoedema.
- Thyroid acropachy.
- Splenomegaly – rare.

Graves' orbitopathy (ophthalmopathy) [10]:

- Uncommon but responsible for considerable morbidity.
- More than 90% of cases occur in patients presenting with hyperthyroidism due to Graves' disease.

Features of Graves' eye disease include [2,10]:

- Pain in primary gaze.
- Pain with eye movement.
- Chemosis.
- Eyelid swelling.
- Eyelid erythema.
- Caruncula swelling.
- Decreased visual acuity.
- Diplopia.
- Proptosis.

9.2.2 Toxic Multinodular Goitre

Features of toxic multinodular goitre (Plummer's disease) include [1,3]:

- Low TSH levels and either raised FT4 or raised FT3 levels.
- Patients are usually aged over 50 years.
- More prevalent in iodine-deficient areas.
- At least two nodules must be present for the diagnosis to be made on radio-isotope scanning.
- Possible features include:
    - Dyspnoea.
    - Dysphagia.
    - Sensation of neck pressure.

9.2.3 Toxic Adenoma

Features include [1,5,9,11]:

- Low TSH levels and either raised FT4 or raised FT3 levels.
- Non-tender thyroid mass which is generally palpable – usually reaches at least 3cm in size before hyperthyroidism occurs.
- More prevalent in iodine-deficient areas.

9.2.4 Drug-Induced Thyrotoxicosis

The medications that can cause thyrotoxicosis include [2]:

- Amiodarone.
- Lithium.
- Interferon alpha.
- Interleukin-2.
- Iodine.
- Tyrosine kinase.
- Iodine-rich herbal remedies and over-the-counter supplements.
- Some antiretroviral agents.

For patients taking drugs known to modify thyroid function tests, consider seeking advice regarding test interpretation from an endocrine specialist [1].

9.2.5 Thyroiditis

Thyroiditis is an inflammation of the thyroid gland [18].

The most common forms are [18]:

- Hashimoto's disease.
- Subacute granulomatous thyroiditis.
- Postpartum thyroiditis.
- Subacute lymphocytic thyroiditis.
- Drug-induced thyroiditis.

Features of thyroiditis include [2,18]:

- Subacute thyroiditis:
  - Malaise, fever, and thyroidal pain as well as tremor and heat intolerance.
  - Tender, enlarged, firm, and irregular thyroid gland.
- Painless thyroiditis:
  - May occur in autoimmune thyroiditis, postpartum, during lithium or cytokine treatment, or occasionally with amiodarone.

9.2.6 Factitious Thyrotoxicosis

Factitious hyperthyroidism occurs due to excessive intake of thyroid hormones. Features of factitious thyroiditis may include [19]:

- Low TSH levels and raised FT4 levels.
- Absent goitre.
- Reduced uptake on radio-isotope scanning.
- Low thyroglobulin level.
- Negative autoantibodies.

9.2.7 Subclinical Hyperthyroidism

Differentiate from other causes of a low TSH, e.g. [5][**L2, RGA**]:

- Drugs that suppress serum TSH (e.g., dopamine, glucocorticoids).
- Psychiatric illness.
- Non-thyroidal illness (e.g., euthyroid sick syndrome).
- Hypothalamic-pituitary disorders.

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10 Primary Care / Generalist Management

10.1 Prevention of Cardiac Complications

Due to the risk of cardiac complications, consider prescribing beta-blockers [1,2][**L2, RGA**]:

- In all patients with symptomatic thyrotoxicosis.
- Especially patients who:
  - Are aged over 65 years.
  - Have a resting heart rate greater than 90 bpm; or
  - Have coexistent cardiovascular disease.

Choice of beta-blocker [1,4]:

- Propranolol (20–40 mg every 6 h) or long-acting propranolol (80mg once per day).
- Longer acting beta-blockers (atenolol, bisoprolol or metoprolol).
- Cardio-selective beta-blockers with higher cardioprotective effects and superior prevention of atrial fibrillation for patients with asthma.

NB:

- Consider anticoagulation (warfarin or direct oral anticoagulants) in all patients with atrial fibrillation [4] [**L1, RGA**].

10.2 Management of Graves' Disease

For patients with Graves' disease and/or orbitopathy (ophthalmopathy) [2,10][**L2**, **RGA**]:

- Recommend smoking cessation to all patients who are current smokers:
  - Refer to smoking cessation services, where appropriate.
  - Advise on the risks of second-hand tobacco smoke.
- Provide written information on the early symptoms of Graves' orbitopathy.

