

Guideline version (for example, Draft, Consultation, Final)

Thyroid Disease: Diagnosis and Management of Thyroid Disease

NICE guideline: search strategies

NICE guideline

Search strategies

March 2019

Draft for Consultation

*This guideline was developed by the
National Guideline Centre*

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the [Welsh Government](#), [Scottish Government](#), and [Northern Ireland Executive](#). All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright

© National Institute for Health and Care Excellence, 2018

ISBN

[add for final publication version only, delete this text for consultation version]

Contents

A.1 Information for people with thyroid disease.....	6
A.1.1 Clinical search literature search strategy.....	6
A.2 Thyroid function tests	10
A.2.1 Clinical search literature search strategy.....	10
A.2.2 Health Economics literature search strategy	15
A.3 Indications for testing.....	20
A.3.1 Clinical search literature search strategy.....	20
A.3.2 Health Economics literature search strategy	27
A.4 Imaging for fine needle aspiration.....	32
A.4.1 Clinical search literature search strategy.....	32
A.4.2 Health Economics literature search strategy	37
A.5 Ultrasound guidance for fine needle aspiration	42
A.5.1 Clinical search literature search strategy.....	42
A.5.2 Health Economics literature search strategy	46
A.6 Antibodies in hyperthyroidism.....	51
A.6.1 Clinical search literature search strategy.....	51
A.6.2 Health Economics literature search strategy	57
A.7 Antibodies in hypothyroidism	62
A.7.1 Clinical search literature search strategy.....	62
A.7.2 Health Economics literature search strategy	66
A.8 Management of non-malignant thyroid enlargement.....	71
A.8.1 Clinical search literature search strategy.....	71
A.8.2 Health Economics literature search strategy	75
A.9 Management of hypothyroidism.....	81
Management of subclinical hypothyroidism.....	81
A.9.1 Clinical search literature search strategy.....	81
A.9.2 Health Economics literature search strategy	85
A.10Management of Thyrotoxicosis: Drugs vs Surgery vs Radioactive iodine	90
Management of Thyrotoxicosis: pharmacological options	90
Management of Thyrotoxicosis: radioactive iodine options	90
Management of Thyrotoxicosis: surgical options.....	90
Management of subclinical thyrotoxicosis	90
A.10.1 Clinical search literature search strategy.....	90
A.10.2 Health Economics literature search strategy	94
A.11Monitoring Thyroid disease	99
A.11.1 Clinical search literature search strategy.....	99
A.11.2 Health Economics literature search strategy	104

Thyroid Disease: DRAFT FOR CONSULTATION
Contents

Thyroids Disease search strategy 1

This literature search strategy was used for the following reviews;

A.1 Information for people with thyroid disease

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.1.1 Clinical search literature search strategy

Searches for patient views were run in Medline (OVID), Embase (OVID), CINAHL, Current Nursing and Allied Health Literature (EBSCO) and PsycINFO (ProQuest). Search filters were applied to the search where appropriate.

Table 1: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Qualitative studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Qualitative studies
CINAHL, Current Nursing and Allied Health Literature (EBSCO)	Inception – 07 January 2019	Qualitative studies
PsycINFO (ProQuest)	Inception – 07 January 2019	Qualitative studies

Medline (Ovid) search terms

1.	exp thyroid diseases/
2.	hyperthyroid*.ti,ab.
3.	hypothyroid*.ti,ab.
4.	thyrotoxicosis.ti,ab.
5.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16

18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	"patient acceptance of health care"/ or exp patient satisfaction/ or consumer health information/ or needs assessment/
28.	Patient Education as Topic/ or exp patients/ or exp family/ or caregivers/ or patient preference/
29.	((information* or advice or advising or advised or support*) adj3 (patient* or need* or requirement* or assess* or seek* or access* or disseminat*).ti,ab.
30.	(information* adj2 support*).ti,ab.
31.	((client* or patient* or user* or carer* or consumer* or customer* or parent* or famil* or spouse*) adj2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or preference* or focus group*).ti,ab.
32.	or/27-31
33.	Qualitative research/ or Narration/ or exp Interviews as Topic/ or exp "Surveys and Questionnaires"/ or Health care surveys/
34.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
35.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaiuzzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
36.	or/33-35
37.	26 and 32 and 36

Embase (Ovid) search terms

1.	exp thyroid diseases/
2.	hyperthyroid*.ti,ab.
3.	hypothyroid*.ti,ab.
4.	thyrotoxicosis.ti,ab.
5.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13

15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	patient attitude/ or patient preference/ or patient satisfaction/ or consumer attitude/ or needs assessment/
26.	patient information/ or consumer health information/ or patients/ or family/ or caregivers/
27.	((information* or advice or advising or advised or support*) adj3 (patient* or need* or requirement* or assess* or seek* or access* or disseminat*).ti,ab.
28.	(information* adj2 support*).ti,ab.
29.	((client* or patient* or user* or carer* or consumer* or customer* or parent* or famil* or spouse*) adj2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or preference* or focus group*).ti,ab.
30.	patient education/
31.	or/25-30
32.	health survey/ or exp questionnaire/ or exp interview/ or qualitative research/ or narrative/
33.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
34.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaiuzzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricœur* or spiegelberg* or merleau*).ti,ab.
35.	or/32-34
36.	24 and 31 and 35

CINAHL (EBSCO) search terms

S1.	(MH "Thyroid Diseases+")
S2.	hyperthyroid*
S3.	hypothyroid*
S4.	thyrotoxicosis
S5.	(thyroid n3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
S6.	s1 or s2 or s3 or s4 or s5
S7.	(MH "Consumer Satisfaction+") OR (MH "Patient Education") OR (MH "Health Education")
S8.	((information* or advice or advising or advised or support*) n3 (patient* or need* or requirement* or assess* or seek* or access* or disseminat*))
S9.	(information* n2 support*)
S10.	((client* or patient* or user* or carer* or consumer* or customer*) n2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion*))

S11.	S7 OR S8 OR S9 OR S10
S12.	(MH "Qualitative Studies+")
S13.	(MH "Qualitative Validity+")
S14.	(MH "Interviews+") OR (MH "Focus Groups") OR (MH "Surveys") OR (MH "Questionnaires+")
S15.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*)
S16.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* n3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*)
S17.	S12 OR S13 OR S14 OR S15 OR S16
S18.	S6 AND S11 AND S17
	Limit to English language

PsycINFO (ProQuest) search terms

1.	(MAINSUBJECT.EXACT.EXPLODE("Thyroid Disorders") OR TI,AB(HYPERTHYROID* OR HYPOTHYROID* OR THYROTOXICOSIS) OR TI,AB(THYROID NEAR/3 (SWELL* OR DYSFUNCTION* OR ENLARG* OR NODULE* OR NODE* OR DISEASE* OR CONDITION* OR DISORDER*))) AND (SU.EXACT("Client Education") OR SU.EXACT.EXPLODE("Client Attitudes") OR TI,AB((information* OR advice OR advising OR advised OR support*) NEAR/3 (patient* OR need* OR requirement* OR assess* OR seek* OR access* OR disseminat*)) OR TI,AB((information* NEAR/2 support*) OR TI,AB((client* OR patient* OR user* OR carer* OR consumer* OR customer*) NEAR/2 (attitud* OR priorit* OR perception* OR preferen* OR expectation* OR choice* OR perspective* OR view* OR satisfact* OR inform* OR experience OR experiences OR opinion*))) AND ((su.exact.explore("qualitative research") or su.exact("narratives") or su.exact.explore("questionnaires") or su.exact.explore("interviews") or su.exact.explore("health care services") or ti,ab(qualitative or interview* or focus group* or theme* or questionnaire* or survey*) or ti,ab(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* near/3 analys*) or theoretical-sampl* or purposive-sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*)))
	Limit to English language

Thyroid disease search strategy 2

This literature search strategy was used for the following reviews;

A.2 Thyroid function tests

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.2.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 2: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 1 or 12 CENTRAL to 2019 Issue 1 or 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Medline (Ovid) search terms

38.	exp thyroid diseases/
39.	hyperthyroid*.ti,ab.
40.	hypothyroid*.ti,ab.
41.	thyrotoxicosis.ti,ab.
42.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
43.	or/1-5
44.	letter/
45.	editorial/
46.	news/
47.	exp historical article/

48.	Anecdotes as Topic/
49.	comment/
50.	case report/
51.	(letter or comment*).ti.
52.	or/7-14
53.	randomized controlled trial/ or random*.ti,ab.
54.	15 not 16
55.	animals/ not humans/
56.	exp Animals, Laboratory/
57.	exp Animal Experimentation/
58.	exp Models, Animal/
59.	exp Rodentia/
60.	(rat or rats or mouse or mice).ti.
61.	or/17-23
62.	6 not 24
63.	thyroid function tests/
64.	Thyroxine/ or Triiodothyronine/ or thyrotropin/
65.	(T3 or T4 or fT3 or fT4 or T3RU or T3 uptake or T3 resin uptake or TSH or hTSH).ti,ab.
66.	(thyroxine or triiodothyronine).ti,ab.
67.	(Thyroid stimulating hormone or thyroid-stimulating hormone or thyrotropin or thyrotropic hormone or hormone).ti,ab.
68.	or/27-30
69.	25 and 31
70.	limit 32 to English language
71.	randomized controlled trial.pt.
72.	controlled clinical trial.pt.
73.	randomi#ed.ti,ab.
74.	placebo.ab.
75.	randomly.ti,ab.
76.	Clinical Trials as topic.sh.
77.	trial.ti.
78.	or/34-40
79.	Meta-Analysis/
80.	exp Meta-Analysis as Topic/
81.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
82.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
83.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
84.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
85.	(search* adj4 literature).ab.
86.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
87.	cochrane.jw.
88.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
89.	or/42-51

90.	exp "sensitivity and specificity"/
91.	(sensitivity or specificity).ti,ab.
92.	((pre test or pretest or post test) adj probability).ti,ab.
93.	(predictive value* or PPV or NPV).ti,ab.
94.	likelihood ratio*.ti,ab.
95.	likelihood function/
96.	((area under adj4 curve) or AUC).ti,ab.
97.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
98.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
99.	gold standard.ab.
100.	or/53-62
101.	Epidemiologic studies/
102.	Observational study/
103.	exp Cohort studies/
104.	(cohort adj (study or studies or analys* or data)).ti,ab.
105.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
106.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
107.	Controlled Before-After Studies/
108.	Historically Controlled Study/
109.	Interrupted Time Series Analysis/
110.	(before adj2 after adj2 (study or studies or data)).ti,ab.
111.	or/64-73
112.	exp case control study/
113.	case control*.ti,ab.
114.	or/75-76
115.	74 or 77
116.	Cross-sectional studies/
117.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
118.	or/79-80
119.	74 or 81
120.	74 or 77 or 81
121.	33 and (41 or 52 or 63 or 83)

Embase (Ovid) search terms

37.	exp thyroid diseases/
38.	hyperthyroid*.ti,ab.
39.	hypothyroid*.ti,ab.
40.	thyrotoxicosis.ti,ab.
41.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
42.	or/1-5
43.	letter.pt. or letter/
44.	note.pt.
45.	editorial.pt.

46.	case report/ or case study/
47.	(letter or comment*).ti.
48.	or/7-11
49.	randomized controlled trial/ or random*.ti,ab.
50.	12 not 13
51.	animal/ not human/
52.	nonhuman/
53.	exp Animal Experiment/
54.	exp Experimental Animal/
55.	animal model/
56.	exp Rodent/
57.	(rat or rats or mouse or mice).ti.
58.	or/14-21
59.	6 not 22
60.	thyroid function test/
61.	Thyroxine/ or Triiodothyronine/ or thyrotropin/
62.	(T3 or T4 or fT3 or fT4 or T3RU or T3 uptake or T3 resin uptake or TSH or hTSH).ti,ab.
63.	(thyroxine or triiodothyronine).ti,ab.
64.	(Thyroid stimulating hormone or thyroid-stimulating hormone or thyrotropin or thyrotropic hormone or hormone).ti,ab.
65.	or/24-28
66.	23 and 29
67.	limit 30 to English language
68.	random*.ti,ab.
69.	factorial*.ti,ab.
70.	(crossover* or cross over*).ti,ab.
71.	((doubl* or singl*) adj blind*).ti,ab.
72.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
73.	crossover procedure/
74.	single blind procedure/
75.	randomized controlled trial/
76.	double blind procedure/
77.	or/32-40
78.	systematic review/
79.	meta-analysis/
80.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
81.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
82.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
83.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
84.	(search* adj4 literature).ab.
85.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
86.	cochrane.jw.
87.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.

88.	or/42-51
89.	exp "sensitivity and specificity"/
90.	(sensitivity or specificity).ti,ab.
91.	((pre test or pretest or post test) adj probability).ti,ab.
92.	(predictive value* or PPV or NPV).ti,ab.
93.	likelihood ratio*.ti,ab.
94.	((area under adj4 curve) or AUC).ti,ab.
95.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
96.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
97.	diagnostic accuracy/
98.	diagnostic test accuracy study/
99.	gold standard.ab.
100.	or/53-63
101.	Clinical study/
102.	Observational study/
103.	family study/
104.	longitudinal study/
105.	retrospective study/
106.	prospective study/
107.	cohort analysis/
108.	follow-up/
109.	cohort*.ti,ab.
110.	72 and 73
111.	(cohort adj (study or studies or analys* or data)).ti,ab.
112.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
113.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
114.	(before adj2 after adj2 (study or studies or data)).ti,ab.
115.	or/65-71,74-78
116.	exp case control study/
117.	case control*.ti,ab.
118.	or/80-81
119.	79 or 82
120.	cross-sectional study/
121.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
122.	or/84-85
123.	79 or 86
124.	79 or 82 or 86
125.	31 and (41 or 52 or 64 or 88)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Thyroid Diseases] explode all trees
#2.	hyperthyroid*:ti,ab
#3.	hypothyroid*:ti,ab

#4.	thyrotoxicosis:ti,ab
#5.	(thyroid near/3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)):ti,ab
#6.	(or #1-#5)
#7.	MeSH descriptor: [Thyroid function tests] explode all trees
#8.	MeSH descriptor: [Thyroxine] explode all trees
#9.	MeSH descriptor: [Triiodothyronine] explode all trees
#10.	MeSH descriptor: [Thyrotropin] explode all trees
#11.	(T3 or T4 or fT3 or fT4 or T3RU or T3 uptake or T3 resin uptake or TSH or hTSH):ti,ab
#12.	(thyroxine or triiodothyronine):ti,ab
#13.	(Thyroid stimulating hormone or thyroid-stimulating hormone or thyrotropin or thyrotropic hormone or hormone):ti,ab
#14.	(or #7-#13)
#15.	#6 and #14

A.2.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a thyroid disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 3: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 07 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

1.	exp thyroid diseases/
2.	hyperthyroid*.ti,ab.
3.	hypothyroid*.ti,ab.
4.	thyrotoxicosis.ti,ab.
5.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
6.	or/1-5

7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	exp models, economic/
45.	*Models, Theoretical/
46.	*Models, Organizational/
47.	markov chains/
48.	monte carlo method/
49.	exp Decision Theory/
50.	(markov* or monte carlo).ti,ab.

51.	econom* model*.ti,ab.
52.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
53.	or/44-52
54.	quality-adjusted life years/
55.	sickness impact profile/
56.	(quality adj2 (wellbeing or well being)).ti,ab.
57.	sickness impact profile.ti,ab.
58.	disability adjusted life.ti,ab.
59.	(qal* or qtime* or qwb* or daly*).ti,ab.
60.	(euroqol* or eq5d* or eq 5*).ti,ab.
61.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
62.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
63.	(hui or hui1 or hui2 or hui3).ti,ab.
64.	(health* year* equivalent* or hye or hyes).ti,ab.
65.	discrete choice*.ti,ab.
66.	rosser.ti,ab.
67.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
68.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
69.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
70.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
71.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
72.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
73.	or/54-72
74.	26 and (43 or 53 or 73)

Embase (Ovid) search terms

1.	exp thyroid diseases/
2.	hyperthyroid*.ti,ab.
3.	hypothyroid*.ti,ab.
4.	thyrotoxicosis*.ti,ab.
5.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/

18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	statistical model/
40.	exp economic aspect/
41.	39 and 40
42.	*theoretical model/
43.	*nonbiological model/
44.	stochastic model/
45.	decision theory/
46.	decision tree/
47.	monte carlo method/
48.	(markov* or monte carlo).ti,ab.
49.	econom* model*.ti,ab.
50.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
51.	or/41-50
52.	quality adjusted life year/
53.	"quality of life index"/
54.	short form 12/ or short form 20/ or short form 36/ or short form 8/
55.	sickness impact profile/
56.	(quality adj2 (wellbeing or well being)).ti,ab.
57.	sickness impact profile.ti,ab.

