Management of Thyroid Disorders in Pregnancy

RCOG Green-top Guideline No. 76: A Clinical Pathway Summary

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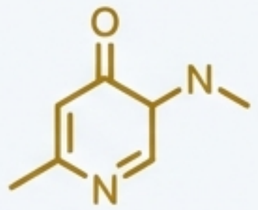
ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

Guideline at a Glance: Key Practice-Changing Recommendations

Diagnostics: Use trimester- & manufacturer-specific TSH/fT4 reference ranges.

[Grade B]

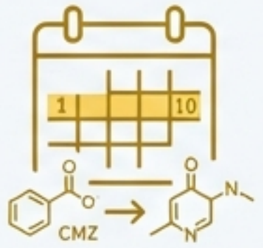


Hyperthyroidism (Preconception): Use propylthiouracil (PTU) instead of carbimazole (CMZ) for women trying to conceive.

[Grade B]

Hypothyroidism (Pre-existing): Counsel patients to self-initiate a ~25% levothyroxine dose increase immediately upon positive pregnancy test.

[Grade A]



Hyperthyroidism (1st Trimester): If on CMZ, switch to PTU as soon as possible before 10 weeks' gestation.

[Grade D]

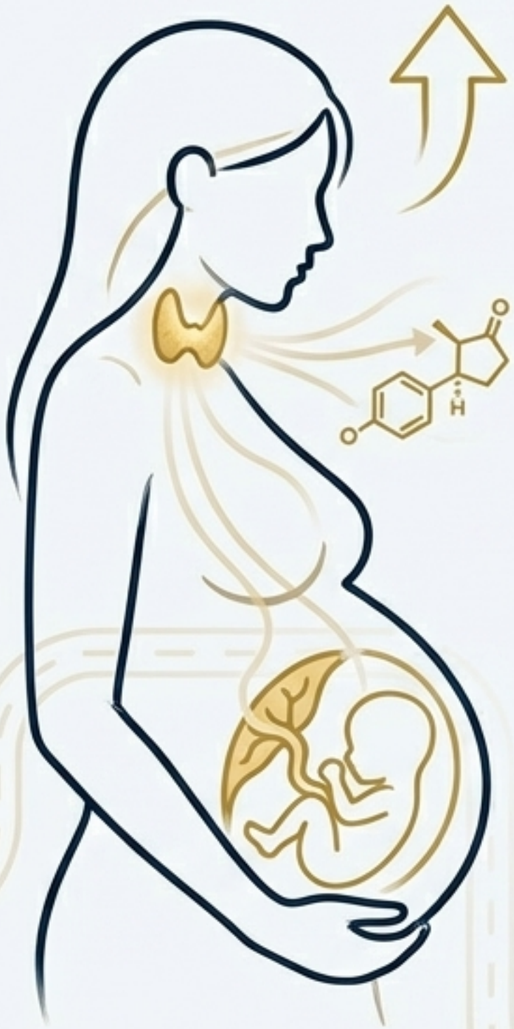
Hypothyroidism (Treatment Target): Aim for TSH ≤ 2.5 mU/L and fT4 within the normal trimester-specific range.

[Grade C for TSH target]

Iodine: Recommend a total daily intake of 200–250µg via diet or a 150µg supplement.

[Grade C]

The Physiological Demands of Pregnancy on the Thyroid



Increased Demand: Maternal thyroid hormone production increases by approximately 50% to supply both mother and fetus.

Hormonal Influence:

- Rising oestrogen increases thyroxine-binding globulin (TBG), requiring more T4/T3 production to maintain free hormone levels.
- First-trimester hCG has weak TSH-like activity, which can transiently increase fT4 and suppress TSH.

Increased Demand: Maternal thyroid hormone production increases by approximately 50% to supply both mother and fetus levels.

Fetal Dependence: The fetus is completely dependent on maternal T4 for neurodevelopment until its own thyroid is functional (18-22 weeks).

Increased Iodine Requirement: Iodine needs increase significantly due to higher thyroid hormone synthesis, increased renal clearance, and fetal uptake starting at 10-12 weeks.

Accurate Diagnosis Requires Trimester-Specific Reference Ranges

Core Recommendation

Use of non-pregnant reference ranges is inapplicable and risks misdiagnosis. Always use trimester- and manufacturer-specific pregnancy reference ranges for TSH and fT4.

[Grade B]

Pragmatic Upper Limit

In the absence of specific ranges, a TSH upper limit of 4.0 mU/L is a reasonable choice.

[Grade C]

Key Distinction

Diagnostic reference ranges should not be confused with treatment targets for patients on medication.