For patients with Graves' orbitopathy [10]:

- Consider prescribing lubricant eye drops.
- See *Section 10.4* for recommendations on referral to secondary care.

10.3 Management of Subclinical Hyperthyroidism

If other causes (see *Section 9.2.7*) have been excluded [2,5][**L2, RGA**]:

- Determine if subclinical hyperthyroidism is persistent, by repeating the thyroid tests in 2-3 months.
- Persistent subclinical hyperthyroidism should prompt referral to a specialist (see *Section 11.1*).

10.4 Referral to Specialist Care

Urgent referral to a specialist is indicated for the following [4,10,20]:

- Emergency evaluation and management of suspected thyroid storm (see *Sections 5.2* and *11.4*).
- If symptoms or signs of new-onset atrial fibrillation or acute heart failure are present, refer to the Emergency Department.
- In emergency sight-threatening situations that occur out of hours, refer to an emergency eye care service.

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Outpatient referral to endocrinology is indicated for the evaluation or management of any of the following [1,20]:

- All cases of confirmed clinical (overt) hyperthyroidism [**R-GDG**].
- Suspected drug-induced hyperthyroidism.
    - Referral is particularly recommended in patients taking amiodarone as management may be complex.
- Inconsistency between clinical findings and laboratory test results.
- Non-thyroidal illness with TSH suppression, i.e. euthyroid sick syndrome.
- Persistent subclinical hyperthyroidism.
- Apathetic thyrotoxicosis in elderly patients.
- TSH-secreting pituitary adenoma (high TSH and high FT4).

Routine dual endocrinology and ophthalmology referral is indicated for evaluation or management of significant Graves' orbitopathy [10].

11 Secondary Care / Specialist Management

11.1 Management of Subclinical Hyperthyroidism

Treatment of subclinical hyperthyroidism should be considered in patients with:

- TSH levels persistently less than 0.1mIU/L *and* any of the following [2,4,5][**L2, RGB**]:
  - Age 65 years and older.
  - Postmenopausal women who are not taking oestrogens or bisphosphonates.
  - Comorbidities including any of the following:
    - Heart disease.
    - Cardiac risk factors.
    - Osteoporosis.
    - Hyperthyroid symptoms.
- Patients under the age of 65 years with a persistent TSH of less than 0.1mIU/L, and hyperthyroid symptoms [2].
- TSH levels 0.1 - 0.5mIU/L (where 0.5mIU/L is the lower limit of the normal range) *and* any of the following:
  - Age 65 years and older [2][**L2, RGB**].
  - Age under 65 years with heart disease or hyperthyroid symptoms [2,5][**L2, RGB**].
  - Perimenopausal women.

Treatment of subclinical hyperthyroidism is NOT generally recommended for:

- Young, asymptomatic patients with low but detectable TSH, although these patients should be monitored [5][**L2, RGB**].

If treatment is required:

- Anti-thyroid drug therapy should be the first line treatment of Graves' subclinical hyperthyroidism [4][**L1, RGA**].

If the patient remains untreated:

- Repeat TFTs every 6-12 months or if clinical picture changes [1,5][**L2, RGA**].

NB: Treatment options should be based on aetiology and follow the same principles as for overt hyperthyroidism [2,5][**L2, RGA**].

11.2 Management of Clinical (Overt) Hyperthyroidism

11.2.1 Management of Graves' Disease and Orbitopathy

The following treatment options are available:

- Anti-thyroid drug therapy (see *Section 11.5*).
- Radioiodine therapy (see *Section 11.6)*.
- Thyroidectomy (see *Section 11.7*).

NB: Patients with newly diagnosed Graves' orbitopathy and thyroid function results indicating hyperthyroidism, should be rendered euthyroid as soon as possible [2,10][**L2, RGA**].

Advise all patients with Graves' eye disease to:

- Stop smoking and avoid exposure to second-hand smoke [2,10][**L2, RGA**]:
  - Refer to a smoking cessation program if smoking.

  - Patients who are exposed to second-hand smoke should be advised of its negative impact.
- Use lubricant eye drops, if signs of corneal exposure are present [10][**L2, RGA**].

The following treatment options are available:

- Patients with **inactive orbitopathy** can be treated with [2,10] [**L2, RGB**]:
  - Anti-thyroid drug therapy (carbimazole) (see *Section 11.5*).
  - Radioiodine therapy (see *Section 11.6*):
    - Radioiodine therapy without steroid cover is appropriate[4].
  - Thyroidectomy (see *Section 11.7*).
  - Steroid prophylaxis can be avoided if there are no other risk factors for Graves' orbitopathy progression [4] [**L1, RGB**].

