

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Thyroid Testing for Hypothyroidism: Clinical Effectiveness and Guidelines

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Research Questions

1. What is the effectiveness of assessing free T3 or T4 to screen for hypothyroidism?
2. What is the effectiveness of assessing free T3 or T4 levels to monitor or adjust levothyroxine dose?
3. What are the evidence-based guidelines regarding thyroid testing for screening or monitoring patients with hypothyroidism?

Key Findings

Two systematic reviews, one non-randomized study, four evidence-based guidelines, and one systematic review of guidelines were identified regarding the assessment of free T3 or T4 to screen for hypothyroidism.

Methods

This report makes use of a literature search developed for a previous CADTH report. The original literature search was conducted in April 2015 on key resources including PubMed, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Filters were applied to limit retrieval to health technology assessments, systematic reviews, and meta-analyses, randomized controlled trials, non-randomized studies, and guidelines. Where possible, retrieval was limited to the human population. The initial search was also limited to English-language documents published between January 1, 2010 and April 9, 2015. For the current report, database searches were rerun on November 1, 2018 to capture any articles published since the initial search date. The search of major health technology agencies was also updated to include documents published since April 2015.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adult patients with suspected or known hypothyroidism, without pituitary or hypothalamic disease
Intervention	Free T3 or T4 levels
Comparator	Q1, 2: Thyroid Stimulating Hormone (TSH) Q3: No comparator
Outcomes	Q1, 2: Clinical effectiveness (benefits [reliable assessment of hypothyroidism or usefulness to manage levothyroxine dose]; harms), evidence-based guidelines Q3: Guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

Two systematic reviews, one non-randomized study, four evidence-based guidelines, and one systematic review of guidelines were identified regarding the assessment of free T3 or T4 to screen for hypothyroidism. No relevant health technology assessments or randomized controlled trials were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

One systematic review (SR)¹ examined the screening and management of thyroid dysfunction before and during pregnancy. The review included two randomized controlled trials (RCTs). Women were part of a universal screening group or a “high-risk” case finding group and were tested for thyroid stimulating hormone (TSH), free T4, and thyroid peroxidase antibody. More women in the screening group were diagnosed with hypothyroidism than in the case finding group.¹ Another SR² was identified that was conducted to support the US Preventive Services Task Force guidelines on screening and treatment of thyroid dysfunction. No evidence was identified that directly compared the benefits and harms of screening with no screening. In addition, there was no mention of which measurements should be used for screening.²

One non-randomized study³ was identified that evaluated the use of T3 measurements to assess levothyroxine over-replacement for hyperthyroid patients. The authors concluded that T3 levels remained normal even in patients who had received too much levothyroxine and that its measurement for this purpose was not of any benefit to these patients.³

Four evidence-based guidelines⁴⁻⁷ were identified. The 2013 Latin American Thyroid Society⁴ and the 2012 American Association of Clinical Endocrinologists and the American Thyroid Association guidelines for the management of hypothyroidism⁶ and the 2012 Endocrine Society guideline on the management of thyroid dysfunction during pregnancy and postpartum⁵ were identified; however, the abstracts of these guidelines did not provide any specific detail regarding the use of free T3 or T4 to screen for hypothyroidism. The 2011 American Thyroid Association guideline for the diagnosis and management of thyroid disease during pregnancy and postpartum⁷ outlines the use of TSH and free T4 testing as screening tools. A systematic review of nine guidelines was also identified that did not provide detail regarding the use of free T3 or T4 testing for thyroid screening in the abstract.⁸

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Spencer L, Bubner T, Bain E, Middleton P. Screening and subsequent management for thyroid dysfunction pre-pregnancy and during pregnancy for improving maternal and infant health. *Cochrane Database Syst Rev*. 2015 Sep 21(9):CD011263.
[PubMed: PM26387772](#)
2. Ruge JB, Bougatsos C, Chou R. U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. Screening for and treatment of thyroid dysfunction: an evidence review for the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality (US); 2014.
[PubMed: PM25927133](#)

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

3. Livingston M, Birch K, Guy M, Kane J, Heald AH. No role for tri-iodothyronine (T3) testing in the assessment of levothyroxine (T4) over-replacement in hypothyroid patients. *Br J Biomed Sci*. 2015;72(4):160-163.
[PubMed: PM26738396](#)

Guidelines and Recommendations

4. Brenta G, Vaisman M, Sgarbi JA, et al. Clinical practice guidelines for the management of hypothyroidism. *Arq Bras Endocrinol Metabol*. 2013 Jun;57(4):265-291.
[PubMed: PM23828433](#)
5. De Groot L, Abalovich M, Alexander EK, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2012 Aug;97(8):2543-2565.
[PubMed: PM22869843](#)
6. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Endocr Pract*. 2012 Nov-Dec;18(6):988-1028.
[PubMed: PM23246686](#)
7. Stagnaro-Green A, Abalovich M, Alexander E, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid*. 2011 Oct;21(10):1081-1125.
[PubMed: PM21787128](#)

Systematic Reviews of Guidelines

8. Fang Y, Yao L, Sun J, et al. Appraisal of clinical practice guidelines on the management of hypothyroidism in pregnancy using the Appraisal of Guidelines for Research and Evaluation II instrument. *Endocrine*. 2018 Apr;60(1):4-14.
[PubMed: PM29445919](#)

Appendix — Further Information

Previous CADTH Reports

9. Free T3 or T4 levels for hypothyroidism: clinical effectiveness and guidelines. Ottawa (ON): CADTH; 2015 Apr: <https://www.cadth.ca/sites/default/files/pdf/htis/apr-2015/RB0847%20Free%20T3%20or%20T4%20Levels%20for%20Hypothyroidism%20Final.pdf> Accessed 2018 Nov 13.