58.	disability adjusted life.ti,ab.
59.	(qal* or qtime* or qwb* or daly*).ti,ab.
60.	(euroqol* or eq5d* or eq 5*).ti,ab.
61.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
62.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
63.	(hui or hui1 or hui2 or hui3).ti,ab.
64.	(health* year* equivalent* or hye or hyes).ti,ab.
65.	discrete choice*.ti,ab.
66.	rosser.ti,ab.
67.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
68.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
69.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
70.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
71.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
72.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
73.	or/52-72
74.	24 and (38 or 51 or 73)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Thyroid Diseases EXPLODE ALL TREES
#2.	hyperthyroid*
#3.	hypothyroid*
#4.	thyrotoxicosis*
#5.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
#6.	#1 OR #2 OR #3 OR #4 or #5

Thyroid disease search strategy 3

This literature search strategy was used for the following reviews;

A.3 Indications for testing

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.3.1 Clinical search literature search strategy

Searches were constructed using the following approach:

- Population AND Prognostic/risk factor terms AND Study filter(s)

Table 4: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Observational studies Prognostic studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Observational studies Prognostic studies

Medline (Ovid) search terms

122.	exp thyroid diseases/
123.	hyperthyroid*.ti,ab.
124.	hypothyroid*.ti,ab.
125.	thyrotoxicosis.ti,ab.
126.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
127.	or/1-5
128.	letter/
129.	editorial/
130.	news/
131.	exp historical article/
132.	Anecdotes as Topic/
133.	comment/
134.	case report/
135.	(letter or comment*).ti.
136.	or/7-14
137.	randomized controlled trial/ or random*.ti,ab.
138.	15 not 16
139.	animals/ not humans/
140.	exp Animals, Laboratory/
141.	exp Animal Experimentation/
142.	exp Models, Animal/

143.	exp Rodentia/
144.	(rat or rats or mouse or mice).ti.
145.	or/17-23
146.	6 not 24
147.	limit 25 to English language
148.	Sleep Apnea, Obstructive/
149.	(obstructive adj2 sleep adj2 apnoea).ti,ab.
150.	"hypopnea syndrome".ti,ab.
151.	Osteoporosis/
152.	(osteoporosis or osteopenia or (bone adj (density or mass or loss)) or hepatic osteodystrophy).ti,ab.
153.	exp autoimmune diseases/
154.	exp Diabetes Mellitus, Type 2/
155.	(Type* adj ("2" or "II" or two) adj (diabete* or diabetic*)).ti,ab.
156.	((Maturit* or adult* or slow*) adj3 onset* adj3 (diabete* or diabetic*)).ti,ab.
157.	((Ketosis-resistant* or stable*) adj3 (diabete* or diabetic*)).ti,ab.
158.	((Non insulin* or Noninsulin*) adj3 depend* adj3 (diabete* or diabetic*)).ti,ab.
159.	NIDDM.ti,ab.
160.	Hashimoto Disease/
161.	(Hashimoto* adj3 (disease* or thyroiditis)).ti,ab.
162.	(thyroid* adj3 (chronic lymphocytic or autoimmun*)).ti,ab.
163.	Arthritis, Rheumatoid/
164.	(rheumatoid adj (arthritis or arthrosis)).ti,ab.
165.	(caplan* adj2 syndrome).ti,ab.
166.	(felty* adj2 syndrome).ti,ab.
167.	(rheumatoid adj2 factor).ti,ab.
168.	((inflammatory or idiopathic) adj2 arthritis).ti.
169.	"inflammatory polyarthritis".ti,ab.
170.	exp Multiple Sclerosis/
171.	((multiple or disseminated) adj scleros*).ti,ab.
172.	encephalomyelitis disseminata.ti,ab.
173.	MS.ti.
174.	celiac disease/
175.	(celiac or coeliac or "gluten sensitive enteropathy" or sprue).ti,ab.
176.	Arrhythmias, Cardiac/
177.	atrial fibrillation/
178.	(atrial adj3 fibrillat*).ti,ab.
179.	(auricular adj3 fibrillat*).ti,ab.
180.	(arrythmia* or Afib or a-fib).ti,ab.
181.	palpitation*.ti,ab.
182.	exp Obesity/
183.	exp Overweight/
184.	Weight Loss/
185.	(obesity or obese).ti.
186.	(weight adj (loss or lost or losing or reduc*)).ti,ab.

187.	(weight adj (gain or increase or rise or rising or risen)).ti,ab.
188.	((over adj (weight or eating)) or overweight).ti,ab.
189.	((under adj (weight or eating)) or underweight).ti,ab.
190.	Turner Syndrome/ or Down syndrome/ or DiGeorge Syndrome/
191.	((turner* or down* or digeorge*) adj syndrome).ti,ab.
192.	myxedema/
193.	(myxedema or myxoedema).ti,ab.
194.	((dry* or wax* or itch* or flak* or crack*) adj3 skin).ti,ab.
195.	Hoarseness/
196.	(hoarseness or ((hoarse or harsh or rasp* or strained) adj3 voice)).ti,ab.
197.	cognitive dysfunction/
198.	(cognitive adj (dysfunction* or impairment* or defec*)).ti,ab.
199.	Muscle Cramp/
200.	(muscle adj3 (spasm* or cramp*)).ti,ab.
201.	depression/
202.	Anxiety/
203.	fatigue/
204.	(tiredness or fatigue or anxiet* or anxious or depression or low mood or tearfulness or irritability or nervousness).ti,ab.
205.	(sleep* adj (disturbance* or difficult* or trouble* or disorder* or problem*)).ti,ab.
206.	body temperature regulation/
207.	(temperature adj2 (disturbance or regulat*)).ti,ab.
208.	Thermogenesis/
209.	thermogenes*.ti,ab.
210.	Menstruation Disturbances/
211.	((long* or heav* or more or increas* or abnormal or irregular or cramp* or pain* or disturb*) adj2 (period* or menses or menstruation)).ti,ab.
212.	exp Dyspnea/
213.	((paroxysmal or exertion*) adj3 (dyspnoea or dyspnea)).ti,ab.
214.	(dyspnoea or dyspnea or "shortness of breath" or breathlessness or air hunger).ti,ab.
215.	Diarrhea/
216.	Constipation/
217.	((digestive or bowel or gut or stool) adj3 (change* or problem* increase or slow-down or slowdown or inconsisten* or irregularit*)).ti,ab.
218.	(constipat* or diarrhoea or diarrhea or bloating or gas or cramping or loose stool* or burping or heartburn or flatulence).ti,ab.
219.	abortion, spontaneous/ or abortion, habitual/
220.	(recurrent miscarriage or habitual abortion or spontaneous abortion or recurrent pregnancy loss or RPL or pregnancy loss).ti,ab.
221.	Photophobia/
222.	photophobia.ti,ab.
223.	((eye* or eyelid*) adj2 (bulge or bulging or staring or grittiness or gritty or dry or water* or swollen or swelling or oedema or edema or fullness or red* or blurr* or double vision or ache or pain or difficult* mov* or retraction)).ti,ab.
224.	Genetic predisposition to disease/
225.	((family or familial or genetic) adj2 (disease* or history)).ti,ab.
226.	((autoimmune or auto immune) adj disease*).ti,ab.

227.	or/27-105
228.	Risk/
229.	Risk Assessment/
230.	Risk Factors/
231.	risk*.ti.
232.	risk factor*.ti,ab.
233.	(risk adj3 assess*).ti,ab.
234.	prevalence/
235.	prevalence.ti,ab.
236.	or/107-114
237.	26 and (106 or 115)
238.	prognosis/
239.	(predict* or prognos*).ti,ab.
240.	Logistic models/
241.	Disease progression/
242.	or/117-120
243.	Epidemiologic studies/
244.	Observational study/
245.	exp Cohort studies/
246.	(cohort adj (study or studies or analys* or data)).ti,ab.
247.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
248.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
249.	Controlled Before-After Studies/
250.	Historically Controlled Study/
251.	Interrupted Time Series Analysis/
252.	(before adj2 after adj2 (study or studies or data)).ti,ab.
253.	or/122-131
254.	exp case control study/
255.	case control*.ti,ab.
256.	or/133-134
257.	132 or 135
258.	Cross-sectional studies/
259.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
260.	or/137-138
261.	132 or 139
262.	132 or 135 or 139
263.	116 and (121 or 141)

Embase (Ovid) search terms

126.	exp thyroid diseases/
127.	hyperthyroid*.ti,ab.
128.	hypothyroid*.ti,ab.
129.	thyrotoxicosis.ti,ab.
130.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or

	condition* or disorder*).ti,ab.
131.	or/1-5
132.	letter.pt. or letter/
133.	note.pt.
134.	editorial.pt.
135.	case report/ or case study/
136.	(letter or comment*).ti.
137.	or/7-11
138.	randomized controlled trial/ or random*.ti,ab.
139.	12 not 13
140.	animal/ not human/
141.	nonhuman/
142.	exp Animal Experiment/
143.	exp Experimental Animal/
144.	animal model/
145.	exp Rodent/
146.	(rat or rats or mouse or mice).ti.
147.	or/14-21
148.	6 not 22
149.	sleep disordered breathing/
150.	(obstructive adj2 sleep adj2 apnoea).ti,ab.
151.	"hypopnea syndrome".ti,ab.
152.	*osteoporosis/
153.	(osteoporosis or osteopenia or (bone adj (density or mass or loss)) or hepatic osteodystrophy).ti,ab.
154.	exp autoimmune disease/
155.	*non insulin dependent diabetes mellitus/
156.	(Type* adj ("2" or "II" or two) adj (diabete* or diabetic*).ti,ab.
157.	((Maturit* or adult* or slow*) adj3 onset* adj3 (diabete* or diabetic*).ti,ab.
158.	((Ketosis-resistant* or stable*) adj3 (diabete* or diabetic*).ti,ab.
159.	((Non insulin* or Noninsulin*) adj3 depend* adj3 (diabete* or diabetic*).ti,ab.
160.	NIDDM.ti,ab.
161.	((autoimmune or auto immune) adj disease*).ti,ab.
162.	*hashimoto disease/
163.	(Hashimoto* adj3 (disease* or thyroiditis)).ti,ab.
164.	(thyroid* adj3 (chronic lymphocytic or autoimmun*).ti,ab.
165.	*rheumatoid arthritis/
166.	(rheumatoid adj (arthritis or arthrosis)).ti,ab.
167.	(caplan* adj2 syndrome).ti,ab.
168.	(felty* adj2 syndrome).ti,ab.
169.	(rheumatoid adj2 factor).ti,ab.
170.	((inflammatory or idiopathic) adj2 arthritis).ti.
171.	"inflammatory polyarthritis".ti,ab.
172.	*multiple sclerosis/
173.	((multiple or disseminated) adj scleros*).ti,ab.

174.	encephalomyelitis disseminata.ti,ab.
175.	MS.ti.
176.	celiac disease/
177.	(celiac or coeliac or "gluten sensitive enteropathy" or sprue).ti,ab.
178.	heart arrhythmia/
179.	atrial fibrillation/
180.	(atrial adj3 fibrillat*).ti,ab.
181.	(auricular adj3 fibrillat*).ti,ab.
182.	(arrythmia* or Afib or a-fib).ti,ab.
183.	palpitation*.ti,ab.
184.	exp obesity/
185.	*weight reduction/
186.	(obesity or obese).ti.
187.	(weight adj (loss or lost or losing or reduc*)).ti,ab.
188.	(weight adj (gain or increase or rise or rising or risen)).ti,ab.
189.	((over adj (weight or eating)) or overweight).ti,ab.
190.	((under adj (weight or eating)) or underweight).ti,ab.
191.	digeorge syndrome/ or turner dysndrome/ or down syndrome/
192.	((turner* or down* or digeorge*) adj syndrome).ti,ab.
193.	myxedema/
194.	(myxedema or myxoedema).ti,ab.
195.	((dry* or wax* or itch* or flak* or crack*) adj3 skin).ti,ab.
196.	hoarseness/
197.	(hoarseness or ((hoarse or harsh or rasp* or strained) adj3 voice)).ti,ab.
198.	*cognitive defect/
199.	(cognitive adj (dysfunction* or impairment* or defec*)).ti,ab.
200.	muscle cramp/
201.	(muscle adj3 (spasm* or cramp*)).ti,ab.
202.	*depression/
203.	*anxiety/
204.	*fatigue/
205.	(tiredness or fatigue or anxiet* or anxious or depression or low mood or tearfulness or irritability or nervousness).ti,ab.
206.	(sleep* adj (disturbance* or difficult* or trouble* or disorder* or problem*)).ti,ab.
207.	thermoregulation/
208.	(temperature adj2 (disturbance or regulat*)).ti,ab.
209.	*thermogenesis/
210.	thermogenes*.ti,ab.
211.	menstruation disorder/
212.	((long* or heav* or more or increas* or abnormal or irregular or cramp* or pain* or disturb*) adj2 (period* or menses or menstruation)).ti,ab.
213.	*dyspnea/
214.	((paroxysmal or exertion*) adj3 (dyspnoea or dyspnea)).ti,ab.
215.	(dyspnoea or dyspnea or "shortness of breath" or breathlessness or air hunger).ti,ab.
216.	*diarrhea/
217.	constipation/

218.	((digestive or bowel or gut or stool) adj3 (change* or problem* increase or slow-down or slowdown or inconsisten* or irregularit*).ti,ab.
219.	(constipat* or diarrhoea or diarrhea or bloating or gas or cramping or loose stool* or burping or heartburn).ti,ab.
220.	*spontaneous abortion/
221.	recurrent abortion/
222.	(recurrent miscarriage or habitual abortion or spontaneous abortion or recurrent pregnancy loss or RPL or pregnancy loss).ti,ab.
223.	*photophobia/
224.	photophobia.ti,ab.
225.	((eye* or eyelid*) adj2 (bulge or bulging or staring or grittiness or gritty or dry or water* or swollen or swelling or oedema or edema or fullness or red* or blurr* or double vision or ache or pain or difficult* mov* or retraction)).ti,ab.
226.	exp genetic predisposition/
227.	((family or familial or genetic) adj2 (disease* or history)).ti,ab.
228.	*risk/
229.	risk factor/
230.	*risk assessment/
231.	risk*.ti.
232.	risk factor*.ti,ab.
233.	(risk adj3 assess*).ti,ab.
234.	prevalence/
235.	prevalence.ti,ab.
236.	or/24-102
237.	or/103-110
238.	23 and (111 or 112)
239.	exp prognosis/
240.	prognostic assessment/
241.	(predict* or prognos*).ti,ab.
242.	disease course/
243.	statistical model/
244.	or/114-118
245.	Clinical study/
246.	Observational study/
247.	family study/
248.	longitudinal study/
249.	retrospective study/
250.	prospective study/
251.	cohort analysis/
252.	follow-up/
253.	cohort*.ti,ab.
254.	127 and 128
255.	(cohort adj (study or studies or analys* or data)).ti,ab.
256.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
257.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.

258.	(before adj2 after adj2 (study or studies or data)).ti,ab.
259.	or/120-126,129-133
260.	exp case control study/
261.	case control*.ti,ab.
262.	or/135-136
263.	134 or 137
264.	cross-sectional study/
265.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
266.	or/139-140
267.	134 or 141
268.	134 or 137 or 141
269.	113 and (119 or 143)
270.	Limit 144 to English language

A.3.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a thyroid disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 5: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 07 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

75.	exp thyroid diseases/
76.	hyperthyroid*.ti,ab.
77.	hypothyroid*.ti,ab.
78.	thyrotoxicosis.ti,ab.
79.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
80.	or/1-5
81.	letter/

82.	editorial/
83.	news/
84.	exp historical article/
85.	Anecdotes as Topic/
86.	comment/
87.	case report/
88.	(letter or comment*).ti.
89.	or/7-14
90.	randomized controlled trial/ or random*.ti,ab.
91.	15 not 16
92.	animals/ not humans/
93.	exp Animals, Laboratory/
94.	exp Animal Experimentation/
95.	exp Models, Animal/
96.	exp Rodentia/
97.	(rat or rats or mouse or mice).ti.
98.	or/17-23
99.	6 not 24
100.	limit 25 to English language
101.	Economics/
102.	Value of life/
103.	exp "Costs and Cost Analysis"/
104.	exp Economics, Hospital/
105.	exp Economics, Medical/
106.	Economics, Nursing/
107.	Economics, Pharmaceutical/
108.	exp "Fees and Charges"/
109.	exp Budgets/
110.	budget*.ti,ab.
111.	cost*.ti.
112.	(economic* or pharmaco?economic*).ti.
113.	(price* or pricing*).ti,ab.
114.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
115.	(financ* or fee or fees).ti,ab.
116.	(value adj2 (money or monetary)).ti,ab.
117.	or/27-42
118.	exp models, economic/
119.	*Models, Theoretical/
120.	*Models, Organizational/
121.	markov chains/
122.	monte carlo method/
123.	exp Decision Theory/
124.	(markov* or monte carlo).ti,ab.
125.	econom* model*.ti,ab.