- Patients with **mild active orbitopathy** [4,10,21][**L1, RGA**]:
  - Anti-thyroid drug therapy (see *Section 11.5*).
  - Steroid prophylaxis is recommended if radioiodine therapy is planned.
  - Temporary treatment with transconjunctival botulinum toxin type A may be reviewed [22] [**L1, RGB**].

- Patients with **active moderate-to-severe** orbitopathy [21–23] [**L1, RGA**]:
  - Anti-thyroid drug therapy (see *Section 11.5*).
  - Thyroidectomy (see *Section 11.7*).
  - Systemic steroid prophylaxis is recommended:
    - Methylprednisolone is recommended intravenous (500 mg/week for 6 weeks then 250 mg/week for 6 weeks).
    - Cumulative doses of methylprednisolone should not exceed 8g [**L1, RGC**].
  - External radiation therapy (20 Gy in 10 fractions over 12 days) is recommended in case of:
    - Corticosteroid dependence or resistance.
    - Predominantly oculomotor forms.
  - Other immunosuppressive therapies to reduce inflammation (rituximab, cyclosporine, methotrexate, mycophenolate mofetil, tocilizumab, etanercept or adalimumab) may be reviewed but are not routinely recommended in case of:
    - Corticosteroid dependence or resistance.
    - Contraindications to external radiation therapy.

- Patients with **sight-threatening orbitopathy** [4,22]:
  - Anti-thyroid drug therapy (see *Section 11.5*).
  - Multi-modal treatment including a combination of immunosuppression, orbital radiation, and orbital decompression.
  - Radioiodine therapy (see *Section 11.6*) as second-line treatment.

NB:

- For patients whose dominant clinical features are due to Graves' eye disease refer directly to a specialised ophthalmology unit or joint thyroid eye clinic [10].
- Ophthalmological emergencies that occur out of hours should be referred to the nearest emergency eye care service [10].

11.2.2 Management of Toxic Multinodular Goitre or Toxic Adenoma

The following treatment options are available [3]:

- Radioiodine therapy (see *Section 11.6*).
- Thyroidectomy (see *Section 11.7*).
- Long term anti-thyroid drug therapy with carbimazole (non-curative) (see *Section 11.5*).

11.2.3 Management of Thyroiditis

Thyroiditis is usually short-lived and self-limiting, and often followed by a hypothyroid phase [1]. For patient with mild symptomatic subacute thyroiditis, consider beta-blockers or non-steroidal anti-inflammatory drugs (NSAIDs) [2][**L2, RGA**]. For patients who fail to respond, or with moderate-to-severe symptoms, consider corticosteroids [2][**L2, RGA**].

11.3 Management of Drug-Induced Thyrotoxicosis

Iodine-induced hyperthyroidism [2]:

- Avoid additional iodine.
- Consider beta-blockers alone or in combination with anti-thyroid drug therapy.
- Radioactive iodine cannot be used until iodine load has been cleared (can take several months).
- Thyroidectomy may be considered in patients allergic or resistant to anti-thyroid drugs.

Cytokine-induced thyrotoxicosis [2]:

- If developed during therapy with interferon-α or interleukin-2, determine the aetiology and treat accordingly[2][**L2, RGA**].

Amiodarone-induced thyrotoxicosis [2,24]:

- Monitor thyroid function tests before and at 1 and 3 months following the initiation of treatment with amiodarone, and at 3-6 month intervals thereafter.
- Consideration to stop amiodarone should be determined:
    - On an individual basis.
    - In consultation with a cardiologist.
    - Based on the presence or absence of effective alternative antiarrhythmic treatment.
- Distinguish between subtypes:
    - Type 1 (iodine-induced) – consider anti-thyroid drugs.
    - Type 2 (thyroiditis) – consider corticosteroids.
- Consider combined anti-thyroid and anti-inflammatory treatment for patients:
    - Failing to respond to single modality therapy.
    - With an unknown type of disease.
- Thyroidectomy should be considered for patients who are unresponsive to aggressive medical therapy with anti-thyroid drugs and corticosteroids [2].
- The radio-iodine therapy is not recommended but may be justified in life threatening conditions [24][**L2, RGC**].

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11.4 Management of Thyroid Storm

Thyroid storm is a rare, life-threatening disorder which should be managed and monitored in an ICU setting [2,4,12][**L2, RGA**]. It is important to have a high index of suspicion in patients with thyrotoxicosis associated with any evidence of systemic decompensation [2].