Table Title: Example Trimester-Specific Reference Ranges (pmol/L for fT4, mU/L for TSH)

Assay Manufacturer	First Trimester	Second Trimester	Third Trimester
Abbott Architect	TSH: 0.09–3.46 fT4: 10.9–18.7	TSH: 0.32–3.31 fT4: 9.7–17.2	TSH: 0.38–4.34 fT4: 8.8–14.9
Beckman Access/Dxl	TSH: 0.06–3.32 fT4: 8.7–15.6	TSH: 0.32–3.31 fT4: 6.8–12.4	TSH: 0.34–5.02 fT4: 6.0–11.7
Roche Cobas/Elecsys	TSH: 0.12–4.10 fT4: 11.6–20.3	TSH: 0.11–4.26 fT4: 9.9–17.7	TSH: 0.50–4.71 fT4: 8.7–15.2
Siemens Advia Centaur	TSH: 0.06–3.67 fT4: 11.9–19.2	TSH: 0.47–4.46 fT4: 11.6–17.6	TSH: 0.60–4.60 fT4: 9.6–16.5

Optimizing Iodine Intake from Preconception Through Breastfeeding

Recommended Daily Intake:
All pregnant and breastfeeding women should aim for a total daily intake of 200–250µg of iodine. [Grade B]

Achieving Intake

This can be met by increasing dietary intake of iodine-rich foods **OR** taking a **daily 150µg supplement** (as potassium iodide). [Grade C]

Cow's milk
(50-100µg/200mL)

Yoghurt
(50-100µg/150g)

Eggs
(20-26µg/egg)

Haddock
(~325-430µg/100g)

Timing

Supplementation should ideally start 3 months before pregnancy or as soon as possible. [GPP]

Caution

Avoid sustained intake exceeding 500µg daily. [Grade C]

Not Recommended

Individual assessment of iodine status (e.g., urinary iodine) is not recommended due to high variability. [Grade B]

A Risk-Based Approach to Thyroid Function Testing in Early Pregnancy

Universal Screening is Not Recommended

Current evidence from large RCTs (like the CATS study) shows no improvement in population-level pregnancy or child cognitive outcomes. [Grade C]

Targeted Testing is Justified

Offer TSH and fT4 testing as soon as possible in pregnancy (preferably first trimester) to women with specific risk factors. [Grade D]

Personal History of Thyroid Condition

Previous thyroid surgery, goitre, nodule, overt/subclinical dysfunction, thyroiditis, known TPOAb positivity, radioiodine ablation, head/neck irradiation.

Associated Autoimmune Conditions

Type 1 diabetes, Systemic Lupus Erythematosus (SLE), Anti-Ro/Anti-La positivity, Antiphospholipid syndrome.

Previous Adverse Pregnancy Outcome

History of stillbirth or second-trimester miscarriage (if not previously tested).

Proactive Management of Hypothyroidism: Preconception and Initial Diagnosis

Part 1: Pre-Pregnancy Optimization

Goal: Titrate levothyroxine to achieve a preconception TSH ≤ 2.5 mU/L. [Grade B for OH/severe SCH; Grade C for milder SCH]

This applies to overt hypothyroidism (OH), severe subclinical hypothyroidism (SCH, TSH >10 mU/L), and should be considered for milder SCH (TSH > upper limit to 10 mU/L), especially if TPOAb positive.

Part 2: The Critical First Step on Positive Pregnancy Test

Action: Counsel women on levothyroxine to self-initiate an empirical dose increase of 25-30% as soon as pregnancy is confirmed. [Grade A]

Option A: Double the dose of levothyroxine on two days of each week.

Option B: Implement a daily dose increment (e.g., +25µg/day for doses ≤100µg; +50µg/day for doses >100µg).