126.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
127.	or/44-52
128.	quality-adjusted life years/
129.	sickness impact profile/
130.	(quality adj2 (wellbeing or well being)).ti,ab.
131.	sickness impact profile.ti,ab.
132.	disability adjusted life.ti,ab.
133.	(qal* or qtime* or qwb* or daly*).ti,ab.
134.	(euroqol* or eq5d* or eq 5*).ti,ab.
135.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
136.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
137.	(hui or hui1 or hui2 or hui3).ti,ab.
138.	(health* year* equivalent* or hye or hyes).ti,ab.
139.	discrete choice*.ti,ab.
140.	rosser.ti,ab.
141.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
142.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
143.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
144.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
145.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
146.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
147.	or/54-72
148.	26 and (43 or 53 or 73)

Embase (Ovid) search terms

75.	exp thyroid diseases/
76.	hyperthyroid*.ti,ab.
77.	hypothyroid*.ti,ab.
78.	thyrotoxicosis*.ti,ab.
79.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
80.	or/1-5
81.	letter.pt. or letter/
82.	note.pt.
83.	editorial.pt.
84.	case report/ or case study/
85.	(letter or comment*).ti.
86.	or/7-11
87.	randomized controlled trial/ or random*.ti,ab.
88.	12 not 13
89.	animal/ not human/
90.	nonhuman/
91.	exp Animal Experiment/
92.	exp Experimental Animal/

93.	animal model/
94.	exp Rodent/
95.	(rat or rats or mouse or mice).ti.
96.	or/14-21
97.	6 not 22
98.	limit 23 to English language
99.	health economics/
100.	exp economic evaluation/
101.	exp health care cost/
102.	exp fee/
103.	budget/
104.	funding/
105.	budget*.ti,ab.
106.	cost*.ti.
107.	(economic* or pharmaco?economic*).ti.
108.	(price* or pricing*).ti,ab.
109.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
110.	(financ* or fee or fees).ti,ab.
111.	(value adj2 (money or monetary)).ti,ab.
112.	or/25-37
113.	statistical model/
114.	exp economic aspect/
115.	39 and 40
116.	*theoretical model/
117.	*nonbiological model/
118.	stochastic model/
119.	decision theory/
120.	decision tree/
121.	monte carlo method/
122.	(markov* or monte carlo).ti,ab.
123.	econom* model*.ti,ab.
124.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
125.	or/41-50
126.	quality adjusted life year/
127.	"quality of life index"/
128.	short form 12/ or short form 20/ or short form 36/ or short form 8/
129.	sickness impact profile/
130.	(quality adj2 (wellbeing or well being)).ti,ab.
131.	sickness impact profile.ti,ab.
132.	disability adjusted life.ti,ab.

133.	(qal* or qtime* or qwb* or daly*).ti,ab.
134.	(euroqol* or eq5d* or eq 5*).ti,ab.
135.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
136.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
137.	(hui or hui1 or hui2 or hui3).ti,ab.
138.	(health* year* equivalent* or hye or hyes).ti,ab.
139.	discrete choice*.ti,ab.
140.	rosser.ti,ab.
141.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
142.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
143.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
144.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
145.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
146.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
147.	or/52-72
148.	24 and (38 or 51 or 73)

NHS EED and HTA (CRD) search terms

#7.	MeSH DESCRIPTOR Thyroid Diseases EXPLODE ALL TREES
#8.	hyperthyroid*
#9.	hypothyroid*
#10.	thyrotoxicosis*
#11.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
#12.	#1 OR #2 OR #3 OR #4 or #5

Thyroid disease search strategy 4

This literature search strategy was used for the following reviews;

A.4 Imaging for fine needle aspiration

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.4.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 6: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 1 or 12 CENTRAL to 2019 Issue 1 or 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Medline (Ovid) search terms

264.	exp thyroid diseases/
265.	hyperthyroid*.ti,ab.
266.	hypothyroid*.ti,ab.
267.	thyrotoxicosis.ti,ab.
268.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
269.	or/1-5
270.	letter/
271.	editorial/
272.	news/
273.	exp historical article/

274.	Anecdotes as Topic/
275.	comment/
276.	case report/
277.	(letter or comment*).ti.
278.	or/7-14
279.	randomized controlled trial/ or random*.ti,ab.
280.	15 not 16
281.	animals/ not humans/
282.	exp Animals, Laboratory/
283.	exp Animal Experimentation/
284.	exp Models, Animal/
285.	exp Rodentia/
286.	(rat or rats or mouse or mice).ti.
287.	or/17-23
288.	6 not 24
289.	Ultrasonography/
290.	Magnetic Resonance Imaging/
291.	Tomography, X-Ray Computed/
292.	(ultrasonograph* or ultrasound* or ultra sound or sonograph* or sonogram* or echograph* or echotomograph* or doppler).ti,ab.
293.	magnetic resonance.ti,ab.
294.	(MR or MRI).ti,ab.
295.	(diffusion weighted imag* or DWI).ti,ab.
296.	(computed adj3 tomography).ti,ab.
297.	(CT or CAT).ti,ab.
298.	or/26-34
299.	25 and 35
300.	limit 36 to English language
301.	randomized controlled trial.pt.
302.	controlled clinical trial.pt.
303.	randomi#ed.ti,ab.
304.	placebo.ab.
305.	randomly.ti,ab.
306.	Clinical Trials as topic.sh.
307.	trial.ti.
308.	or/38-44
309.	exp "sensitivity and specificity"/
310.	(sensitivity or specificity).ti,ab.
311.	((pre test or pretest or post test) adj probability).ti,ab.
312.	(predictive value* or PPV or NPV).ti,ab.
313.	likelihood ratio*.ti,ab.
314.	likelihood function/
315.	((area under adj4 curve) or AUC).ti,ab.
316.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
317.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.

318.	gold standard.ab.
319.	or/46-55
320.	Epidemiologic studies/
321.	Observational study/
322.	exp Cohort studies/
323.	(cohort adj (study or studies or analys* or data)).ti,ab.
324.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
325.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
326.	Controlled Before-After Studies/
327.	Historically Controlled Study/
328.	Interrupted Time Series Analysis/
329.	(before adj2 after adj2 (study or studies or data)).ti,ab.
330.	or/57-66
331.	exp case control study/
332.	case control*.ti,ab.
333.	or/68-69
334.	67 or 70
335.	Cross-sectional studies/
336.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
337.	or/72-73
338.	67 or 74
339.	67 or 70 or 74
340.	Meta-Analysis/
341.	exp Meta-Analysis as Topic/
342.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
343.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
344.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
345.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
346.	(search* adj4 literature).ab.
347.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
348.	cochrane.jw.
349.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
350.	or/77-86
351.	37 and (45 or 56 or 87 or 76)

Embase (Ovid) search terms

271.	exp thyroid disease/
272.	hyperthyroid*.ti,ab.
273.	hypothyroid*.ti,ab.
274.	thyrotoxicosis.ti,ab.
275.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.

276.	or/1-5
277.	letter.pt. or letter/
278.	note.pt.
279.	editorial.pt.
280.	case report/ or case study/
281.	(letter or comment*).ti.
282.	or/7-11
283.	randomized controlled trial/ or random*.ti,ab.
284.	12 not 13
285.	animal/ not human/
286.	nonhuman/
287.	exp Animal Experiment/
288.	exp Experimental Animal/
289.	animal model/
290.	exp Rodent/
291.	(rat or rats or mouse or mice).ti.
292.	or/14-21
293.	6 not 22
294.	limit 23 to English language
295.	echography/
296.	nuclear magnetic resonance imaging/
297.	computer assisted tomography/
298.	(ultrasonograph* or ultrasound* or ultra sound or sonograph* or sonogram* or echograph* or echotomograph* or doppler).ti,ab.
299.	magnetic resonance.ti,ab.
300.	(MR or MRI).ti,ab.
301.	(diffusion weighted imag* or DWI).ti,ab.
302.	(computed adj3 tomography).ti,ab.
303.	(CT or CAT).ti,ab.
304.	or/25-33
305.	24 and 34
306.	exp "sensitivity and specificity"/
307.	(sensitivity or specificity).ti,ab.
308.	((pre test or pretest or post test) adj probability).ti,ab.
309.	(predictive value* or PPV or NPV).ti,ab.
310.	likelihood ratio*.ti,ab.
311.	((area under adj4 curve) or AUC).ti,ab.
312.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
313.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
314.	diagnostic accuracy/
315.	diagnostic test accuracy study/
316.	gold standard.ab.
317.	or/36-46
318.	random*.ti,ab.
319.	factorial*.ti,ab.

320.	(crossover* or cross over*).ti,ab.
321.	((doubl* or singl*) adj blind*).ti,ab.
322.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
323.	crossover procedure/
324.	single blind procedure/
325.	randomized controlled trial/
326.	double blind procedure/
327.	or/48-56
328.	systematic review/
329.	meta-analysis/
330.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
331.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
332.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
333.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
334.	(search* adj4 literature).ab.
335.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
336.	cochrane.jw.
337.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
338.	or/58-67
339.	Clinical study/
340.	Observational study/
341.	family study/
342.	longitudinal study/
343.	retrospective study/
344.	prospective study/
345.	cohort analysis/
346.	follow-up/
347.	cohort*.ti,ab.
348.	76 and 77
349.	(cohort adj (study or studies or analys* or data)).ti,ab.
350.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
351.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
352.	(before adj2 after adj2 (study or studies or data)).ti,ab.
353.	or/69-75,78-82
354.	exp case control study/
355.	case control*.ti,ab.
356.	or/84-85
357.	83 or 86
358.	cross-sectional study/
359.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
360.	or/88-89
361.	83 or 90

362.	83 or 86 or 90
363.	35 and (47 or 57 or 68 or 92)

Cochrane Library (Wiley) search terms

#16.	MeSH descriptor: [Thyroid Diseases] explode all trees
#17.	hyperthyroid*:ti,ab
#18.	hypothyroid*:ti,ab
#19.	thyrotoxicosis:ti,ab
#20.	(thyroid near/3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)):ti,ab
#21.	(or #1-#5)
#22.	MeSH descriptor: [Ultrasonography] explode all trees
#23.	MeSH descriptor: [Magnetic Resonance Imaging] explode all trees
#24.	MeSH descriptor: [Tomography, X-Ray Computed] explode all trees
#25.	(ultrasonograph* or ultrasound* or ultra sound or sonograph* or sonogram* or echograph* or echotomograph* or doppler):ti,ab
#26.	magnetic resonance:ti,ab
#27.	(MR or MRI):ti,ab
#28.	(diffusion weighted imag* or DWI):ti,ab
#29.	(computed near/3 tomography):ti,ab
#30.	(CT or CAT):ti,ab
#31.	(or #7-#15)
#32.	#6 and #16

A.4.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a thyroid disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 7: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 07 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

149.	exp thyroid diseases/
150.	hyperthyroid*.ti,ab.
151.	hypothyroid*.ti,ab.
152.	thyrotoxicosis.ti,ab.
153.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
154.	or/1-5
155.	letter/
156.	editorial/
157.	news/
158.	exp historical article/
159.	Anecdotes as Topic/
160.	comment/
161.	case report/
162.	(letter or comment*).ti.
163.	or/7-14
164.	randomized controlled trial/ or random*.ti,ab.
165.	15 not 16
166.	animals/ not humans/
167.	exp Animals, Laboratory/
168.	exp Animal Experimentation/
169.	exp Models, Animal/
170.	exp Rodentia/
171.	(rat or rats or mouse or mice).ti.
172.	or/17-23
173.	6 not 24
174.	limit 25 to English language
175.	Economics/
176.	Value of life/
177.	exp "Costs and Cost Analysis"/
178.	exp Economics, Hospital/
179.	exp Economics, Medical/
180.	Economics, Nursing/
181.	Economics, Pharmaceutical/
182.	exp "Fees and Charges"/
183.	exp Budgets/
184.	budget*.ti,ab.
185.	cost*.ti.
186.	(economic* or pharmaco?economic*).ti.
187.	(price* or pricing*).ti,ab.
188.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
189.	(financ* or fee or fees).ti,ab.
190.	(value adj2 (money or monetary)).ti,ab.
191.	or/27-42

192.	exp models, economic/
193.	*Models, Theoretical/
194.	*Models, Organizational/
195.	markov chains/
196.	monte carlo method/
197.	exp Decision Theory/
198.	(markov* or monte carlo).ti,ab.
199.	econom* model*.ti,ab.
200.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
201.	or/44-52
202.	quality-adjusted life years/
203.	sickness impact profile/
204.	(quality adj2 (wellbeing or well being)).ti,ab.
205.	sickness impact profile.ti,ab.
206.	disability adjusted life.ti,ab.
207.	(qal* or qtime* or qwb* or daly*).ti,ab.
208.	(euroqol* or eq5d* or eq 5*).ti,ab.
209.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
210.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
211.	(hui or hui1 or hui2 or hui3).ti,ab.
212.	(health* year* equivalent* or hye or hyes).ti,ab.
213.	discrete choice*.ti,ab.
214.	rosser.ti,ab.
215.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
216.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
217.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
218.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
219.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
220.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
221.	or/54-72
222.	26 and (43 or 53 or 73)

Embase (Ovid) search terms

149.	exp thyroid diseases/
150.	hyperthyroid*.ti,ab.
151.	hypothyroid*.ti,ab.
152.	thyrotoxicosis*.ti,ab.
153.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
154.	or/1-5
155.	letter.pt. or letter/
156.	note.pt.
157.	editorial.pt.
158.	case report/ or case study/
159.	(letter or comment*).ti.

160.	or/7-11
161.	randomized controlled trial/ or random*.ti,ab.
162.	12 not 13
163.	animal/ not human/
164.	nonhuman/
165.	exp Animal Experiment/
166.	exp Experimental Animal/
167.	animal model/
168.	exp Rodent/
169.	(rat or rats or mouse or mice).ti.
170.	or/14-21
171.	6 not 22
172.	limit 23 to English language
173.	health economics/
174.	exp economic evaluation/
175.	exp health care cost/
176.	exp fee/
177.	budget/
178.	funding/
179.	budget*.ti,ab.
180.	cost*.ti.
181.	(economic* or pharmaco?economic*).ti.
182.	(price* or pricing*).ti,ab.
183.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
184.	(financ* or fee or fees).ti,ab.
185.	(value adj2 (money or monetary)).ti,ab.
186.	or/25-37
187.	statistical model/
188.	exp economic aspect/
189.	39 and 40
190.	*theoretical model/
191.	*nonbiological model/
192.	stochastic model/
193.	decision theory/
194.	decision tree/
195.	monte carlo method/
196.	(markov* or monte carlo).ti,ab.
197.	econom* model*.ti,ab.
198.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
199.	or/41-50

200.	quality adjusted life year/
201.	"quality of life index"/
202.	short form 12/ or short form 20/ or short form 36/ or short form 8/
203.	sickness impact profile/
204.	(quality adj2 (wellbeing or well being)).ti,ab.
205.	sickness impact profile.ti,ab.
206.	disability adjusted life.ti,ab.
207.	(qal* or qtime* or qwb* or daly*).ti,ab.
208.	(euroqol* or eq5d* or eq 5*).ti,ab.
209.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
210.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
211.	(hui or hui1 or hui2 or hui3).ti,ab.
212.	(health* year* equivalent* or hye or hyes).ti,ab.
213.	discrete choice*.ti,ab.
214.	rosser.ti,ab.
215.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
216.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
217.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
218.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
219.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
220.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
221.	or/52-72
222.	24 and (38 or 51 or 73)

NHS EED and HTA (CRD) search terms

#13.	MeSH DESCRIPTOR Thyroid Diseases EXPLODE ALL TREES
#14.	hyperthyroid*
#15.	hypothyroid*
#16.	thyrotoxicosis*
#17.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
#18.	#1 OR #2 OR #3 OR #4 or #5

Thyroid disease search strategy 5

This literature search strategy was used for the following reviews;

A.5 Ultrasound guidance for fine needle aspiration

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.5.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 8: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Randomised controlled trials Observational studies Diagnostic tests studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Randomised controlled trials Observational studies Diagnostic tests studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 1 or 12 CENTRAL to 2019 Issue 1 or 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Medline (Ovid) search terms

352.	exp thyroid diseases/
353.	hyperthyroid*.ti,ab.
354.	hypothyroid*.ti,ab.
355.	thyrotoxicosis.ti,ab.
356.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
357.	or/1-5
358.	letter/
359.	editorial/
360.	news/
361.	exp historical article/
362.	Anecdotes as Topic/

363.	comment/
364.	case report/
365.	(letter or comment*).ti.
366.	or/7-14
367.	randomized controlled trial/ or random*.ti,ab.
368.	15 not 16
369.	animals/ not humans/
370.	exp Animals, Laboratory/
371.	exp Animal Experimentation/
372.	exp Models, Animal/
373.	exp Rodentia/
374.	(rat or rats or mouse or mice).ti.
375.	or/17-23
376.	6 not 24
377.	Biopsy, Fine-Needle/
378.	(FNA or FNAB or FNA biops* or fine needle aspiration or fine needle aspiration biops* or fine-needle aspiration or fine-needle aspiration biops* or (palpation guid* adj3 aspiration)).ti,ab.
379.	26 or 27
380.	25 and 28
381.	randomized controlled trial.pt.
382.	controlled clinical trial.pt.
383.	randomi#ed.ti,ab.
384.	placebo.ab.
385.	randomly.ti,ab.
386.	Clinical Trials as topic.sh.
387.	trial.ti.
388.	or/30-36
389.	exp "sensitivity and specificity"/
390.	(sensitivity or specificity).ti,ab.
391.	((pre test or pretest or post test) adj probability).ti,ab.
392.	(predictive value* or PPV or NPV).ti,ab.
393.	likelihood ratio*.ti,ab.
394.	likelihood function/
395.	((area under adj4 curve) or AUC).ti,ab.
396.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
397.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
398.	gold standard.ab.
399.	or/38-47
400.	Epidemiologic studies/
401.	Observational study/
402.	exp Cohort studies/
403.	(cohort adj (study or studies or analys* or data)).ti,ab.
404.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.