Early recognition and aggressive multimodality treatment of thyroid storm are important [4,12][**L1, RGA**]:

- Beta-adrenergic blockade [4,12]:
  - Propranolol 40 mg every 6 h.
  - Landiolol or esmolol when heart rate is >80 bpm, systolic blood pressure >80 mmHg or cardiac index is >2.2 L/min/m2.
  - Verapamil or diltiazem for patients with severe pulmonary disease, such as asthma and COPD.
  - Digitalis for patients with normal renal function without hemodynamic failure.

- Anti-thyroid drug therapy [4,12]:
  - Propylthiouracil (400-600 mg) every 8 h.
  - Recommended when thyroid storm in Graves' disease is diagnosed [12] [**L1, RGA**].
  - Not recommended when thyroid storm by destructive thyroiditis is diagnosed [12] [**L1, RGB**].

- Glucocorticoids [4,12]:
  - Methylprednisolone 50 mg intravenous.
  - Hydrocortisone 300 mg/day.
  - Dexamethasone 8 mg/day.

- Inorganic iodide [12].

- Acid-suppressive drugs to decrease the risk of gastrointestinal haemorrhage [12].
  - Proton pump inhibitors.
  - Histamine-2 receptor antagonists.

- Aggressive cooling with acetaminophen and cooling blankets [4,12].

- Volume resuscitation.

- Respiratory and nutritional support.

- Consider psychotropic medications to manage neurologic manifestation [12].

- Consider benzodiazepines (diazepam) or alternative drugs (fosphenytoin, phenobarbital, and sodium thiopental) if convulsions are present [12].

NB: If acute congestive heart failure occurs, invasive hemodynamic monitoring (Swan-Ganz catheter) is recommended for patients with symptoms and signs of pulmonary oedema [12][**L2, RGA**].

11.5 Anti-Thyroid Drug Therapy

Anti-thyroid drug therapy (ATD) may be used [1,2,4]:

- Short term whilst awaiting definitive treatment (e.g., radioiodine or surgery).
- Medium term with the aim of inducing remission of Graves' disease.
- Long term in patients for whom definitive treatment is contraindicated, or according to patient preference.

Before initiating ATD, carry out the following tests [2,6][**L2**, **RGB**]:

- Full blood count – including white cell count and differential:
  - The absolute neutrophil count should be above 1000/mm^3.
- Liver profile – including bilirubin and transaminase:
  - The levels of liver enzymes should not exceed three times the upper limit of the normal range.

Before stopping ATD, carry out the measurement of TSH-R-Ab levels [1,4][**L1, RGA**]:

- Normal levels indicate a greater chance of remission.

Note:

- Consider prescribing beta-blockers in the early stages before ATD takes effect [4] [**L1, RGA**].
- Thyrotoxicosis alone may reduce the white cell count and elevate transaminases.

11.5.1 Administration of ATD

For first-line treatment, consider a thioamide such as [1,2,4,5]:

- Carbimazole:
  - The initial dose is 15–40 mg/day [4].
  - The maximal dose is 40 mg/day.
  - Low doses should be used for the treatment of subclinical hyperthyroidism, where indicated [5][**L2, RGA**].

- Propylthiouracil:
  - Is of benefit in severe thyrotoxicosis and thyroid storm[4,7].
  - Not recommended for use in children due to its potential severe hepatotoxicity, and should only be used in [6]:
    - Exceptional circumstances.
    - For short periods of time.
    - With close monitoring for signs of hepatic dysfunction.
    - Before radical treatment.
    - In patients experiencing severe side effects on carbimazole.
  - The dose is 100 mg every 8 h [4].
  - The usual maintenance dose in the titration regimen is 50–100 mg/day [4].

Advise patients to stop anti-thyroid medication and seek medical attention if they develop symptoms of agranulocytosis or hepatic injury, e.g. [2][**L2**, **RGA**]:

- Pharyngitis.
- Pruritic rash.
- Jaundice.
- Acholic stool or dark urine.
- Arthralgias.

- Abdominal pain.
- Nausea.
- Fatigue.
- Fever.

Check the following [2][**L2**, **RGA**]:

- White cell count if the patient experiences a febrile illness or pharyngitis.
- Liver function tests - if the patient experiences symptoms suggestive of hepatic injury.

11.5.2 Monitoring of ATD

The optimal duration of ATD treatment for the titration regimen is 12–18 months [4] with the maximum remission rate of 50–55%. A substantial proportion of patients may reach euthyroidism within 3–4 weeks of treatment [4]. Discontinue ATD treatment after 12-18 months if TSH is normal [2,4][**L1, RGA**].