A Clinical Algorithm for Managing Hypothyroidism in Pregnancy

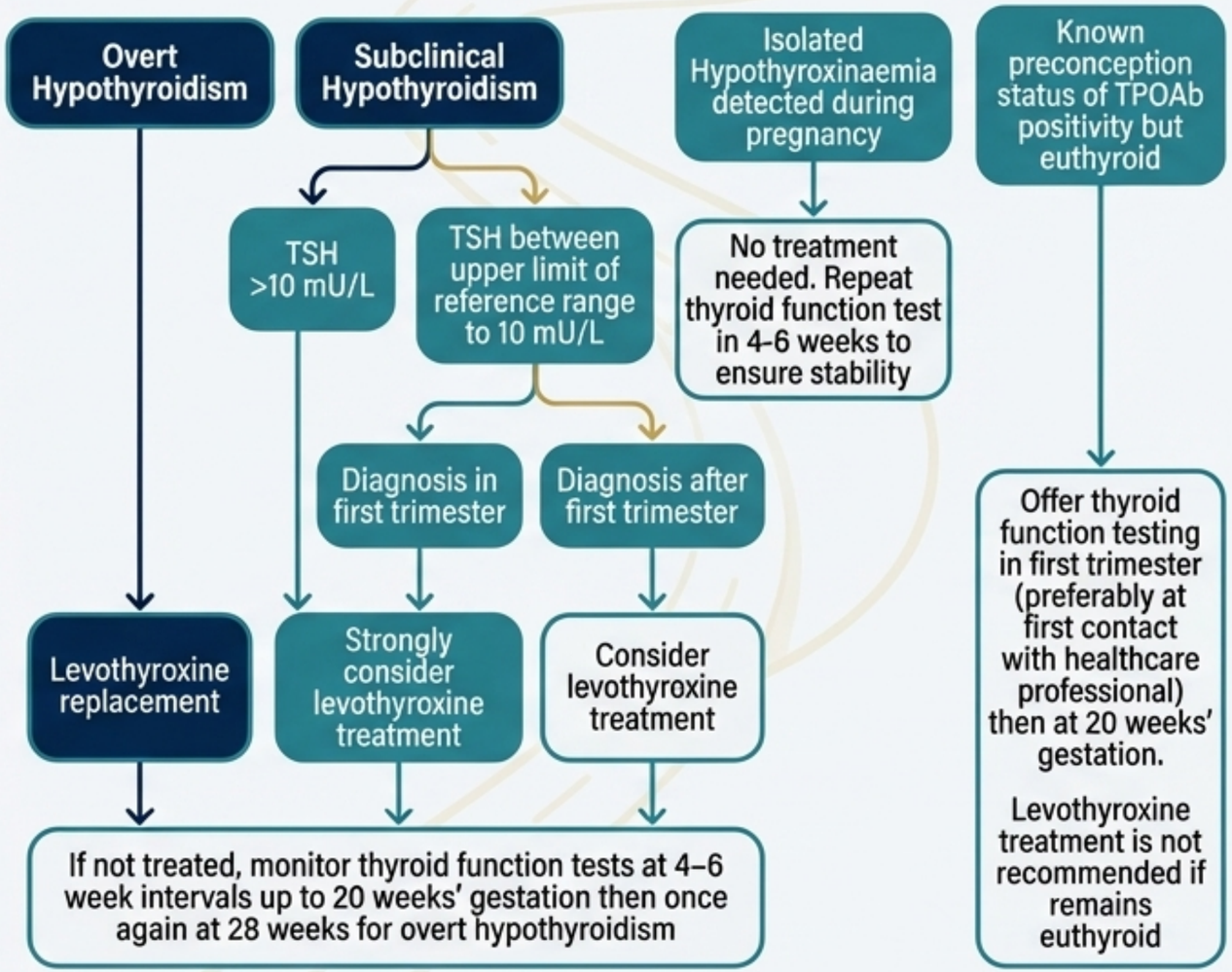
Monitoring Frequency: Check TSH and fT4 every 4–6 weeks until 20 weeks, then once more at 28 weeks. [Grade A]

Treatment Target: Aim to keep TSH below 2.5 mU/L, while fT4 remains within the normal trimester-specific pregnancy range. [Grade C]

Initial Dosing for New Diagnosis:
- **Overt Hypothyroidism (OH) & Severe SCH (TSH >10):** Start levothyroxine at 1.6µg per kg per day. [Grade B]
- **SCH (TSH between upper limit and 10):** Consider levothyroxine at 1.0–1.2µg per kg per day, especially if diagnosed in the first trimester. [Grade C]

Isolated Hypothyroxinaemia (IH): Routine levothyroxine is not recommended. Recheck TFTs in 4-6 weeks to ensure stability. [Grade C]

Known TPOAb Positive but Euthyroid: Levothyroxine is not recommended. Monitor TFTs at first contact and at 20 weeks. [Grade A/C]



Optimizing Hyperthyroidism Care Before Conception

Pre-Pregnancy Counselling is Essential: Discuss all management options to minimize maternal and fetal risk. [GPP]

Definitive Treatment: Discuss radioiodine or thyroidectomy, especially for severe disease. Wait at least 6 months post-treatment before attempting conception. [Grade C]

TRAb Levels: High TRAb levels (>3x upper limit) upper limit) post-treatment are associated with fetal Graves' disease; consider delaying conception further. [Grade D]

Antithyroid Drug (ATD) Choice for Conception

- Use **Propylthiouracil (PTU)** in preference to Carbimazole (CMZ) while trying to conceive. [Grade B]
- **Dosing Goal:** Use the lowest effective dose to maintain fT4 in the upper half of the reference range.