405.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
406.	Controlled Before-After Studies/
407.	Historically Controlled Study/
408.	Interrupted Time Series Analysis/
409.	(before adj2 after adj2 (study or studies or data)).ti,ab.
410.	or/49-58
411.	exp case control study/
412.	case control*.ti,ab.
413.	or/60-61
414.	59 or 62
415.	Cross-sectional studies/
416.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
417.	or/64-65
418.	59 or 66
419.	59 or 62 or 66
420.	29 and (37 or 48 or 68)
421.	limit 69 to English language

Embase (Ovid) search terms

364.	exp thyroid diseases/
365.	hyperthyroid*.ti,ab.
366.	hypothyroid*.ti,ab.
367.	thyrotoxicosis.ti,ab.
368.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
369.	or/1-5
370.	letter.pt. or letter/
371.	note.pt.
372.	editorial.pt.
373.	case report/ or case study/
374.	(letter or comment*).ti.
375.	or/7-11
376.	randomized controlled trial/ or random*.ti,ab.
377.	12 not 13
378.	animal/ not human/
379.	nonhuman/
380.	exp Animal Experiment/
381.	exp Experimental Animal/
382.	animal model/
383.	exp Rodent/
384.	(rat or rats or mouse or mice).ti.
385.	or/14-21
386.	6 not 22
387.	fine needle aspiration biopsy/
388.	(FNA or FNAB or FNA biops* or fine needle aspiration or fine needle aspiration biops* or fine-needle aspiration or fine-needle aspiration biops* or (palpation guid* adj3

	aspiration)).ti,ab.
389.	24 or 25
390.	23 and 26
391.	random*.ti,ab.
392.	factorial*.ti,ab.
393.	(crossover* or cross over*).ti,ab.
394.	((doubl* or singl*) adj blind*).ti,ab.
395.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
396.	crossover procedure/
397.	single blind procedure/
398.	randomized controlled trial/
399.	double blind procedure/
400.	or/28-36
401.	exp "sensitivity and specificity"/
402.	(sensitivity or specificity).ti,ab.
403.	((pre test or pretest or post test) adj probability).ti,ab.
404.	(predictive value* or PPV or NPV).ti,ab.
405.	likelihood ratio*.ti,ab.
406.	((area under adj4 curve) or AUC).ti,ab.
407.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
408.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
409.	diagnostic accuracy/
410.	diagnostic test accuracy study/
411.	gold standard.ab.
412.	or/38-48
413.	Clinical study/
414.	Observational study/
415.	family study/
416.	longitudinal study/
417.	retrospective study/
418.	prospective study/
419.	cohort analysis/
420.	follow-up/
421.	cohort*.ti,ab.
422.	57 and 58
423.	(cohort adj (study or studies or analys* or data)).ti,ab.
424.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
425.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
426.	(before adj2 after adj2 (study or studies or data)).ti,ab.
427.	or/50-56,59-63
428.	exp case control study/
429.	case control*.ti,ab.
430.	or/65-66

431.	64 or 67
432.	cross-sectional study/
433.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
434.	or/69-70
435.	64 or 71
436.	64 or 67 or 71
437.	27 and (37 or 49 or 73)
438.	limit 74 to English language

Cochrane Library (Wiley) search terms

#33.	MeSH descriptor: [Thyroid Diseases] explode all trees
#34.	hyperthyroid*:ti,ab
#35.	hypothyroid*:ti,ab
#36.	thyrotoxicosis:ti,ab
#37.	(thyroid near/3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)) ti,ab
#38.	(or #1-#5)
#39.	MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#40.	(FNA or FNAB or FNA biops* or fine needle aspiration or fine needle aspiration biops* or fine-needle aspiration or fine-needle aspiration biops* or (palpation guid* near/3 aspiration)):ti,ab
#41.	#7 or #8
#42.	#6 and #9

A.5.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a thyroid disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 9: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 07 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

223.	exp thyroid diseases/
224.	hyperthyroid*.ti,ab.
225.	hypothyroid*.ti,ab.
226.	thyrotoxicosis.ti,ab.
227.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
228.	or/1-5
229.	letter/
230.	editorial/
231.	news/
232.	exp historical article/
233.	Anecdotes as Topic/
234.	comment/
235.	case report/
236.	(letter or comment*).ti.
237.	or/7-14
238.	randomized controlled trial/ or random*.ti,ab.
239.	15 not 16
240.	animals/ not humans/
241.	exp Animals, Laboratory/
242.	exp Animal Experimentation/
243.	exp Models, Animal/
244.	exp Rodentia/
245.	(rat or rats or mouse or mice).ti.
246.	or/17-23
247.	6 not 24
248.	limit 25 to English language
249.	Economics/
250.	Value of life/
251.	exp "Costs and Cost Analysis"/
252.	exp Economics, Hospital/
253.	exp Economics, Medical/
254.	Economics, Nursing/
255.	Economics, Pharmaceutical/
256.	exp "Fees and Charges"/
257.	exp Budgets/
258.	budget*.ti,ab.
259.	cost*.ti.
260.	(economic* or pharmaco?economic*).ti.
261.	(price* or pricing*).ti,ab.
262.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
263.	(financ* or fee or fees).ti,ab.
264.	(value adj2 (money or monetary)).ti,ab.
265.	or/27-42

266.	exp models, economic/
267.	*Models, Theoretical/
268.	*Models, Organizational/
269.	markov chains/
270.	monte carlo method/
271.	exp Decision Theory/
272.	(markov* or monte carlo).ti,ab.
273.	econom* model*.ti,ab.
274.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
275.	or/44-52
276.	quality-adjusted life years/
277.	sickness impact profile/
278.	(quality adj2 (wellbeing or well being)).ti,ab.
279.	sickness impact profile.ti,ab.
280.	disability adjusted life.ti,ab.
281.	(qal* or qtime* or qwb* or daly*).ti,ab.
282.	(euroqol* or eq5d* or eq 5*).ti,ab.
283.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
284.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
285.	(hui or hui1 or hui2 or hui3).ti,ab.
286.	(health* year* equivalent* or hye or hyes).ti,ab.
287.	discrete choice*.ti,ab.
288.	rosser.ti,ab.
289.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
290.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
291.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
292.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
293.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
294.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
295.	or/54-72
296.	26 and (43 or 53 or 73)

Embase (Ovid) search terms

223.	exp thyroid diseases/
224.	hyperthyroid*.ti,ab.
225.	hypothyroid*.ti,ab.
226.	thyrotoxicosis*.ti,ab.
227.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*).ti,ab.
228.	or/1-5
229.	letter.pt. or letter/
230.	note.pt.
231.	editorial.pt.
232.	case report/ or case study/
233.	(letter or comment*).ti.

234.	or/7-11
235.	randomized controlled trial/ or random*.ti,ab.
236.	12 not 13
237.	animal/ not human/
238.	nonhuman/
239.	exp Animal Experiment/
240.	exp Experimental Animal/
241.	animal model/
242.	exp Rodent/
243.	(rat or rats or mouse or mice).ti.
244.	or/14-21
245.	6 not 22
246.	limit 23 to English language
247.	health economics/
248.	exp economic evaluation/
249.	exp health care cost/
250.	exp fee/
251.	budget/
252.	funding/
253.	budget*.ti,ab.
254.	cost*.ti.
255.	(economic* or pharmaco?economic*).ti.
256.	(price* or pricing*).ti,ab.
257.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
258.	(financ* or fee or fees).ti,ab.
259.	(value adj2 (money or monetary)).ti,ab.
260.	or/25-37
261.	statistical model/
262.	exp economic aspect/
263.	39 and 40
264.	*theoretical model/
265.	*nonbiological model/
266.	stochastic model/
267.	decision theory/
268.	decision tree/
269.	monte carlo method/
270.	(markov* or monte carlo).ti,ab.
271.	econom* model*.ti,ab.
272.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
273.	or/41-50

274.	quality adjusted life year/
275.	"quality of life index"/
276.	short form 12/ or short form 20/ or short form 36/ or short form 8/
277.	sickness impact profile/
278.	(quality adj2 (wellbeing or well being)).ti,ab.
279.	sickness impact profile.ti,ab.
280.	disability adjusted life.ti,ab.
281.	(qal* or qtime* or qwb* or daly*).ti,ab.
282.	(euroqol* or eq5d* or eq 5*).ti,ab.
283.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
284.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
285.	(hui or hui1 or hui2 or hui3).ti,ab.
286.	(health* year* equivalent* or hye or hyes).ti,ab.
287.	discrete choice*.ti,ab.
288.	rosser.ti,ab.
289.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
290.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
291.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
292.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
293.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
294.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
295.	or/52-72
296.	24 and (38 or 51 or 73)

NHS EED and HTA (CRD) search terms

#19.	MeSH DESCRIPTOR Thyroid Diseases EXPLODE ALL TREES
#20.	hyperthyroid*
#21.	hypothyroid*
#22.	thyrotoxicosis*
#23.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
#24.	#1 OR #2 OR #3 OR #4 or #5

Thyroid disease search strategy 6

This literature search strategy was used for the following reviews;

A.6 Antibodies in hyperthyroidism

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.6.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 10: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 1 or 12 CENTRAL to 2019 Issue 1 or 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Medline (Ovid) search terms

422.	exp goiter/
423.	exp Hyperthyroidism/
424.	(hyperthyroid* or thyrotoxicosis).ti,ab.
425.	(toxic adj4 (node* or nodul* or multi?nodul* or goitre or goiter)).ti,ab.
426.	(graves' disease or plummer's disease).ti,ab.
427.	or/1-5
428.	letter/
429.	editorial/
430.	news/
431.	exp historical article/
432.	Anecdotes as Topic/
433.	comment/
434.	case report/
435.	(letter or comment*).ti.
436.	or/7-14
437.	randomized controlled trial/ or random*.ti,ab.
438.	15 not 16
439.	animals/ not humans/
440.	exp Animals, Laboratory/
441.	exp Animal Experimentation/
442.	exp Models, Animal/
443.	exp Rodentia/
444.	(rat or rats or mouse or mice).ti.
445.	or/17-23
446.	6 not 24
447.	limit 25 to English language
448.	autoantibodies/
449.	anti-TPO.ti,ab.
450.	((anti thyroid or antithyroid or TPO) adj2 (peroxidase or antibod* or autoantibod*)).ti,ab.
451.	((iodide adj2 peroxidase) or thyroperoxidase or microsomal antigen).ti,ab.
452.	TRAbs.ti,ab.
453.	((TSH or thyrotropin) adj2 receptor* adj2 (antigen* or antibod* or anti bod*)).ti,ab.
454.	(TSI or TBI or TBII or (thyroid adj2 (antibod* or anti bod*)) or binding inhibitory immunoglobulin).ti,ab.
455.	Ultrasonography/
456.	(ultrasonic or ultra sonic or ultra sonograph* or ultrasonograph* or ultrasound* or ultra sound* or sonograph* or sonogram* or echograph* or echotomograph* or doppler).ti,ab.
457.	(computed adj3 tomography).ti,ab.
458.	((isotope* or radioisotope* or radio isotope) adj4 scan*).ti,ab.
459.	radionuclide imaging/
460.	iodine radioisotopes/
461.	((iodine 131 or 131-I or I-131 or iodine 123 or 123-I or I-123 or radioiodine or radio-iodine or radionuclide) adj4 (scan* or test* or imag* or image*)).ti,ab.

462.	(radioactive iodine uptake or RAI or RAUI or RAIU).ti,ab.
463.	or/27-41
464.	randomized controlled trial.pt.
465.	controlled clinical trial.pt.
466.	randomi#ed.ti,ab.
467.	placebo.ab.
468.	randomly.ti,ab.
469.	Clinical Trials as topic.sh.
470.	trial.ti.
471.	or/43-49
472.	Meta-Analysis/
473.	exp Meta-Analysis as Topic/
474.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
475.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
476.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
477.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
478.	(search* adj4 literature).ab.
479.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
480.	cochrane.jw.
481.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
482.	or/51-60
483.	exp "sensitivity and specificity"/
484.	(sensitivity or specificity).ti,ab.
485.	((pre test or pretest or post test) adj probability).ti,ab.
486.	(predictive value* or PPV or NPV).ti,ab.
487.	likelihood ratio*.ti,ab.
488.	likelihood function/
489.	((area under adj4 curve) or AUC).ti,ab.
490.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
491.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
492.	gold standard.ab.
493.	or/62-71
494.	Epidemiologic studies/
495.	Observational study/
496.	exp Cohort studies/
497.	(cohort adj (study or studies or analys* or data)).ti,ab.
498.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
499.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
500.	Controlled Before-After Studies/
501.	Historically Controlled Study/
502.	Interrupted Time Series Analysis/

503.	(before adj2 after adj2 (study or studies or data)).ti,ab.
504.	or/73-82
505.	exp case control study/
506.	case control*.ti,ab.
507.	or/84-85
508.	83 or 86
509.	Cross-sectional studies/
510.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
511.	or/88-89
512.	83 or 90
513.	83 or 86 or 90
514.	26 and 42 and (50 or 61 or 72 or 92)

Embase (Ovid) search terms

439.	goiter/
440.	hyperthyroidism/ or graves disease/ or thyrotoxicosis/ or toxic goiter/
441.	(hyperthyroid* or thyrotoxicosis).ti,ab.
442.	(toxic adj4 (node* or nodul* or multi?nodul* or goitre or goiter)).ti,ab.
443.	(graves' disease or plummer's disease).ti,ab.
444.	or/1-5
445.	letter.pt. or letter/
446.	note.pt.
447.	editorial.pt.
448.	case report/ or case study/
449.	(letter or comment*).ti.
450.	or/7-11
451.	randomized controlled trial/ or random*.ti,ab.
452.	12 not 13
453.	animal/ not human/
454.	nonhuman/
455.	exp Animal Experiment/
456.	exp Experimental Animal/
457.	animal model/
458.	exp Rodent/
459.	(rat or rats or mouse or mice).ti.
460.	or/14-21
461.	6 not 22
462.	limit 23 to English language
463.	Autoantibodies/
464.	anti-TPO.ti,ab.
465.	((anti thyroid or antithyroid or TPO) adj2 (peroxidase or antibod* or autoantibod*)).ti,ab.
466.	((iodide adj2 peroxidase) or thyroperoxidase or microsomal antigen).ti,ab.
467.	TRAbs.ti,ab.
468.	((TSH or thyrotropin) adj2 receptor* adj2 (antigen* or antibod* or anti bod*)).ti,ab.
469.	(TSI or TBI or TBII or (thyroid adj2 (antibod* or anti bod*)) or binding inhibitory immunoglobulin).ti,ab.