Measurement of TSH-R-Ab levels prior to stopping ATD therapy is recommended, as it aids in predicting which patients can be weaned from the medication, with normal levels indicating a greater chance of remission [**R-GDG**]. Patients with persistently high TSH-R-Ab at 12–18 months can continue therapy, repeating the TSH-R-Ab measurement after an additional 12 months, or opt for radio-iodine or thyroidectomy [**R-GDG**].

Monitoring may be carried out in secondary care:

- TFTs should be reviewed 3–4 weeks after starting treatment [4][**L1, RGA**].
- Continue monitoring thyroid function every 3-6 weeks during the first 3–4 months of treatment [6] [**L2, RGA**].
- Once at a maintenance dose, less frequent monitoring is required (every 3–4 months) [6][**L2, RGA**].

The dose of ATD should be titrated based on FT4 and FT3 levels [4][**L1, RGA**]. Persistent suppression of serum TSH should not in itself prompt an increase in the thioamide dose [1,2]. If the patient exhibits reversible adverse reactions, consider a concomitant transitory antihistamine treatment without stopping the ATD treatment [4,6][**L2, RGA**].

If the patient exhibits persistent minor side effects to medication, consider [2,4][**L2, RGA**]:

- Changing treatment to radioactive iodine therapy (see *Section 11.6*) or thyroidectomy (see *Section 11.7*); or
- Switching to an alternative anti-thyroid medication if radioactive iodine therapy or surgery are contraindicated.
    - If serious allergic reaction occurs, do not prescribe an alternative anti-thyroid drug.

Long-term ATD treatment should be considered as an alternative treatment for Graves' disease [4,6–8]. Long term may also be appropriate in patients in whom definitive treatment is contraindicated, where regular monitoring is possible, and in those who prefer this option[2].

11.5.3 Follow-Up After ATD

A patient can be considered to be in remission if they have a normal serum TSH, FT4, and FT3 for 1 year after discontinuation of anti-thyroid medication [2].

Follow-up all patients closely for relapse during the first year after treatment [2]:

- Repeat testing at 1-3 month intervals for 6-12 months.
- Repeat testing TSH at 1, 3, and 6 months in delivered women that had hyperthyroidism remission during pregnancy.

Patients may be discharged back to the care of their primary care physician for annual monitoring of TFTs, if they remain in remission after one year of stopping anti-thyroid treatment [**R-GDG**].

11.5.4 Relapse After ATD

ATD treatment has a high relapse rate (approximately 50%). When medication has been used as the primary treatment for Graves' disease, approximately two thirds of relapses occur in the first year after the treatment has been stopped [25].

The following factors predict reoccurrence [4]:

- Lower age.
- Higher serum TSH-R-Ab and FT4.
- Larger goitre at diagnosis.

If a patient relapses after a course of ATD, consider [2][**L2, RGB**]:

- Radioactive iodine therapy (see *Section 11.6*).
- Thyroidectomy (see *Section 11.7*).
- A long term anti-thyroid drug treatment with a low-dose carbimazole may be considered in patients who prefer this approach.

11.6 Radioactive Iodine Therapy

Pre-administration considerations [2][**L2, RGA**]:

- Treatment of any comorbid conditions should be optimised prior to administering radioactive iodine.
- A pregnancy test should be obtained at most within 72 hours of initiating treatment in any female patient of childbearing age – a negative pregnancy test result should be verified by the clinician [2,26].
- Breast-feeding should be definitively terminated at least 4 weeks before treatment [26].
- Written and verbal advice concerning radiation safety precautions following treatment should be provided. If precautions cannot be followed, an alternative treatment should be used.
- For patients with Graves' disease with conditions that put them at risk of complications from worsening hyperthyroidism (such as the extremely symptomatic or those with FT4 estimates 2-3 times the upper limit of normal) [2]:
    - Treat with a beta-blocker prior to radioactive therapy [2][**L2, RGA**].
    - Consider pre-treatment with anti-thyroid drugs [2][**L2, RGB**].
- For patients with toxic multinodular goitre or toxic adenoma, with conditions that put them at increased risk for complications due to worsening of hyperthyroidism (such as the elderly, cardiovascular disease or severe hyperthyroidism)[2]:
    - Treat with beta-blocker prior to radioactive therapy and until euthyroid [2][**L2, RGA**].

- Consider pre-treatment with anti-thyroid drugs [2][**L2, RGB**].
- If carbimazole is used, avoid radioiodine therapy when TSH is normal or elevated to prevent direct iodine treatment of perinodular and contralateral normal thyroid tissue [2].

- ATD should be temporarily paused for a week before radioiodine treatment [4].
- Propylthiouracil may induce relative radio resistance [1,27].
  - This may be overcome by stopping propylthiouracil for a minimum of 2 weeks before radioiodine administration or by giving a larger dose.