Non-Randomized Studies

Alternative Comparator

10. Birk-Urovitz E, Del Giudice ME, Meaney C. Use of thyroid-stimulating hormone tests for identifying primary hypothyroidism in family medicine patients. *Can Fam Med.* 2017 Sep;63: <http://www.cfp.ca/content/cfp/63/9/e389.full.pdf> Accessed 2018 Nov 13.
11. Gibbons V, Lawrenson R, Sleight P, Yarnley T, Conaglen JV. Investigating the pathways in primary practice leading to the diagnosis of central hypothyroidism. *N Z Med J.* 2012 Oct 26;125(1364):83-90.
[PubMed: PM23242401](#)

Clinical Practice Guidelines and Position Statements – Unspecified Methodology

12. Saskatchewan Disease Control Laboratory. Laboratory testing guidelines for the diagnosis and monitoring of thyroid disease. Government of Saskatchewan; 2018 Sep: <https://rrpl-testviewer.ehealthsask.ca/SCI/Sample%20Collection%20and%20Packaging%20Information/Testing%20Guidelines%20for%20the%20Diagnosis%20and%20Monitoring%20of%20Thyroid%20Disease%20v2.0.pdf>
Accessed 2018 Nov 13.
13. Thyroid function testing for adult diagnosis and monitoring: position statement. Surrey, Australia: The Royal College of Pathologists of Australasia; 2017 Jul: <https://www.rcpa.edu.au/getattachment/7bed9076-bcd5-44ac-9d12-ed9a1f69852a/Thyroid-Function-Testing-for-Adult-Diagnosis-and-M.aspx>
Accessed 2018 Nov 13.
14. United Healthcare Services. Clinical guidelines: evaluation of thyroid dysfunction; 2016 Jan: https://www.uhcprovider.com/content/dam/provider/docs/public/policies/lab-benefit-mgmt/PDS-014_EVALUATION-OF-THYROID-DYSFUNCTION_UHC_20140530_v1.pdf
Accessed 2018 Nov 13.
15. The New Zealand laboratory schedule and test guidelines: biochemistry tests. *BPJ.* 2014 Feb: <https://bpac.org.nz/BT/2014/February/docs/BT22-biochemistry.pdf>
See: *Tests of Thyroid Function, page 5*
Accessed 2018 Nov 13.
16. Toward Optimized Practice (TOP) Endocrine Working Group. Investigation and management of primary thyroid dysfunction. Edmonton, AB: Toward Optimized Practice; 2014 Apr: http://www.topalbertadoctors.org/download/350/thyroid_guideline.pdf
Accessed 2018 Nov 13.

17. BC Guidelines and Protocols Advisory Committee. Thyroid function tests: diagnoses and monitoring of thyroid function disorders in adults; 2010 Jan:
<http://www2.gov.bc.ca/gov/DownloadAsset?assetId=581E65D32B7140E0A87E79002E94BE1C&filename=thyroid.pdf> Accessed 2018 Nov 13.
18. Management of thyroid dysfunction in adults. *BPJ*. 2010;33:
http://www.bpac.org.nz/BPJ/2010/December/docs/bpj_33_thyroid_pages_22-32.pdf
 Accessed 2018 Nov 13.

Review Articles

19. Sheehan MT. Biochemical testing of the thyroid: TSH is the best and, oftentimes, only test needed – a review for primary care. *Clin Med Res*. 2016 Jun;14(2):83-92.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5321289/>
20. Thompson L, et al. Technologies scoping report 22: In the context of hypothyroidism, what is the evidence for the effectiveness of diagnostic tests and thyroid hormone replacement therapies? Glasgow, Scotland: NHS Quality Improvement Scotland (NHS QIS), 2014 Feb:
http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/shtg_scoping_reports/technologies_scoping_report_22.aspx?theme=mobile Accessed 2018 Nov 13. *Will need to download report once URL is accessed.*

Additional References

21. Gilmour J, Mukerji G. Less is more with T3 and T4: a toolkit for reducing free thyroid hormone testing (Choosing Wisely); 2017 Aug: https://choosingwiselycanada.org/wp-content/uploads/2017/09/CWC_T3T4_Toolkit_V1.pdf
 Accessed 2018 Nov 13.
22. Sawka AM, Jonklaas J. Hypothyroidism. *CMAJ*. 2015 Feb;187(3): 205.
<http://www.cmaj.ca/content/187/3/205>
 Accessed 2018 Nov 13.
23. Faix JD, Thienpont LM, Thyroid-stimulating hormone: why efforts to harmonize testing are critical to patient care. *AACC LaboraStories*; 2013 May:
<https://www.aacc.org/publications/cln/articles/2013/may/tsh-harmonization>
 Accessed 2018 Nov 13.