470.	echography/
471.	(ultrasonic or ultra sonic or ultra sonograph* or ultrasonograph* or ultrasound* or sonograph* or sonogram* or echograph* or echotomograph* or doppler).ti,ab.
472.	(computed adj3 tomography).ti,ab.
473.	((isotope* or radioisotope* or radio isotope) adj4 scan*).ti,ab.
474.	scintiscanning/
475.	radioactive iodine/
476.	((iodine 131 or 131-I or I-131 or iodine 123 or 123-I or I-123 or radioiodine or radio-iodine or radionuclide) adj4 (scan* or test* or imag* or image*)).ti,ab.
477.	(radioactive iodine uptake or RAI or RAUI or RAIU).ti,ab.
478.	or/27-39
479.	random*.ti,ab.
480.	factorial*.ti,ab.
481.	(crossover* or cross over*).ti,ab.
482.	((doubl* or singl*) adj blind*).ti,ab.
483.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
484.	crossover procedure/
485.	single blind procedure/
486.	randomized controlled trial/
487.	double blind procedure/
488.	or/41-49
489.	systematic review/
490.	meta-analysis/
491.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
492.	((systematic* or evidence*) adj3 (review* or overview*).ti,ab.
493.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
494.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
495.	(search* adj4 literature).ab.
496.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
497.	cochrane.jw.
498.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
499.	or/51-60
500.	exp "sensitivity and specificity"/
501.	(sensitivity or specificity).ti,ab.
502.	((pre test or pretest or post test) adj probability).ti,ab.
503.	(predictive value* or PPV or NPV).ti,ab.
504.	likelihood ratio*.ti,ab.
505.	((area under adj4 curve) or AUC).ti,ab.
506.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
507.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
508.	diagnostic accuracy/
509.	diagnostic test accuracy study/

510.	gold standard.ab.
511.	or/62-72
512.	Clinical study/
513.	Observational study/
514.	family study/
515.	longitudinal study/
516.	retrospective study/
517.	prospective study/
518.	cohort analysis/
519.	follow-up/
520.	cohort*.ti,ab.
521.	81 and 82
522.	(cohort adj (study or studies or analys* or data)).ti,ab.
523.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
524.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
525.	(before adj2 after adj2 (study or studies or data)).ti,ab.
526.	or/74-80,83-87
527.	exp case control study/
528.	case control*.ti,ab.
529.	or/89-90
530.	88 or 91
531.	cross-sectional study/
532.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
533.	or/93-94
534.	88 or 95
535.	88 or 91 or 95
536.	24 and 40 and (50 or 61 or 73 or 97)

Cochrane Library (Wiley) search terms

#43.	MeSH descriptor: [Goiter] explode all trees
#44.	MeSH descriptor: [Hyperthyroidism] explode all trees
#45.	(hyperthyroid* or thyrotoxicosis):ti,ab
#46.	(toxic near/4 (node* or nodul* or multinodul* or multi-nodul* or goitre or goiter)):ti,ab
#47.	MeSH descriptor: [Graves Disease] explode all trees
#48.	(grave* near/4 (thyrotoxicos* or hyperthyrr*)):ti,ab
#49.	graves' disease:ti,ab
#50.	(or #1-#7)
#51.	MeSH descriptor: [Autoantibodies] explode all trees
#52.	anti-TPO:ti,ab
#53.	((anti thyroid or antithyroid or TPO) near/2 (peroxidase or antibod* or autoantibod*)):ti,ab
#54.	((iodide near/2 peroxidase) or thyroperoxidase or microsomal antigen):ti,ab
#55.	TRAbs:ti,ab
#56.	((TSH or thyrotropin) near/2 receptor* near/2 (antigen* or antibod* or anti bod*)):ti,ab

#57.	(TSI or TBI or TBII or (thyroid near/2 (antibod* or anti bod*)) or binding inhibitory immunoglobulin):ti,ab
#58.	MeSH descriptor: [Ultrasonography] explode all trees
#59.	(ultrasonic or ultra sonic or ultra sonograph* or ultrasonograph* or ultrasound* or ultra sound* or sonograph* or sonogram* or echograph* or echotomograph* or doppler):ti,ab
#60.	(computed near/3 tomography):ti,ab
#61.	((isotope* or radioisotope* or radio isotope) near/4 scan*):ti,ab
#62.	MeSH descriptor: [Radionuclide imaging] explode all trees
#63.	MeSH descriptor: [Iodine radioisotopes] explode all trees
#64.	((iodine 131 or 131-I or I-131 or iodine 123 or 123-I or I-123 or radioiodine or radio-iodine or radionuclide) near/4 (scan* or test* or imag* or image*)):ti,ab
#65.	(radioactive iodine uptake or RAI or RAUI or RAIU):ti,ab
#66.	(or #9-#23)
#67.	#8 and #24

A.6.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a thyroid disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 11: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 07 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

297.	exp thyroid diseases/
298.	hyperthyroid*.ti,ab.
299.	hypothyroid*.ti,ab.
300.	thyrotoxicosis.ti,ab.
301.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
302.	or/1-5
303.	letter/

304.	editorial/
305.	news/
306.	exp historical article/
307.	Anecdotes as Topic/
308.	comment/
309.	case report/
310.	(letter or comment*).ti.
311.	or/7-14
312.	randomized controlled trial/ or random*.ti,ab.
313.	15 not 16
314.	animals/ not humans/
315.	exp Animals, Laboratory/
316.	exp Animal Experimentation/
317.	exp Models, Animal/
318.	exp Rodentia/
319.	(rat or rats or mouse or mice).ti.
320.	or/17-23
321.	6 not 24
322.	limit 25 to English language
323.	Economics/
324.	Value of life/
325.	exp "Costs and Cost Analysis"/
326.	exp Economics, Hospital/
327.	exp Economics, Medical/
328.	Economics, Nursing/
329.	Economics, Pharmaceutical/
330.	exp "Fees and Charges"/
331.	exp Budgets/
332.	budget*.ti,ab.
333.	cost*.ti.
334.	(economic* or pharmaco?economic*).ti.
335.	(price* or pricing*).ti,ab.
336.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
337.	(financ* or fee or fees).ti,ab.
338.	(value adj2 (money or monetary)).ti,ab.
339.	or/27-42
340.	exp models, economic/
341.	*Models, Theoretical/
342.	*Models, Organizational/
343.	markov chains/
344.	monte carlo method/
345.	exp Decision Theory/
346.	(markov* or monte carlo).ti,ab.
347.	econom* model*.ti,ab.

348.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
349.	or/44-52
350.	quality-adjusted life years/
351.	sickness impact profile/
352.	(quality adj2 (wellbeing or well being)).ti,ab.
353.	sickness impact profile.ti,ab.
354.	disability adjusted life.ti,ab.
355.	(qal* or qtime* or qwb* or daly*).ti,ab.
356.	(euroqol* or eq5d* or eq 5*).ti,ab.
357.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
358.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
359.	(hui or hui1 or hui2 or hui3).ti,ab.
360.	(health* year* equivalent* or hye or hyes).ti,ab.
361.	discrete choice*.ti,ab.
362.	rosser.ti,ab.
363.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
364.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
365.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
366.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
367.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
368.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
369.	or/54-72
370.	26 and (43 or 53 or 73)

Embase (Ovid) search terms

297.	exp thyroid diseases/
298.	hyperthyroid*.ti,ab.
299.	hypothyroid*.ti,ab.
300.	thyrotoxicosis*.ti,ab.
301.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*).ti,ab.
302.	or/1-5
303.	letter.pt. or letter/
304.	note.pt.
305.	editorial.pt.
306.	case report/ or case study/
307.	(letter or comment*).ti.
308.	or/7-11
309.	randomized controlled trial/ or random*.ti,ab.
310.	12 not 13
311.	animal/ not human/
312.	nonhuman/
313.	exp Animal Experiment/
314.	exp Experimental Animal/

315.	animal model/
316.	exp Rodent/
317.	(rat or rats or mouse or mice).ti.
318.	or/14-21
319.	6 not 22
320.	limit 23 to English language
321.	health economics/
322.	exp economic evaluation/
323.	exp health care cost/
324.	exp fee/
325.	budget/
326.	funding/
327.	budget*.ti,ab.
328.	cost*.ti.
329.	(economic* or pharmaco?economic*).ti.
330.	(price* or pricing*).ti,ab.
331.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
332.	(financ* or fee or fees).ti,ab.
333.	(value adj2 (money or monetary)).ti,ab.
334.	or/25-37
335.	statistical model/
336.	exp economic aspect/
337.	39 and 40
338.	*theoretical model/
339.	*nonbiological model/
340.	stochastic model/
341.	decision theory/
342.	decision tree/
343.	monte carlo method/
344.	(markov* or monte carlo).ti,ab.
345.	econom* model*.ti,ab.
346.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
347.	or/41-50
348.	quality adjusted life year/
349.	"quality of life index"/
350.	short form 12/ or short form 20/ or short form 36/ or short form 8/
351.	sickness impact profile/
352.	(quality adj2 (wellbeing or well being)).ti,ab.
353.	sickness impact profile.ti,ab.
354.	disability adjusted life.ti,ab.

355.	(qal* or qtime* or qwb* or daly*).ti,ab.
356.	(euroqol* or eq5d* or eq 5*).ti,ab.
357.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
358.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
359.	(hui or hui1 or hui2 or hui3).ti,ab.
360.	(health* year* equivalent* or hye or hyes).ti,ab.
361.	discrete choice*.ti,ab.
362.	rosser.ti,ab.
363.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
364.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
365.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
366.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
367.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
368.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
369.	or/52-72
370.	24 and (38 or 51 or 73)

NHS EED and HTA (CRD) search terms

#25.	MeSH DESCRIPTOR Thyroid Diseases EXPLODE ALL TREES
#26.	hyperthyroid*
#27.	hypothyroid*
#28.	thyrotoxicosis*
#29.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
#30.	#1 OR #2 OR #3 OR #4 or #5

Thyroid disease search strategy 7

This literature search strategy was used for the following reviews;

A.7 Antibodies in hypothyroidism

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.7.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 12: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 1 or 12 CENTRAL to 2019 Issue 1 or 12	None

Medline (Ovid) search terms

515.	exp hypothyroidism/ or thyroiditis, autoimmune/
516.	(thyroid adj3 (defic* or insuffic* or underactiv*)).ti,ab.
517.	(hypothyr* or hypo-thyr* or autoimmune thyroiditis).ti,ab.
518.	or/1-3
519.	letter/
520.	editorial/
521.	news/
522.	exp historical article/
523.	Anecdotes as Topic/
524.	comment/
525.	case report/
526.	(letter or comment*).ti.
527.	or/5-12
528.	randomized controlled trial/ or random*.ti,ab.

529.	13 not 14
530.	animals/ not humans/
531.	exp Animals, Laboratory/
532.	exp Animal Experimentation/
533.	exp Models, Animal/
534.	exp Rodentia/
535.	(rat or rats or mouse or mice).ti.
536.	or/15-21
537.	4 not 22
538.	limit 23 to English language
539.	exp autoantibodies/
540.	anti-TPO.ti,ab.
541.	((anti thyroid or antithyroid or TPO) adj2 (peroxidase or antibod* or autoantibod*).ti,ab.
542.	((iodide adj2 peroxidase) or thyroperoxidase or microsomal antigen*).ti,ab.
543.	(antithyroglobulin* or anti thyroglobulin* or thyroglobulin antibod*).ti,ab.
544.	(anti-Tg or TgAb or anti TgAb).ti,ab.
545.	or/25-30
546.	randomized controlled trial.pt.
547.	controlled clinical trial.pt.
548.	randomi#ed.ti,ab.
549.	placebo.ab.
550.	randomly.ti,ab.
551.	Clinical Trials as topic.sh.
552.	trial.ti.
553.	or/32-38
554.	Meta-Analysis/
555.	exp Meta-Analysis as Topic/
556.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
557.	((systematic* or evidence*) adj3 (review* or overview*).ti,ab.
558.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
559.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
560.	(search* adj4 literature).ab.
561.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
562.	cochrane.jw.
563.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
564.	or/40-49
565.	Epidemiologic studies/
566.	Observational study/
567.	exp Cohort studies/
568.	(cohort adj (study or studies or analys* or data)).ti,ab.
569.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
570.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.

571.	Controlled Before-After Studies/
572.	Historically Controlled Study/
573.	Interrupted Time Series Analysis/
574.	(before adj2 after adj2 (study or studies or data)).ti,ab.
575.	or/51-60
576.	exp case control study/
577.	case control*.ti,ab.
578.	or/62-63
579.	61 or 64
580.	Cross-sectional studies/
581.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
582.	or/66-67
583.	61 or 68
584.	61 or 64 or 68
585.	24 and 31
586.	71 and (39 or 50 or 70)

Embase (Ovid) search terms

537.	exp hypothyroidism/ or autoimmune thyroiditis/
538.	(thyroid adj3 (defic* or insuffic* or underactiv*)).ti,ab.
539.	(hypothyr* or hypo-thyr* or autoimmune thyroiditis).ti,ab.
540.	or/1-3
541.	letter.pt. or letter/
542.	note.pt.
543.	editorial.pt.
544.	case report/ or case study/
545.	(letter or comment*).ti.
546.	or/5-9
547.	randomized controlled trial/ or random*.ti,ab.
548.	10 not 11
549.	animal/ not human/
550.	nonhuman/
551.	exp Animal Experiment/
552.	exp Experimental Animal/
553.	animal model/
554.	exp Rodent/
555.	(rat or rats or mouse or mice).ti.
556.	or/12-19
557.	4 not 20
558.	limit 21 to English language
559.	exp autoantibody/
560.	anti-TPO.ti,ab.
561.	((anti thyroid or antithyroid or TPO) adj2 (peroxidase or antibod* or autoantibod*)).ti,ab.
562.	((iodide adj2 peroxidase) or thyroperoxidase or microsomal antigen*).ti,ab.
563.	(anti thyroglobulin* or anti thyroglobulin* or thyroglobulin antibod*).ti,ab.
564.	(anti-Tg or TgAb or anti TgAb).ti,ab.

565.	or/23-28
566.	random*.ti,ab.
567.	factorial*.ti,ab.
568.	(crossover* or cross over*).ti,ab.
569.	((doubl* or singl*) adj blind*).ti,ab.
570.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
571.	crossover procedure/
572.	single blind procedure/
573.	randomized controlled trial/
574.	double blind procedure/
575.	or/30-38
576.	systematic review/
577.	meta-analysis/
578.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
579.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
580.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
581.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
582.	(search* adj4 literature).ab.
583.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
584.	cochrane.jw.
585.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
586.	or/40-49
587.	Epidemiologic studies/
588.	Observational study/
589.	exp Cohort studies/
590.	(cohort adj (study or studies or analys* or data)).ti,ab.
591.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
592.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
593.	Controlled Before-After Studies/
594.	Historically Controlled Study/
595.	Interrupted Time Series Analysis/
596.	(before adj2 after adj2 (study or studies or data)).ti,ab.
597.	or/51-60
598.	exp case control study/
599.	case control*.ti,ab.
600.	or/62-63
601.	61 or 64
602.	Cross-sectional studies/
603.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
604.	or/66-67
605.	61 or 68
606.	61 or 64 or 68

607.	22 and 29 and (39 or 50 or 70)
------	--------------------------------

Cochrane Library (Wiley) search terms

#68.	MeSH descriptor: [Hypothyroidism] explode all trees
#69.	MeSH descriptor: [Thyroiditis] explode all trees
#70.	(thyroid near/3 (defic* or insuffic* or underactiv*)):ti,ab
#71.	(hypothyr* or hypo-thyr* or autoimmune thyroiditis):ti,ab
#72.	(or #1-#4)
#73.	MeSH descriptor: [Autoantibodies] explode all trees
#74.	anti-TPO:ti,ab
#75.	((anti thyroid or antithyroid or TPO) near/2 (peroxidase or antibod* or autoantibod*)):ti,ab
#76.	((iodide near/2 peroxidase) or thyroperoxidase or microsomal antigen*):ti,ab
#77.	(antithyroglobulin* or anti thyroglobulin* or thyroglobulin antibod*):ti,ab
#78.	(anti-Tg or TgAb or anti TgAb):ti,ab
#79.	(or #6-#11)
#80.	#5 and #12

A.7.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a thyroid disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 13: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 07 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

371.	exp thyroid diseases/
372.	hyperthyroid*.ti,ab.
373.	hypothyroid*.ti,ab.
374.	thyrotoxicosis.ti,ab.
375.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or

	condition* or disorder*).ti,ab.
376.	or/1-5
377.	letter/
378.	editorial/
379.	news/
380.	exp historical article/
381.	Anecdotes as Topic/
382.	comment/
383.	case report/
384.	(letter or comment*).ti.
385.	or/7-14
386.	randomized controlled trial/ or random*.ti,ab.
387.	15 not 16
388.	animals/ not humans/
389.	exp Animals, Laboratory/
390.	exp Animal Experimentation/
391.	exp Models, Animal/
392.	exp Rodentia/
393.	(rat or rats or mouse or mice).ti.
394.	or/17-23
395.	6 not 24
396.	limit 25 to English language
397.	Economics/
398.	Value of life/
399.	exp "Costs and Cost Analysis"/
400.	exp Economics, Hospital/
401.	exp Economics, Medical/
402.	Economics, Nursing/
403.	Economics, Pharmaceutical/
404.	exp "Fees and Charges"/
405.	exp Budgets/
406.	budget*.ti,ab.
407.	cost*.ti.
408.	(economic* or pharmaco?economic*).ti.
409.	(price* or pricing*).ti,ab.
410.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
411.	(financ* or fee or fees).ti,ab.
412.	(value adj2 (money or monetary)).ti,ab.
413.	or/27-42
414.	exp models, economic/
415.	*Models, Theoretical/
416.	*Models, Organizational/
417.	markov chains/
418.	monte carlo method/