NB: Verbal and written information on all aspects of radioiodine therapy should be provided to the patient. The patient should be informed that a repeated treatment with radioiodine may be required [4].

11.6.1 Administration of Radioactive Iodine Therapy

There is varying opinion on the optimal dosage, however sufficient radiation should be administered in a single dose to render the patient hypothyroid [2,27][**L2, RGA**].

Post-administration considerations:

- Radioactive iodine has been associated with exacerbation of pre-existing eye disease [2,28]:
  - This risk appears to be reduced with a course of steroids given concurrently with and following radioiodine and is indicated in those patients with mild-active eye disease who are smokers, or who have other risk factors for Graves' orbitopathy.
- If given as pre-treatment, anti-thyroid drugs should be [2,27]:
  - Restarted a week after treatment [4]; and
  - Start tapering the dose over 4-6 weeks as the thyroid function normalises.
  - If thyroid hormone levels become elevated on withdrawal, repeat radioiodine therapy 6 months after the initial treatment.

Contraindications [2,4,17]:

- Pregnancy or breastfeeding.
- Male or female patients planning conception within 6 months after the therapy.
- Co-existence or suspicion of thyroid cancer.
- Patients unable to comply with safety guidelines.

11.6.2 Monitoring of Radioactive Iodine Therapy

In the majority of patients, thyroid function is normalized within 3–12 months after radioiodine therapy [4]. The size of thyroid is normalized within a year of radioiodine therapy [4].

Radioiodine treatment may be associated with thyroid pain, swelling, and sialoadenitis [4]. Target these comorbidities if needed.

Thyroid storm following the therapy is extremely rare [4].

Assess TFTs 1-2 months after radioiodine treatment [2][**L2, RGA**]:

- Assessment should include measurement of levels of FT4, FT3, TSH [1,2][**L2, RGA**]:
- Assess TFTs 6 weeks after treatment and then every 3 months for the first year and then annually thereafter [**R-GDG**].
- If the patient continues to be thyrotoxic, repeat testing at 4-6 week intervals until stable [2][**L2, RGA**].

11.6.3 Follow-Up After Radioactive Iodine Therapy

If the patient remains euthyroid after 1 year of follow-up, consider referring back to primary care with clear instructions, to monitor for the development of hypothyroid symptoms [27].

Hypothyroidism following radioiodine therapy [2]:

- Can occur from week 4 but is more common between months 2 and 6.
- Occasionally transient hypothyroidism occurs and is followed by either complete recovery of thyroid function or recurrent hyperthyroidism.

NB: Smokers are more likely to have a progression or de novo occurrence of eye disease following radioactive iodine treatment [4].

11.6.4 Persistent Hyperthyroidism

If hyperthyroidism persists [2][**L2, RGB**]:

- After 6 months following radioiodine therapy for Graves' disease, or there is minimal response 3 months after treatment, retreatment with *radioiodine* is suggested.
- Beyond 6 months following radioiodine therapy for toxic multinodular goitre or toxic adenoma, retreatment with *iodine* is suggested.

11.7 Thyroidectomy

Total or near-total thyroidectomy may be indicated for the following [2,4][**L1**]:

- Removal of severe goitre (e.g., toxic multinodular goitre causing pressure symptoms).
- Hyperthyroidism from a hyperfunctioning nodule or Graves' disease and any of the following:
    - Intolerance or inadequate response to anti-thyroid drugs or radioactive iodine therapy.
    - Contraindication to radioactive iodine; or
    - Rapid remission is required.
    - The patient prefers to have surgery.
- Malignant thyroid tumours.
- Severe thyroid eye disease.
- Amiodarone-induced thyrotoxicosis that fails to respond to medical therapy.

NB:

- Total or bilateral subtotal thyroidectomy is the procedure of choice [4].
- They have the same risk of complications by the rate of recurrent hyperthyroidism after the total thyroidectomy is lower.
- An ipsilateral thyroid lobectomy, or isthmusectomy, should be performed for toxic adenoma if the adenoma is in the isthmus [2][**L2, RGA**].

NB: The surgeon performing the procedure should be thoroughly trained and have an active practice in thyroid surgery [4][L1, RGA].

Contraindications to thyroidectomy include [2]:

- Substantial comorbidity.
- Pregnancy is a relative contraindication - only to be used when rapid control is needed and anti-thyroid medications cannot be used. If surgery is to be performed, this should preferably be undertaken in the second trimester [**R-GDG**].