Considering Discontinuation: If a woman is euthyroid for ≥6 months on a low ATD dose (CMZ <10mg or PTU <200mg), consider stopping the drug before conception, with close monitoring. [Grade D]

Managing Graves' Disease Through Pregnancy: Medication, Monitoring, and Fetal Surveillance

First Trimester

Medication: PTU is the recommended drug. [Grade D]

Action: If a woman conceives on CMZ, **switch to PTU as soon as possible before 10 weeks' gestation**. (Advised dose ratio CMZ:PTU is 1:20). No benefit to switching after 10 weeks. [Grade D]

Monitoring Frequency: Every 2–4 weeks

Second Trimester

Monitoring Frequency: Every 4–8 weeks after 20 weeks

Third Trimester

Fetal Surveillance: Required if patient has uncontrolled Graves' disease, requires ATDs, or has TRAb >3x upper limit.

26 weeks

Protocol: Serial ultrasound scans for fetal biometry with umbilical artery Doppler **monthly from 26-28 weeks**. [Grade D]

Treatment Target: Titrate ATDs to target **fT4 concentrations in the upper half of the trimester-specific range.** This minimizes risk of fetal hypothyroidism. TSH may remain suppressed. [Grade D]

Distinguishing Gestational Transient Thyrotoxicosis (GTT) from Graves' Disease

Feature	Gestational Transient Thyrotoxicosis (GTT)	Graves' Disease
Symptoms Before Pregnancy	No	Often
Hyperemesis Gravidarum	Yes (~60% of cases)	Often not present
Goitre	No	Diffuse goitre in 90%
Thyroid Eye Disease	No	In ~20%
TSH-Receptor Antibodies (TRAb)	Normal	**Increased**
fT3 Concentration	Normal in 85%	**Increased**

Management Takeaway

- **Graves' Disease:** Requires prompt treatment with antithyroid drugs.

- **Gestational Transient Thyrotoxicosis:** Does not require antithyroid drugs. Management is symptomatic and supportive only. [Grade C]

Managing Thyroid Nodules and Cancer Discovered in Pregnancy

Step 1

Initial Assessment

For any new or enlarging thyroid nodule/goitre:

1. Check thyroid function (TSH/fT4).
2. Refer to a specialist for assessment. [Grade D]

Step 2

Diagnostic Pathway

Ultrasound: The primary imaging modality.

Fine Needle Aspiration (FNA): If malignancy is suspected on ultrasound, FNA can be performed safely at any gestation. [Grade B]

Radioactive isotope scans are contraindicated.

Step 3

Surgical Intervention

If required (e.g., for compressive symptoms or aggressive cancer), surgery should ideally be performed between

14 and 22 weeks of gestation

to reduce risks of miscarriage and preterm labor. [Grade C]

Prognosis of Differentiated Thyroid Cancer

Reassurance: There is no difference in the rate of recurrence or long-term survival for well-differentiated thyroid cancer identified during pregnancy compared to non-pregnant diagnoses. [Grade B]

The Postpartum Transition: Dose Adjustments and Breastfeeding Safety

For Hypothyroidism

- **Pre-existing on Levothyroxine**: Revert to the preconception dose of levothyroxine **2 weeks postpartum**. [Grade D]

- **Started Levothyroxine in Pregnancy**: Stop levothyroxine after birth and check thyroid function at **6 weeks postpartum** to reassess need for therapy. [Grade D]

For Hyperthyroidism

- **Risk of Relapse**: Increased autoimmunity postpartum raises the risk of Graves' disease relapse or new onset. Perform a thyroid function test 6–8 weeks after birth. [Grade C]

Breastfeeding Safety

- **Safe Medications:** Both Carbimazole (CMZ, up to 20mg/day) and Propylthiouracil (PTU, up to 450mg/day) are considered safe during breastfeeding. [Grade C]
- **Dosing Principle**: Use the lowest effective dose. Routine thyroid function testing of the infant is not required unless there are concerns or high doses are used.