419.	exp Decision Theory/
420.	(markov* or monte carlo).ti,ab.
421.	econom* model*.ti,ab.
422.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
423.	or/44-52
424.	quality-adjusted life years/
425.	sickness impact profile/
426.	(quality adj2 (wellbeing or well being)).ti,ab.
427.	sickness impact profile.ti,ab.
428.	disability adjusted life.ti,ab.
429.	(qal* or qtime* or qwb* or daly*).ti,ab.
430.	(euroqol* or eq5d* or eq 5*).ti,ab.
431.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
432.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
433.	(hui or hui1 or hui2 or hui3).ti,ab.
434.	(health* year* equivalent* or hye or hyes).ti,ab.
435.	discrete choice*.ti,ab.
436.	rosser.ti,ab.
437.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
438.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
439.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
440.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
441.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
442.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
443.	or/54-72
444.	26 and (43 or 53 or 73)

Embase (Ovid) search terms

371.	exp thyroid diseases/
372.	hyperthyroid*.ti,ab.
373.	hypothyroid*.ti,ab.
374.	thyrotoxicosis*.ti,ab.
375.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*).ti,ab.
376.	or/1-5
377.	letter.pt. or letter/
378.	note.pt.
379.	editorial.pt.
380.	case report/ or case study/
381.	(letter or comment*).ti.
382.	or/7-11
383.	randomized controlled trial/ or random*.ti,ab.
384.	12 not 13
385.	animal/ not human/

386.	nonhuman/
387.	exp Animal Experiment/
388.	exp Experimental Animal/
389.	animal model/
390.	exp Rodent/
391.	(rat or rats or mouse or mice).ti.
392.	or/14-21
393.	6 not 22
394.	limit 23 to English language
395.	health economics/
396.	exp economic evaluation/
397.	exp health care cost/
398.	exp fee/
399.	budget/
400.	funding/
401.	budget*.ti,ab.
402.	cost*.ti.
403.	(economic* or pharmaco?economic*).ti.
404.	(price* or pricing*).ti,ab.
405.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
406.	(financ* or fee or fees).ti,ab.
407.	(value adj2 (money or monetary)).ti,ab.
408.	or/25-37
409.	statistical model/
410.	exp economic aspect/
411.	39 and 40
412.	*theoretical model/
413.	*nonbiological model/
414.	stochastic model/
415.	decision theory/
416.	decision tree/
417.	monte carlo method/
418.	(markov* or monte carlo).ti,ab.
419.	econom* model*.ti,ab.
420.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
421.	or/41-50
422.	quality adjusted life year/
423.	"quality of life index"/
424.	short form 12/ or short form 20/ or short form 36/ or short form 8/
425.	sickness impact profile/

426.	(quality adj2 (wellbeing or well being)).ti,ab.
427.	sickness impact profile.ti,ab.
428.	disability adjusted life.ti,ab.
429.	(qal* or qtime* or qwb* or daly*).ti,ab.
430.	(euroqol* or eq5d* or eq 5*).ti,ab.
431.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
432.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
433.	(hui or hui1 or hui2 or hui3).ti,ab.
434.	(health* year* equivalent* or hye or hyes).ti,ab.
435.	discrete choice*.ti,ab.
436.	rosser.ti,ab.
437.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
438.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
439.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
440.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
441.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
442.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
443.	or/52-72
444.	24 and (38 or 51 or 73)

NHS EED and HTA (CRD) search terms

#31.	MeSH DESCRIPTOR Thyroid Diseases EXPLODE ALL TREES
#32.	hyperthyroid*
#33.	hypothyroid*
#34.	thyrotoxicosis*
#35.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
#36.	#1 OR #2 OR #3 OR #4 or #5

Thyroid disease search strategy 8

This literature search strategy was used for the following reviews;

A.8 Management of non-malignant thyroid enlargement

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.8.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 1 or 12 CENTRAL to 2019 Issue 1 or 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Medline (Ovid) search terms

587.	((thyroid adj4 (swell* or enlarg* or nodule* or node*)) or (goitre* or goiter*)) adj5 (non-malignan* or nonmalignan* or benign)).ti,ab.
588.	Thyroid Nodule/
589.	1 or 2
590.	letter/
591.	editorial/
592.	news/
593.	exp historical article/
594.	Anecdotes as Topic/
595.	comment/
596.	case report/

597.	(letter or comment*).ti.
598.	or/4-11
599.	randomized controlled trial/ or random*.ti,ab.
600.	12 not 13
601.	animals/ not humans/
602.	exp Animals, Laboratory/
603.	exp Animal Experimentation/
604.	exp Models, Animal/
605.	exp Rodentia/
606.	(rat or rats or mouse or mice).ti.
607.	or/14-20
608.	3 not 21
609.	Thyroidectomy/
610.	(thyroidectomy or total thyroidectomy or total-thyroidectomy or lobectomy or hemithyroidectomy or hemi-thyroidectomy or near total thyroidectomy or near-total thyroidectomy or isthmusectomy or surg* or interstitial laser photocoagulation or ILP).ti,ab.
611.	((radioiodine or microwave or radiofrequency or ethanol) adj3 ablation).ti,ab.
612.	(radioactive iodine or RAI).ti,ab.
613.	High-Intensity Focused Ultrasound Ablation/
614.	(high intensity focused ultrasound or HIFU).ti,ab.
615.	(Magnetic resonance guided focused ultrasound or MRgFUS).ti,ab.
616.	(percutaneous ethanol injection or PEI).ti,ab.
617.	levothyroxine.ti,ab.
618.	or/23-31
619.	22 and 32
620.	randomized controlled trial.pt.
621.	controlled clinical trial.pt.
622.	randomi#ed.ti,ab.
623.	placebo.ab.
624.	randomly.ti,ab.
625.	Clinical Trials as topic.sh.
626.	trial.ti.
627.	or/34-40
628.	Meta-Analysis/
629.	exp Meta-Analysis as Topic/
630.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
631.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
632.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
633.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
634.	(search* adj4 literature).ab.
635.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
636.	cochrane.jw.
637.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.

638.	or/42-51
639.	Epidemiologic studies/
640.	Observational study/
641.	exp Cohort studies/
642.	(cohort adj (study or studies or analys* or data)).ti,ab.
643.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
644.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
645.	Controlled Before-After Studies/
646.	Historically Controlled Study/
647.	Interrupted Time Series Analysis/
648.	(before adj2 after adj2 (study or studies or data)).ti,ab.
649.	or/53-62
650.	exp case control study/
651.	case control*.ti,ab.
652.	or/64-65
653.	63 or 66
654.	Cross-sectional studies/
655.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
656.	or/68-69
657.	63 or 70
658.	63 or 66 or 70
659.	33 and (41 or 52 or 72)
660.	limit 73 to English language

Embase (Ovid) search terms

608.	((thyroid adj4 (swell* or enlarg* or nodule* or node*)) or (goitre* or goiter*)) adj5 (non-malignan* or nonmalignan* or benign)).ti,ab.
609.	Thyroid Nodule/
610.	1 or 2
611.	letter.pt. or letter/
612.	note.pt.
613.	editorial.pt.
614.	case report/ or case study/
615.	(letter or comment*).ti.
616.	or/4-8
617.	randomized controlled trial/ or random*.ti,ab.
618.	9 not 10
619.	animal/ not human/
620.	nonhuman/
621.	exp Animal Experiment/
622.	exp Experimental Animal/
623.	animal model/
624.	exp Rodent/
625.	(rat or rats or mouse or mice).ti.

626.	or/11-18
627.	3 not 19
628.	Thyroidectomy/
629.	(thyroidectomy or total thyroideectomy or total-thyroidectomy or lobectomy or hemithyroidectomy or hemi-thyroidectomy or near total thyroideectomy or near-total thyroideectomy or isthmusectomy or surg* or interstitial laser photocoagulation or ILP).ti,ab.
630.	((radioiodine or microwave or radiofrequency or ethanol) adj3 ablation).ti,ab.
631.	radioactive iodine/
632.	(radioactive iodine or RAI).ti,ab.
633.	High-Intensity Focused Ultrasound Ablation/
634.	(high intensity focused ultrasound or HIFU).ti,ab.
635.	(Magnetic resonance guided focused ultrasound or MRgFUS).ti,ab.
636.	(percutaneous ethanol injection or PEI).ti,ab.
637.	levothyroxine/
638.	or/21-30
639.	20 and 31
640.	random*.ti,ab.
641.	factorial*.ti,ab.
642.	(crossover* or cross over*).ti,ab.
643.	((doubl* or singl*) adj blind*).ti,ab.
644.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
645.	crossover procedure/
646.	single blind procedure/
647.	randomized controlled trial/
648.	double blind procedure/
649.	or/33-41
650.	systematic review/
651.	meta-analysis/
652.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
653.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
654.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
655.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
656.	(search* adj4 literature).ab.
657.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
658.	cochrane.jw.
659.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
660.	or/43-52
661.	Clinical study/
662.	Observational study/
663.	family study/
664.	longitudinal study/
665.	retrospective study/
666.	prospective study/

667.	cohort analysis/
668.	follow-up/
669.	cohort*.ti,ab.
670.	61 and 62
671.	(cohort adj (study or studies or analys* or data)).ti,ab.
672.	((follow up or observational or uncontrolled or non randomised or epidemiologic*) adj (study or studies or data)).ti,ab.
673.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
674.	(before adj2 after adj2 (study or studies or data)).ti,ab.
675.	or/54-60,63-67
676.	exp case control study/
677.	case control*.ti,ab.
678.	or/69-70
679.	68 or 71
680.	cross-sectional study/
681.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
682.	or/73-74
683.	68 or 75
684.	68 or 71 or 75
685.	32 and (42 or 53 or 77)
686.	limit 78 to English language

Cochrane Library (Wiley) search terms

#81.	((thyroid near/4 (swell* or enlarg* or nodule* or node*)) or (goitre* or goiter*)) near/5 (non-malignan* or nonmalignan* or benign)):ti,ab
#82.	MeSH descriptor: [Thyroid Nodule] explode all trees
#83.	#1 or #2
#84.	MeSH descriptor: [Thyroidectomy] explode all trees
#85.	("total thyroideectomy" or "total-thyroideectomy" or "lobectomy" or "hemithyroideectomy" or "hemi-thyroideectomy" or "near total thyroideectomy" or "near-total thyroidectomy" or "isthmusectomy" or "surg*" or "interstitial laser photocoagulation" or "ILP"):ti,ab
#86.	(radioactive iodine or RAI):ti,ab
#87.	(high intensity focused ultrasound or HIFU):ti,ab
#88.	(Magnetic resonance guided focused ultrasound or MRgFUS):ti,ab
#89.	(percutaneous ethanol injection or PEI):ti,ab
#90.	levothyroxine:ti,ab
#91.	(or #4-#10)
#92.	#3 and #11

A.8.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a thyroid disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 14: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 07 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

445.	exp thyroid diseases/
446.	hyperthyroid*.ti,ab.
447.	hypothyroid*.ti,ab.
448.	thyrotoxicosis.ti,ab.
449.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
450.	or/1-5
451.	letter/
452.	editorial/
453.	news/
454.	exp historical article/
455.	Anecdotes as Topic/
456.	comment/
457.	case report/
458.	(letter or comment*).ti.
459.	or/7-14
460.	randomized controlled trial/ or random*.ti,ab.
461.	15 not 16
462.	animals/ not humans/
463.	exp Animals, Laboratory/
464.	exp Animal Experimentation/
465.	exp Models, Animal/
466.	exp Rodentia/
467.	(rat or rats or mouse or mice).ti.
468.	or/17-23
469.	6 not 24
470.	limit 25 to English language
471.	Economics/
472.	Value of life/

473.	exp "Costs and Cost Analysis"/
474.	exp Economics, Hospital/
475.	exp Economics, Medical/
476.	Economics, Nursing/
477.	Economics, Pharmaceutical/
478.	exp "Fees and Charges"/
479.	exp Budgets/
480.	budget*.ti,ab.
481.	cost*.ti.
482.	(economic* or pharmaco?economic*).ti.
483.	(price* or pricing*).ti,ab.
484.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
485.	(financ* or fee or fees).ti,ab.
486.	(value adj2 (money or monetary)).ti,ab.
487.	or/27-42
488.	exp models, economic/
489.	*Models, Theoretical/
490.	*Models, Organizational/
491.	markov chains/
492.	monte carlo method/
493.	exp Decision Theory/
494.	(markov* or monte carlo).ti,ab.
495.	econom* model*.ti,ab.
496.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
497.	or/44-52
498.	quality-adjusted life years/
499.	sickness impact profile/
500.	(quality adj2 (wellbeing or well being)).ti,ab.
501.	sickness impact profile.ti,ab.
502.	disability adjusted life.ti,ab.
503.	(qal* or qtime* or qwb* or daly*).ti,ab.
504.	(euroqol* or eq5d* or eq 5*).ti,ab.
505.	(qol* or hq1* or hqol* or hr qol* or hrqol* or hr qol*).ti,ab.
506.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
507.	(hui or hui1 or hui2 or hui3).ti,ab.
508.	(health* year* equivalent* or hye or hyes).ti,ab.
509.	discrete choice*.ti,ab.
510.	rosser.ti,ab.
511.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
512.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
513.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
514.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
515.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
516.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.

517.	or/54-72
518.	26 and (43 or 53 or 73)

Embase (Ovid) search terms

445.	exp thyroid diseases/
446.	hyperthyroid*.ti,ab.
447.	hypothyroid*.ti,ab.
448.	thyrotoxicosis*.ti,ab.
449.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
450.	or/1-5
451.	letter.pt. or letter/
452.	note.pt.
453.	editorial.pt.
454.	case report/ or case study/
455.	(letter or comment*).ti.
456.	or/7-11
457.	randomized controlled trial/ or random*.ti,ab.
458.	12 not 13
459.	animal/ not human/
460.	nonhuman/
461.	exp Animal Experiment/
462.	exp Experimental Animal/
463.	animal model/
464.	exp Rodent/
465.	(rat or rats or mouse or mice).ti.
466.	or/14-21
467.	6 not 22
468.	limit 23 to English language
469.	health economics/
470.	exp economic evaluation/
471.	exp health care cost/
472.	exp fee/
473.	budget/
474.	funding/
475.	budget*.ti,ab.
476.	cost*.ti.
477.	(economic* or pharmaco?economic*).ti.
478.	(price* or pricing*).ti,ab.
479.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
480.	(financ* or fee or fees).ti,ab.

481.	(value adj2 (money or monetary)).ti,ab.
482.	or/25-37
483.	statistical model/
484.	exp economic aspect/
485.	39 and 40
486.	*theoretical model/
487.	*nonbiological model/
488.	stochastic model/
489.	decision theory/
490.	decision tree/
491.	monte carlo method/
492.	(markov* or monte carlo).ti,ab.
493.	econom* model*.ti,ab.
494.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
495.	or/41-50
496.	quality adjusted life year/
497.	"quality of life index"/
498.	short form 12/ or short form 20/ or short form 36/ or short form 8/
499.	sickness impact profile/
500.	(quality adj2 (wellbeing or well being)).ti,ab.
501.	sickness impact profile.ti,ab.
502.	disability adjusted life.ti,ab.
503.	(qal* or qtime* or qwb* or daly*).ti,ab.
504.	(euroqol* or eq5d* or eq 5*).ti,ab.
505.	(qol* or hq1* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
506.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
507.	(hui or hui1 or hui2 or hui3).ti,ab.
508.	(health* year* equivalent* or hye or hyes).ti,ab.
509.	discrete choice*.ti,ab.
510.	rosser.ti,ab.
511.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
512.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
513.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
514.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
515.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
516.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
517.	or/52-72
518.	24 and (38 or 51 or 73)

NHS EED and HTA (CRD) search terms

#37.	MeSH DESCRIPTOR Thyroid Diseases EXPLODE ALL TREES
------	--

<Click this field on the first page and insert document title / header text>

#38.	hyperthyroid*
#39.	hypothyroid*
#40.	thyrotoxicosis*
#41.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
#42.	#1 OR #2 OR #3 OR #4 or #5

<Click this field on the first page and insert footer text if required>

Thyroid disease search strategy 9

This literature search strategy was used for the following reviews;

A.9 Management of hypothyroidism

Management of subclinical hypothyroidism

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.9.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 1 or 12 CENTRAL to 2019 Issue 1 or 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Medline (Ovid) search terms

661.	exp thyroid diseases/
662.	hyperthyroid*.ti,ab.
663.	hypothyroid*.ti,ab.
664.	thyrotoxicosis.ti,ab.
665.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
666.	or/1-5
667.	letter/
668.	editorial/
669.	news/
670.	exp historical article/
671.	Anecdotes as Topic/

672.	comment/
673.	case report/
674.	(letter or comment*).ti.
675.	or/7-14
676.	randomized controlled trial/ or random*.ti,ab.
677.	15 not 16
678.	animals/ not humans/
679.	exp Animals, Laboratory/
680.	exp Animal Experimentation/
681.	exp Models, Animal/
682.	exp Rodentia/
683.	(rat or rats or mouse or mice).ti.
684.	or/17-23
685.	6 not 24
686.	limit 25 to English language
687.	((iodine or selenium) adj2 supplement*).ti,ab.
688.	(desiccated adj3 (thyroid or hormone* or extract or extracts)).ti,ab.
689.	(thyroid adj2 (extract or extracts)).ti,ab.
690.	(natural adj4 thyroid).ti,ab.
691.	(natural adj3 (extract or extracts)).ti,ab.
692.	armour*.ti,ab.
693.	(thyroxine or levothyroxine or liothyronine or triiodothyronine or tri-iodothyronine).ti,ab.
694.	Thyroxine/ or Triiodothyronine/
695.	(T3 or T4).ti,ab.
696.	(TSH or thyroid stimulating hormone or thyrotropin).ti,ab.
697.	or/27-36
698.	26 and 37
699.	randomized controlled trial.pt.
700.	controlled clinical trial.pt.
701.	randomi#ed.ti,ab.
702.	placebo.ab.
703.	randomly.ti,ab.
704.	Clinical Trials as topic.sh.
705.	trial.ti.
706.	or/39-45
707.	Meta-Analysis/
708.	exp Meta-Analysis as Topic/
709.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
710.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
711.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
712.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
713.	(search* adj4 literature).ab.
714.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.