11.7.1 Pre-Operative Care Planning

Pre-operative care planning [2,4,28]:

- Ensure adequate calcium and vitamin D replacement prior to surgery.
- Render the patient euthyroid preoperatively.
- In Graves' disease:
  - Use ATD [2][**L2, RGA**].
  - In the immediate preoperative period, consider the use of potassium iodide for 10 days [4][**L1, RGA**].
  - Beta blockade and potassium iodide can be used without thioamides in exceptional circumstances when it is not possible to render the patient euthyroid prior to surgery, they have a contraindication or allergy to anti-thyroid medication, or the need to thyroidectomy is urgent [1,2][**L2, RGB**].
- In toxic multinodular goitre or toxic adenoma:
  - ATD with or without beta blockers should be used. Preoperative iodide should not be used in this setting [2][**L2, RGB**].

Potential complications of surgery include [2,4]:

- Hypoparathyroidism.
- Hypocalcaemia.
- Recurrent or superior laryngeal nerve injury.
- Postoperative bleeding.
- Wound infection.
- Complications related to general anaesthesia.

11.7.2 Follow-Up After Thyroidectomy

Following surgery for Graves' disease or toxic multinodular goitre [2][**L2, RGA**]:

- Anti-thyroid medication should be stopped.
- Wean patients off beta-blockers.
- Measure serum calcium or intact parathyroid hormone levels, and prescribe oral calcium and calcitriol supplementation, as appropriate [2][**L2, RGB**].
- Initiate L-T4 therapy taking into account patient weight and age.
- Measure TSH 6-8 weeks post-operatively, every 1-2 months until stable, and then annually.

Following surgery for toxic adenoma [2][**L2, RGA**]:

- Check TSH and FT4 4-6 weeks after surgery.
- Thyroid therapy should be started if there is a persistent rise in TSH above the normal range.
- After lobectomy, serum calcium levels do not need to be obtained, and supplements do not need to be given.

Note:

- Lifelong thyroid function testing is required for all patients who have received surgery for hyperthyroidism [1][**L2, RGA**].Following inadequate surgery for toxic multinodular goitre or toxic adenoma with persistent or recurrent hyperthyroidism, radioactive iodine therapy should be used for retreatment [2][**L2, RGA**].

12 Key Considerations for Patient Preferences

Patient preferences refer to patient perspectives, beliefs, expectations, and goals for health and life, and to the steps employed by individuals in assessing the potential benefits, harms, costs, and limitations of the management options in relation to one another. Patients may have preferences when it comes to defining their problems, identifying the range of management options and selecting or ranking the outcomes used to compare these options.

It is important for healthcare professionals to develop an understanding of the patient as an individual and the unique way in which each person experiences a condition and its impact on their life.

The following recommendations are therefore made for physicians and other healthcare professionals regarding general principles of patient care in Qatar:

- **Respect Patients:** Treat patients with respect, kindness, dignity, courtesy and honesty. Ensure that the environment is conducive to discussion and that the patient's privacy is respected, particularly when discussing sensitive, personal issues. Ask the patient how they wish to be addressed and ensure that their choice is respected and used.

- **Maintain Confidentiality:** Respect the patient's right to confidentiality and avoid disclosing or sharing patients' information without their informed consent. In this context, students and anyone not directly involved in the delivery of care should first be introduced to the patient before starting consultations or meetings, and let the patient decide if they want them to stay.

- **Clarify Third-Party Involvement:** Clarify with the patient at the first point of contact whether and how they like their partner, family members or carers to be involved in key decisions about their care or management and review this regularly. If the patient agrees, share information with their partner, family members or carers.

- **Obtain Informed Consent:** Obtain and document informed consent from patients, in accordance with MOPH policy and guidance.

- **Encourage Shared Decision Making:** Ensure that patients are involved in decision making about their own care, or their dependent's care, and that factors that could impact the patient's participation in their own consultation and care including physical or learning disabilities, sight, speech or hearing impairments and problems with understanding, reading or speaking English are addressed.

- **Disclose Medical Errors:** Disclose errors when they occur and show empathy to patients.

- **Ensure Effective Communication:** Explore ways to improve communication including using pictures, symbols or involving an interpreter or family members. Avoid using medical jargon. Use words the patient will understand and confirm understanding by asking questions.

- **Ensure Continuity of Care:** Provide clear and timely sharing of patient information between healthcare professionals especially at the point of any transitions in care.

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13 Performance Measures

A list of performance measures is given in the table below. Healthcare organisations are encouraged to monitor service performance using the indicator definitions below.