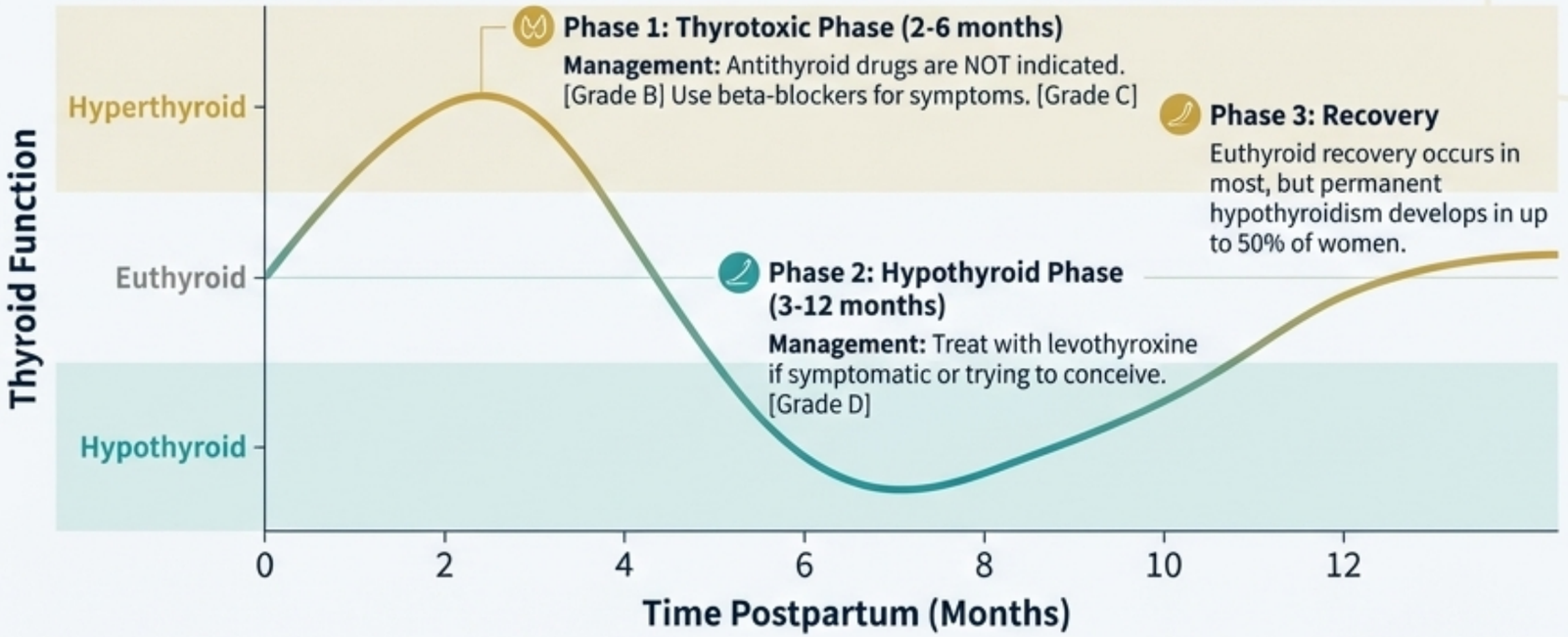
Identifying and Managing Postpartum Thyroiditis (PPT)

Definition

An autoimmune disorder causing thyroid dysfunction within 12 months postpartum in a previously euthyroid woman.

Occurs in 5–10% of pregnancies.

Clinical Course of Postpartum Thyroiditis (PPT)



Long-term Follow-up

Monitor serum TSH **annually** in all women with a history of PPT due to the high risk of developing permanent hypothyroidism. [Grade C]

Integrating Guidelines into Practice: An Auditable Checklist

- [ ] **Diagnostics**
  Are we using and quoting trimester- & manufacturer-specific reference ranges for at least **95%** of thyroid function tests in pregnancy?

- [ ] **Targeted Testing**
  Are at least **90%** of women with defined risk factors offered TFTs in the first trimester?

- [ ] **Hypothyroidism Dose Increase**
  Are at least **90%** of women on pre-existing levothyroxine counselled to empirically increase their dose upon pregnancy confirmation?

- [ ] **Hypothyroidism Monitoring**
  Is the levothyroxine dose titrated based on repeat TFTs every 4–6 weeks for at least **95%** of dose changes?

- [ ] **Hyperthyroidism Preconception**
  Has an informed discussion about management options and pregnancy preparation occurred with all women of childbearing age with hyperthyroidism?

- [ ] **CMZ to PTU Switch**
  Are at least **90%** of women who conceive on CMZ advised to switch to PTU before 10 weeks' gestation?

- [ ] **Hyperthyroidism Treatment Target**
  Are ATDs titrated to maintain fT4 in the upper half of the reference range in **95%** of cases?