715.	cochrane.jw.
716.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
717.	or/47-56
718.	38 and (46 or 57)

Embase (Ovid) search terms

687.	exp thyroid disease/
688.	hyperthyroid*.ti,ab.
689.	hypothyroid*.ti,ab.
690.	thyrotoxicosis.ti,ab.
691.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
692.	or/1-5
693.	letter.pt. or letter/
694.	note.pt.
695.	editorial.pt.
696.	case report/ or case study/
697.	(letter or comment*).ti.
698.	or/7-11
699.	randomized controlled trial/ or random*.ti,ab.
700.	12 not 13
701.	animal/ not human/
702.	nonhuman/
703.	exp Animal Experiment/
704.	exp Experimental Animal/
705.	animal model/
706.	exp Rodent/
707.	(rat or rats or mouse or mice).ti.
708.	or/14-21
709.	6 not 22
710.	limit 23 to English language
711.	((iodine or selenium) adj2 supplement*).ti,ab.
712.	(desiccated adj3 (thyroid or hormone* or extract or extracts)).ti,ab.
713.	(thyroid adj2 (extract or extracts)).ti,ab.
714.	(natural adj4 thyroid).ti,ab.
715.	armour*.ti,ab.
716.	*thyroxine/ or *levothyroxine/ or *liothyronine/ or *triiodothyronine/
717.	(thyroxine or levothyroxine or liothyronine or triiodothyronine or tri-iodothyronine).ti,ab.
718.	(T3 or T4).ti,ab.
719.	(TSH or thyroid stimulating hormone or thyrotropin).ti,ab.
720.	*thyrotropin/
721.	or/25-34
722.	24 and 35
723.	random*.ti,ab.
724.	factorial*.ti,ab.
725.	(crossover* or cross over*).ti,ab.

726.	((doubl* or singl*) adj blind*).ti,ab.
727.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
728.	crossover procedure/
729.	single blind procedure/
730.	randomized controlled trial/
731.	double blind procedure/
732.	or/37-45
733.	systematic review/
734.	meta-analysis/
735.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
736.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
737.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
738.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
739.	(search* adj4 literature).ab.
740.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
741.	cochrane.jw.
742.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
743.	or/47-56
744.	36 and (46 or 57)

Cochrane Library (Wiley) search terms

#93.	MeSH descriptor: [Thyroid Diseases] explode all trees
#94.	hyperthyroid*:ti,ab
#95.	hypothyroid*:ti,ab
#96.	thyrotoxicosis:ti,ab
#97.	(thyroid near/3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)):ti,ab
#98.	(or #1-#5)
#99.	((iodine or selenium) near/2 supplement*):ti,ab
#100.	(desiccated near/3 (thyroid or hormone* or extract or extracts)):ti,ab
#101.	(thyroid near/2 (extract or extracts)):ti,ab
#102.	(natural near/4 thyroid):ti,ab
#103.	(natural near/3 (extract or extracts)):ti,ab
#104.	armour*:ti,ab
#105.	(thyroxine or levothyroxine or liothyronine or triiodothyronine or tri-iodothyronine):ti,ab
#106.	MeSH descriptor: [Thyroxine] explode all trees
#107.	MeSH descriptor: [Triiodothyronine] explode all trees
#108.	(T3 or T4):ti,ab
#109.	(TSH or thyroid stimulating hormone or thyrotropin):ti,ab
#110.	(or #7-#17)
#111.	#6 and #18

A.9.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a thyroid disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 15: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 07 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

519.	exp thyroid diseases/
520.	hyperthyroid*.ti,ab.
521.	hypothyroid*.ti,ab.
522.	thyrotoxicosis.ti,ab.
523.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
524.	or/1-5
525.	letter/
526.	editorial/
527.	news/
528.	exp historical article/
529.	Anecdotes as Topic/
530.	comment/
531.	case report/
532.	(letter or comment*).ti.
533.	or/7-14
534.	randomized controlled trial/ or random*.ti,ab.
535.	15 not 16
536.	animals/ not humans/
537.	exp Animals, Laboratory/
538.	exp Animal Experimentation/
539.	exp Models, Animal/

540.	exp Rodentia/
541.	(rat or rats or mouse or mice).ti.
542.	or/17-23
543.	6 not 24
544.	limit 25 to English language
545.	Economics/
546.	Value of life/
547.	exp "Costs and Cost Analysis"/
548.	exp Economics, Hospital/
549.	exp Economics, Medical/
550.	Economics, Nursing/
551.	Economics, Pharmaceutical/
552.	exp "Fees and Charges"/
553.	exp Budgets/
554.	budget*.ti,ab.
555.	cost*.ti.
556.	(economic* or pharmaco?economic*).ti.
557.	(price* or pricing*).ti,ab.
558.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
559.	(financ* or fee or fees).ti,ab.
560.	(value adj2 (money or monetary)).ti,ab.
561.	or/27-42
562.	exp models, economic/
563.	*Models, Theoretical/
564.	*Models, Organizational/
565.	markov chains/
566.	monte carlo method/
567.	exp Decision Theory/
568.	(markov* or monte carlo).ti,ab.
569.	econom* model*.ti,ab.
570.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
571.	or/44-52
572.	quality-adjusted life years/
573.	sickness impact profile/
574.	(quality adj2 (wellbeing or well being)).ti,ab.
575.	sickness impact profile.ti,ab.
576.	disability adjusted life.ti,ab.
577.	(qal* or qtime* or qwb* or daly*).ti,ab.
578.	(euroqol* or eq5d* or eq 5*).ti,ab.
579.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
580.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
581.	(hui or hui1 or hui2 or hui3).ti,ab.
582.	(health* year* equivalent* or hye or hyes).ti,ab.
583.	discrete choice*.ti,ab.

584.	rosser.ti,ab.
585.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
586.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
587.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
588.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
589.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
590.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
591.	or/54-72
592.	26 and (43 or 53 or 73)

Embase (Ovid) search terms

519.	exp thyroid diseases/
520.	hyperthyroid*.ti,ab.
521.	hypothyroid*.ti,ab.
522.	thyrotoxicosis*.ti,ab.
523.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
524.	or/1-5
525.	letter.pt. or letter/
526.	note.pt.
527.	editorial.pt.
528.	case report/ or case study/
529.	(letter or comment*).ti.
530.	or/7-11
531.	randomized controlled trial/ or random*.ti,ab.
532.	12 not 13
533.	animal/ not human/
534.	nonhuman/
535.	exp Animal Experiment/
536.	exp Experimental Animal/
537.	animal model/
538.	exp Rodent/
539.	(rat or rats or mouse or mice).ti.
540.	or/14-21
541.	6 not 22
542.	limit 23 to English language
543.	health economics/
544.	exp economic evaluation/
545.	exp health care cost/
546.	exp fee/
547.	budget/
548.	funding/

549.	budget*.ti,ab.
550.	cost*.ti.
551.	(economic* or pharmaco?economic*).ti.
552.	(price* or pricing*).ti,ab.
553.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ti,ab.
554.	(financ* or fee or fees).ti,ab.
555.	(value adj2 (money or monetary)).ti,ab.
556.	or/25-37
557.	statistical model/
558.	exp economic aspect/
559.	39 and 40
560.	*theoretical model/
561.	*nonbiological model/
562.	stochastic model/
563.	decision theory/
564.	decision tree/
565.	monte carlo method/
566.	(markov* or monte carlo).ti,ab.
567.	econom* model*.ti,ab.
568.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
569.	or/41-50
570.	quality adjusted life year/
571.	"quality of life index"/
572.	short form 12/ or short form 20/ or short form 36/ or short form 8/
573.	sickness impact profile/
574.	(quality adj2 (wellbeing or well being)).ti,ab.
575.	sickness impact profile.ti,ab.
576.	disability adjusted life.ti,ab.
577.	(qal* or qtime* or qwb* or daly*).ti,ab.
578.	(euroqol* or eq5d* or eq 5*).ti,ab.
579.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
580.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
581.	(hui or hui1 or hui2 or hui3).ti,ab.
582.	(health* year* equivalent* or hye or hyes).ti,ab.
583.	discrete choice*.ti,ab.
584.	rosser.ti,ab.
585.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
586.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
587.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
588.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.

589.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
590.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
591.	or/52-72
592.	24 and (38 or 51 or 73)

NHS EED and HTA (CRD) search terms

#43.	MeSH DESCRIPTOR Thyroid Diseases EXPLODE ALL TREES
#44.	hyperthyroid*
#45.	hypothyroid*
#46.	thyrotoxicosis*
#47.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
#48.	#1 OR #2 OR #3 OR #4 or #5

Thyroid disease search strategy 10

This literature search strategy was used for the following reviews;

A.10 Management of Thyrotoxicosis: Drugs vs Surgery vs Radioactive iodine

Management of Thyrotoxicosis: pharmacological options

Management of Thyrotoxicosis: radioactive iodine options

Management of Thyrotoxicosis: surgical options

Management of subclinical thyrotoxicosis

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.10.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 16: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 1 or 12 CENTRAL to 2019 Issue 1 or 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Medline (Ovid) search terms

719.	exp goiter/
720.	exp Hyperthyroidism/

721.	(hyperthyroid* or thyrotoxicosis).ti,ab.
722.	(toxic adj4 (node* or nodul* or multi?nodul* or goitre or goiter)).ti,ab.
723.	(graves' disease or plummer's disease).ti,ab.
724.	5
725.	letter/
726.	editorial/
727.	news/
728.	exp historical article/
729.	Anecdotes as Topic/
730.	comment/
731.	case report/
732.	(letter or comment*).ti.
733.	or/7-14
734.	randomized controlled trial/ or random*.ti,ab.
735.	15 not 16
736.	animals/ not humans/
737.	exp Animals, Laboratory/
738.	exp Animal Experimentation/
739.	exp Models, Animal/
740.	exp Rodentia/
741.	(rat or rats or mouse or mice).ti.
742.	or/17-23
743.	randomized controlled trial.pt.
744.	controlled clinical trial.pt.
745.	randomi#ed.ti,ab.
746.	placebo.ab.
747.	randomly.ti,ab.
748.	Clinical Trials as topic.sh.
749.	trial.ti.
750.	or/25-31
751.	Meta-Analysis/
752.	exp Meta-Analysis as Topic/
753.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
754.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
755.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
756.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
757.	(search* adj4 literature).ab.
758.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
759.	cochrane.jw.
760.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
761.	or/33-42
762.	Epidemiologic studies/
763.	Observational study/

764.	exp Cohort studies/
765.	(cohort adj (study or studies or analys* or data)).ti,ab.
766.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
767.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
768.	Controlled Before-After Studies/
769.	Historically Controlled Study/
770.	Interrupted Time Series Analysis/
771.	(before adj2 after adj2 (study or studies or data)).ti,ab.
772.	or/4-53
773.	exp case control study/
774.	case control*.ti,ab.
775.	or/55-56
776.	54 or 57
777.	Cross-sectional studies/
778.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
779.	or/59-60
780.	54 or 61
781.	54 or 57 or 61
782.	6 not 24
783.	limit 64 to English language
784.	65 and (32 or 43 or 64)

Embase (Ovid) search terms

745.	goiter/
746.	hyperthyroidism/ or graves disease/ or thyrotoxicosis/ or toxic goiter/
747.	(hyperthyroid* or thyrotoxicosis).ti,ab.
748.	(toxic adj4 (node* of nodul* or multi?nodul* or goitre or goiter)).ti,ab.
749.	(graves' disease or plummer's disease).ti,ab.
750.	or/1-5
751.	letter.pt. or letter/
752.	note.pt.
753.	editorial.pt.
754.	case report/ or case study/
755.	(letter or comment*).ti.
756.	or/7-11
757.	randomized controlled trial/ or random*.ti,ab.
758.	12 not 13
759.	animal/ not human/
760.	nonhuman/
761.	exp Animal Experiment/
762.	exp Experimental Animal/
763.	animal model/
764.	exp Rodent/
765.	(rat or rats or mouse or mice).ti.

766.	or/14-21
767.	6 not 22
768.	random*.ti,ab.
769.	factorial*.ti,ab.
770.	(crossover* or cross over*).ti,ab.
771.	((doubl* or singl*) adj blind*).ti,ab.
772.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
773.	crossover procedure/
774.	single blind procedure/
775.	randomized controlled trial/
776.	double blind procedure/
777.	or/24-32
778.	systematic review/
779.	meta-analysis/
780.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
781.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
782.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
783.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
784.	(search* adj4 literature).ab.
785.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
786.	cochrane.jw.
787.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
788.	or/34-43
789.	Clinical study/
790.	Observational study/
791.	family study/
792.	longitudinal study/
793.	retrospective study/
794.	prospective study/
795.	cohort analysis/
796.	follow-up/
797.	cohort*.ti,ab.
798.	52 and 53
799.	(cohort adj (study or studies or analys* or data)).ti,ab.
800.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
801.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
802.	(before adj2 after adj2 (study or studies or data)).ti,ab.
803.	or/45-51,54-58
804.	exp case control study/
805.	case control*.ti,ab.
806.	or/60-61
807.	59 or 62

808.	cross-sectional study/
809.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
810.	or/64-65
811.	59 or 66
812.	59 or 62 or 66
813.	23 and (33 or 44 or 68)
814.	limit 69 to English language

Cochrane Library (Wiley) search terms

#112.	MeSH descriptor: [Goiter] explode all trees
#113.	MeSH descriptor: [Hyperthyroidism] explode all trees
#114.	(hyperthyroid* or thyrotoxicosis):ti,ab
#115.	(toxic near/4 (node* or nodul* or multinodul* or multi-nodul* or goitre or goiter)):ti,ab
#116.	MeSH descriptor: [Graves Disease] explode all trees
#117.	(grave* near/4 (thyrotoxicos* or hyperthy*)):ti,ab
#118.	graves' disease:ti,ab
#119.	(or #1-#7)

A.10.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a thyroid disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 17: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 07 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

593.	exp thyroid diseases/
594.	hyperthyroid*.ti,ab.
595.	hypothyroid*.ti,ab.
596.	thyrotoxicosis.ti,ab.
597.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or

	condition* or disorder*).ti,ab.
598.	or/1-5
599.	letter/
600.	editorial/
601.	news/
602.	exp historical article/
603.	Anecdotes as Topic/
604.	comment/
605.	case report/
606.	(letter or comment*).ti.
607.	or/7-14
608.	randomized controlled trial/ or random*.ti,ab.
609.	15 not 16
610.	animals/ not humans/
611.	exp Animals, Laboratory/
612.	exp Animal Experimentation/
613.	exp Models, Animal/
614.	exp Rodentia/
615.	(rat or rats or mouse or mice).ti.
616.	or/17-23
617.	6 not 24
618.	limit 25 to English language
619.	Economics/
620.	Value of life/
621.	exp "Costs and Cost Analysis"/
622.	exp Economics, Hospital/
623.	exp Economics, Medical/
624.	Economics, Nursing/
625.	Economics, Pharmaceutical/
626.	exp "Fees and Charges"/
627.	exp Budgets/
628.	budget*.ti,ab.
629.	cost*.ti.
630.	(economic* or pharmaco?economic*).ti.
631.	(price* or pricing*).ti,ab.
632.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
633.	(financ* or fee or fees).ti,ab.
634.	(value adj2 (money or monetary)).ti,ab.
635.	or/27-42
636.	exp models, economic/
637.	*Models, Theoretical/
638.	*Models, Organizational/
639.	markov chains/
640.	monte carlo method/