Number	Numerator	Denominator
TH01	Number of patients with a record of an eye examination.	All patients with a recorded diagnosis of hyperthyroidism.
TH02	Number of patients who have TFTs within 6-12 months of initial diagnosis.	All patients with a recorded diagnosis of subclinical hyperthyroidism.
TH03	Number of patients with Grave's disease who have smoking status recorded.	All patients with a recorded diagnosis of Grave's disease.

Table 13.1: Performance measures.

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Appendix: Detailed Description of the Literature Search

A systematic search for existing literature on hyperthyroidism was performed in the period April 17th-24th, 2019.

The search for clinical practice guidelines on hyperthyroidism diagnosis and/or management was performed in the *PubMed* database and websites of relevant organisations and societies including the *Thyroid* UK, the *British Thyroid Foundation*, and the *American Thyroid Association*.

Peer-reviewed scientific publications were found in *PubMed* and via *Google Scholar* Internet search engine. Non-peer reviewed studies were identified in *bioRxiv*. Books were checked on PubMed. Personal opinions of healthcare professionals, information published on medical websites, and drug prescribing information sheets were found via Google search engine.

The included publications were identified using the term "*hyperthyroidism*" and, if needed, specified with the following terms in combinations:

Graves' disease/orbitopathy, thyroiditis, thyroid storm, subclinical, prevalence, anti-thyroid drug, radioactive iodine, thyroidectomy.

The date limit for the search was set up as March 19th, 2017 based on the last update of the present guideline.

Figure A.1 below demonstrates graphically the results of the search and application of exclusion criteria.

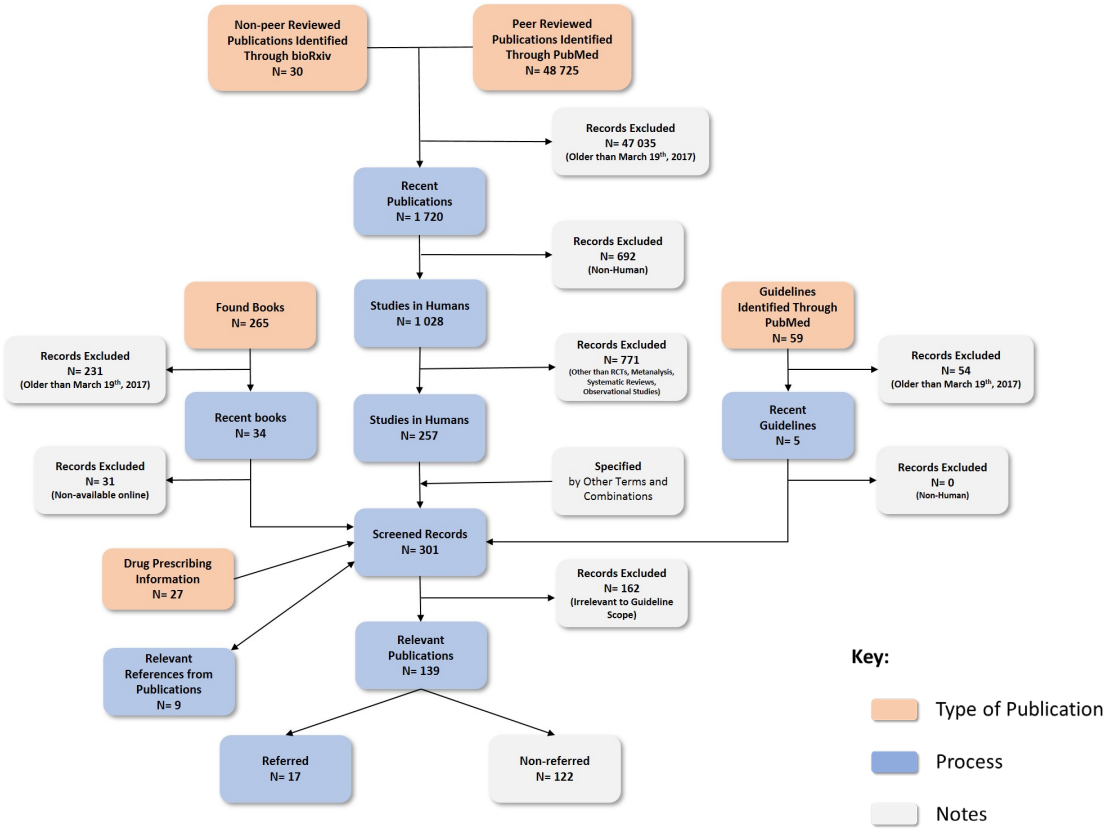

Fig A.1: Literature search results and application of exclusion criteria.

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