641.	exp Decision Theory/
642.	(markov* or monte carlo).ti,ab.
643.	econom* model*.ti,ab.
644.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
645.	or/44-52
646.	quality-adjusted life years/
647.	sickness impact profile/
648.	(quality adj2 (wellbeing or well being)).ti,ab.
649.	sickness impact profile.ti,ab.
650.	disability adjusted life.ti,ab.
651.	(qal* or qtime* or qwb* or daly*).ti,ab.
652.	(euroqol* or eq5d* or eq 5*).ti,ab.
653.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
654.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
655.	(hui or hui1 or hui2 or hui3).ti,ab.
656.	(health* year* equivalent* or hye or hyes).ti,ab.
657.	discrete choice*.ti,ab.
658.	rosser.ti,ab.
659.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
660.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
661.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
662.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
663.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
664.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
665.	or/54-72
666.	26 and (43 or 53 or 73)

Embase (Ovid) search terms

593.	exp thyroid diseases/
594.	hyperthyroid*.ti,ab.
595.	hypothyroid*.ti,ab.
596.	thyrotoxicosis*.ti,ab.
597.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
598.	or/1-5
599.	letter.pt. or letter/
600.	note.pt.
601.	editorial.pt.
602.	case report/ or case study/
603.	(letter or comment*).ti.
604.	or/7-11
605.	randomized controlled trial/ or random*.ti,ab.
606.	12 not 13
607.	animal/ not human/

608.	nonhuman/
609.	exp Animal Experiment/
610.	exp Experimental Animal/
611.	animal model/
612.	exp Rodent/
613.	(rat or rats or mouse or mice).ti.
614.	or/14-21
615.	6 not 22
616.	limit 23 to English language
617.	health economics/
618.	exp economic evaluation/
619.	exp health care cost/
620.	exp fee/
621.	budget/
622.	funding/
623.	budget*.ti,ab.
624.	cost*.ti.
625.	(economic* or pharmaco?economic*).ti.
626.	(price* or pricing*).ti,ab.
627.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
628.	(financ* or fee or fees).ti,ab.
629.	(value adj2 (money or monetary)).ti,ab.
630.	or/25-37
631.	statistical model/
632.	exp economic aspect/
633.	39 and 40
634.	*theoretical model/
635.	*nonbiological model/
636.	stochastic model/
637.	decision theory/
638.	decision tree/
639.	monte carlo method/
640.	(markov* or monte carlo).ti,ab.
641.	econom* model*.ti,ab.
642.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
643.	or/41-50
644.	quality adjusted life year/
645.	"quality of life index"/
646.	short form 12/ or short form 20/ or short form 36/ or short form 8/
647.	sickness impact profile/

648.	(quality adj2 (wellbeing or well being)).ti,ab.
649.	sickness impact profile.ti,ab.
650.	disability adjusted life.ti,ab.
651.	(qal* or qtime* or qwb* or daly*).ti,ab.
652.	(euroqol* or eq5d* or eq 5*).ti,ab.
653.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
654.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
655.	(hui or hui1 or hui2 or hui3).ti,ab.
656.	(health* year* equivalent* or hye or hyes).ti,ab.
657.	discrete choice*.ti,ab.
658.	rosser.ti,ab.
659.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
660.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
661.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
662.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
663.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
664.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
665.	or/52-72
666.	24 and (38 or 51 or 73)

NHS EED and HTA (CRD) search terms

#49.	MeSH DESCRIPTOR Thyroid Diseases EXPLODE ALL TREES
#50.	hyperthyroid*
#51.	hypothyroid*
#52.	thyrotoxicosis*
#53.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
#54.	#1 OR #2 OR #3 OR #4 or #5

Thyroid disease search strategy 11

This literature search strategy was used for the following reviews;

A.11 Monitoring Thyroid disease

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017
<https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869>

For more detailed information, please see the Methodology Review. [Add cross reference]

A.11.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 18: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 1 or 12 CENTRAL to 2019 Issue 1 or 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Medline (Ovid) search terms

785.	exp thyroid diseases/
786.	hyperthyroid*.ti,ab.
787.	hypothyroid*.ti,ab.
788.	thyrotoxicosis.ti,ab.
789.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
790.	exp goiter/
791.	exp Hyperthyroidism/
792.	(hyperthyroid* or thyrotoxicosis).ti,ab.
793.	(toxic adj4 (node* or nodul* or multi?nodul* or goitre or goiter)).ti,ab.
794.	(graves' disease or plummer's disease).ti,ab.
795.	((thyroid adj4 (swell* or enlarg* or nodule* or node*)) or (goitre* or goiter*)) adj5 (non-malignan* or nonmalignan* or benign)).ti,ab.

796.	Thyroid Nodule/
797.	or/1-12
798.	letter/
799.	editorial/
800.	news/
801.	exp historical article/
802.	Anecdotes as Topic/
803.	comment/
804.	case report/
805.	(letter or comment*).ti.
806.	or/14-21
807.	randomized controlled trial/ or random*.ti,ab.
808.	22 not 23
809.	animals/ not humans/
810.	exp Animals, Laboratory/
811.	exp Animal Experimentation/
812.	exp Models, Animal/
813.	exp Rodentia/
814.	(rat or rats or mouse or mice).ti.
815.	or/25-30
816.	13 not 31
817.	Monitoring, Physiologic/
818.	Patient Outcome Assessment/
819.	monitoring.ti,ab.
820.	((followup or follow-up or check* or evaluat* or appointment* or observation or observations) adj3 (timing* or interval* or year* or annual* or month* or periodic* or frequen* or routine*)).ti,ab.
821.	((monitor* or time point* or interval*) adj3 (year* or annual* or month* or periodic* or frequen* or routine*)).ti,ab.
822.	or/33-37
823.	32 and 38
824.	limit 39 to English language
825.	randomized controlled trial.pt.
826.	controlled clinical trial.pt.
827.	randomi#ed.ti,ab.
828.	placebo.ab.
829.	randomly.ti,ab.
830.	Clinical Trials as topic.sh.
831.	trial.ti.
832.	or/41-47
833.	Meta-Analysis/
834.	exp Meta-Analysis as Topic/
835.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
836.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
837.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.

838.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
839.	(search* adj4 literature).ab.
840.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
841.	cochrane.jw.
842.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
843.	or/49-58
844.	Epidemiologic studies/
845.	Observational study/
846.	exp Cohort studies/
847.	(cohort adj (study or studies or analys* or data)).ti,ab.
848.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
849.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
850.	Controlled Before-After Studies/
851.	Historically Controlled Study/
852.	Interrupted Time Series Analysis/
853.	(before adj2 after adj2 (study or studies or data)).ti,ab.
854.	or/60-69
855.	exp case control study/
856.	case control*.ti,ab.
857.	or/71-72
858.	70 or 73
859.	Cross-sectional studies/
860.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
861.	or/75-76
862.	70 or 77
863.	70 or 73 or 77
864.	40 and (48 or 59 or 79)

Embase (Ovid) search terms

815.	exp thyroid disease/
816.	hyperthyroid*.ti,ab.
817.	hypothyroid*.ti,ab.
818.	thyrotoxicosis.ti,ab.
819.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
820.	((thyroid adj4 (swell* or enlarg* or nodule* or node*)) or (goitre* or goiter*)) adj5 (non-malignan* or nonmalignan* or benign)).ti,ab.
821.	Thyroid Nodule/
822.	hyperthyroidism/ or graves disease/ or thyrotoxicosis/ or toxic goiter/
823.	(hyperthyroid* or thyrotoxicosis).ti,ab.
824.	(toxic adj4 (node* or nodul* or multi?nodul* or goitre or goiter)).ti,ab.
825.	(graves' disease or plummer's disease).ti,ab.
826.	or/1-11

827.	letter.pt. or letter/
828.	note.pt.
829.	editorial.pt.
830.	case report/ or case study/
831.	(letter or comment*).ti.
832.	or/13-17
833.	randomized controlled trial/ or random*.ti,ab.
834.	18 not 19
835.	animal/ not human/
836.	nonhuman/
837.	exp Animal Experiment/
838.	exp Experimental Animal/
839.	animal model/
840.	exp Rodent/
841.	(rat or rats or mouse or mice).ti.
842.	or/20-27
843.	12 not 28
844.	physiologic monitoring/
845.	patient monitoring/
846.	patient monitoring/
847.	monitoring.ti,ab.
848.	((followup or follow-up or check* or evaluat* or appointment* or observation or observations) adj3 (timing* or interval* or year* or annual* or month* or periodic* or frequen* or routine*)).ti,ab.
849.	((monitor* or time point* or interval*) adj3 (year* or annual* or month* or periodic* or frequen* or routine*)).ti,ab.
850.	or/30-35
851.	29 and 36
852.	limit 37 to English language
853.	random*.ti,ab.
854.	factorial*.ti,ab.
855.	(crossover* or cross over*).ti,ab.
856.	((doubl* or singl*) adj blind*).ti,ab.
857.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
858.	crossover procedure/
859.	single blind procedure/
860.	randomized controlled trial/
861.	double blind procedure/
862.	or/39-47
863.	systematic review/
864.	meta-analysis/
865.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
866.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
867.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
868.	(search strategy or search criteria or systematic search or study selection or data

	extraction).ab.
869.	(search* adj4 literature).ab.
870.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
871.	cochrane.jw.
872.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
873.	or/49-58
874.	Clinical study/
875.	Observational study/
876.	family study/
877.	longitudinal study/
878.	retrospective study/
879.	prospective study/
880.	cohort analysis/
881.	follow-up/
882.	cohort*.ti,ab.
883.	67 and 68
884.	(cohort adj (study or studies or analys* or data)).ti,ab.
885.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
886.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
887.	(before adj2 after adj2 (study or studies or data)).ti,ab.
888.	or/60-66,69-73
889.	exp case control study/
890.	case control*.ti,ab.
891.	or/75-76
892.	74 or 77
893.	cross-sectional study/
894.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
895.	or/79-80
896.	74 or 81
897.	74 or 77 or 81
898.	38 and (48 or 59 or 83)

Cochrane Library (Wiley) search terms

#120.	MeSH descriptor: [Thyroid Diseases] explode all trees
#121.	hyperthyroid*:ti,ab
#122.	hypothyroid*:ti,ab
#123.	thyrotoxicosis:ti,ab
#124.	(thyroid near/3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)):ti,ab
#125.	MeSH descriptor: [Goiter] explode all trees
#126.	MeSH descriptor: [Hyperthyroidism] explode all trees
#127.	(hyperthyroid* or thyrotoxicosis):ti,ab
#128.	(toxic near/4 (node* or nodul* or multi?nodul* or goitre or goiter)):ti,ab
#129.	(graves' disease or plummer's disease):ti,ab

#130.	((thyroid near/4 (swell* or enlarg* or nodule* or node*)) or (goitre* or goiter*)) near/5 (non-malignan* or nonmalignan* or benign)):ti,ab
#131.	MeSH descriptor: [Thyroid Nodule] explode all trees
#132.	(or #1-#12)
#133.	MeSH descriptor: [Monitoring, Physiologic] explode all trees
#134.	MeSH descriptor: [Patient Outcome Assessment] explode all trees
#135.	monitoring:ti,ab
#136.	((followup or follow-up or check* or evaluat* or appointment* or observation or observations) near/3 (timing* or interval* or year* or annual* or month* or periodic* or frequen* or routine*)):ti,ab
#137.	((monitor* or time point* or interval*) near/3 (year* or annual* or month* or periodic* or frequen* or routine*)):ti,ab
#138.	(or #14-#18)
#139.	#13 and #19

A.11.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a thyroid disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 19: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	2014 – 07 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 07 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

667.	exp thyroid diseases/
668.	hyperthyroid*.ti,ab.
669.	hypothyroid*.ti,ab.
670.	thyrotoxicosis.ti,ab.
671.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
672.	or/1-5
673.	letter/

674.	editorial/
675.	news/
676.	exp historical article/
677.	Anecdotes as Topic/
678.	comment/
679.	case report/
680.	(letter or comment*).ti.
681.	or/7-14
682.	randomized controlled trial/ or random*.ti,ab.
683.	15 not 16
684.	animals/ not humans/
685.	exp Animals, Laboratory/
686.	exp Animal Experimentation/
687.	exp Models, Animal/
688.	exp Rodentia/
689.	(rat or rats or mouse or mice).ti.
690.	or/17-23
691.	6 not 24
692.	limit 25 to English language
693.	Economics/
694.	Value of life/
695.	exp "Costs and Cost Analysis"/
696.	exp Economics, Hospital/
697.	exp Economics, Medical/
698.	Economics, Nursing/
699.	Economics, Pharmaceutical/
700.	exp "Fees and Charges"/
701.	exp Budgets/
702.	budget*.ti,ab.
703.	cost*.ti.
704.	(economic* or pharmaco?economic*).ti.
705.	(price* or pricing*).ti,ab.
706.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
707.	(financ* or fee or fees).ti,ab.
708.	(value adj2 (money or monetary)).ti,ab.
709.	or/27-42
710.	exp models, economic/
711.	*Models, Theoretical/
712.	*Models, Organizational/
713.	markov chains/
714.	monte carlo method/
715.	exp Decision Theory/
716.	(markov* or monte carlo).ti,ab.
717.	econom* model*.ti,ab.

718.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
719.	or/44-52
720.	quality-adjusted life years/
721.	sickness impact profile/
722.	(quality adj2 (wellbeing or well being)).ti,ab.
723.	sickness impact profile.ti,ab.
724.	disability adjusted life.ti,ab.
725.	(qal* or qtime* or qwb* or daly*).ti,ab.
726.	(euroqol* or eq5d* or eq 5*).ti,ab.
727.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
728.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
729.	(hui or hui1 or hui2 or hui3).ti,ab.
730.	(health* year* equivalent* or hye or hyes).ti,ab.
731.	discrete choice*.ti,ab.
732.	rosser.ti,ab.
733.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
734.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
735.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
736.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
737.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
738.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
739.	or/54-72
740.	26 and (43 or 53 or 73)

Embase (Ovid) search terms

667.	exp thyroid diseases/
668.	hyperthyroid*.ti,ab.
669.	hypothyroid*.ti,ab.
670.	thyrotoxicosis*.ti,ab.
671.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*).ti,ab.
672.	or/1-5
673.	letter.pt. or letter/
674.	note.pt.
675.	editorial.pt.
676.	case report/ or case study/
677.	(letter or comment*).ti.
678.	or/7-11
679.	randomized controlled trial/ or random*.ti,ab.
680.	12 not 13
681.	animal/ not human/
682.	nonhuman/
683.	exp Animal Experiment/
684.	exp Experimental Animal/

685.	animal model/
686.	exp Rodent/
687.	(rat or rats or mouse or mice).ti.
688.	or/14-21
689.	6 not 22
690.	limit 23 to English language
691.	health economics/
692.	exp economic evaluation/
693.	exp health care cost/
694.	exp fee/
695.	budget/
696.	funding/
697.	budget*.ti,ab.
698.	cost*.ti.
699.	(economic* or pharmaco?economic*).ti.
700.	(price* or pricing*).ti,ab.
701.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
702.	(financ* or fee or fees).ti,ab.
703.	(value adj2 (money or monetary)).ti,ab.
704.	or/25-37
705.	statistical model/
706.	exp economic aspect/
707.	39 and 40
708.	*theoretical model/
709.	*nonbiological model/
710.	stochastic model/
711.	decision theory/
712.	decision tree/
713.	monte carlo method/
714.	(markov* or monte carlo).ti,ab.
715.	econom* model*.ti,ab.
716.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
717.	or/41-50
718.	quality adjusted life year/
719.	"quality of life index"/
720.	short form 12/ or short form 20/ or short form 36/ or short form 8/
721.	sickness impact profile/
722.	(quality adj2 (wellbeing or well being)).ti,ab.
723.	sickness impact profile.ti,ab.
724.	disability adjusted life.ti,ab.

725.	(qal* or qtime* or qwb* or daly*).ti,ab.
726.	(euroqol* or eq5d* or eq 5*).ti,ab.
727.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
728.	(health utility* or utility score* or disutility* or utility value*).ti,ab.
729.	(hui or hui1 or hui2 or hui3).ti,ab.
730.	(health* year* equivalent* or hye or hyes).ti,ab.
731.	discrete choice*.ti,ab.
732.	rosser.ti,ab.
733.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
734.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
735.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
736.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
737.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
738.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
739.	or/52-72
740.	24 and (38 or 51 or 73)

NHS EED and HTA (CRD) search terms

#55.	MeSH DESCRIPTOR Thyroid Diseases EXPLODE ALL TREES
#56.	hyperthyroid*
#57.	hypothyroid*
#58.	thyrotoxicosis*
#59.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
#60.	#1 OR #2 OR #3 OR #4 or #5