Appendix A

Pilot Study

We conducted a pilot study to test the search string and data management and data extraction. The title and abstract screening, full text screening and data extraction were carried out by two researchers working independently.

Search design

The search string was developed using synonyms to encompass the two parts of the research question: Endocrine Disrupting Chemicals (EDCs) and effect on thyroid hormone (TH).

The search string was designed to be very general in its terms and an provided an initial look at the scope of literature in this area.

#1. **endocrine disrupting chemicals**

Keywords: endocrine disrupting chemicals OR EDCs or endocrine disruptors OR thyroid disrupting chemicals OR thyroid disruptors

MeSH: "Endocrine Disruptors"[Mesh]

Search string:

"Endocrine Disruptors"[Mesh] OR “endocrine disrupting chemical*” OR EDC OR “endocrine disruptor*” OR “thyroid disrupting chemical*” OR “thyroid disruptor*”

#2. **T4**

Keywords: thyroid hormone OR thyroxine

MeSH: "Thyroxine"[Mesh]

Search string: "Thyroxine"[Mesh]

The actual term ‘T4’ was not included as too many non-specific references were generated.

#3. **Thyroid stimulating hormone TSH**

Keywords: “thyroid stimulating hormone”

MeSH: "Thyrotropin"[Mesh]

Search string: "Thyrotropin"[Mesh] OR “thyroid stimulating hormone”

Query (#1, #2, #3 combined):

The search string**: (("Endocrine Disruptors"[Mesh] OR "endocrine disrupting chemical*" OR EDC OR "endocrine disruptor*" OR "thyroid disrupting chemical*" OR "thyroid disruptor*") AND ("Thyroxine"[Mesh])) AND ("Thyrotropin"[Mesh] OR "thyroid stimulating hormone")**

The was run in Pubmed, Scopus and Web of Science, giving: **63** results in Pubmed, **82** results in Web of Science and **269** results in Scopus.

Data management

All references were uploaded to the reference management software Mendeley and transferred to the systematic review software Cadima for de-duplication, screening and data extraction.

Data Extraction

Data extraction templates were created in Excel. The parameters recorded are given in the two tables below:

Table 1 Parameters for data extraction from human epidemiology studies

Data extraction - Human epidemiology	
Author	
Article ID	
Funding source	
Conflict of interest	
EDC	
Subjects	Study population
	Geography
	Demographics
	Number of subjects
	Inclusion / exclusion criteria
Methods	Study design
	Health outcome
	Diagnostic method
	Confounders
	Exposure assessment (EDC)
	TH assessment (sample)
	Measurement of Thyroid hormones
	Statistical methods
	EDC
Hormone level measurement	T4
	FT4
	TT4
	T3
	FT3
	TT3
	TSH
	FT3:FT4
	TSH/T4
	Comment

Table 2 Parameters for data extraction from animal studies

Data extraction - Animal studies	
Article ID	
Title	
Author	
primary date	
Funding	Source
	chemical
Animal model	Species
	Strain
Life stage at start of dosing	
Life stage at outcome assessment	
Treatment duration and frequency	
Dosing route	
Dose levels (mg/kg/d)	
Methods	Design (single dosing, chronic, multi-generation)
	Negative control
	Positive control
	Method to measure TH level
	Statistical methods
	thyroid histopathology
male adult	T4
	FT4
	TSH
	T3
	FT3
	fT3/fT4
female adult	T4
	FT4
	TSH
	T3
	FT3
	fT3/fT4
male offspring	T4
	FT4
	TSH
	T3
	FT3
female offspring	T4
	FT4
	TSH
	T3
	FT3
EDC	chemical
	source
	purity
	vehicle
Comment	Comment

Outcome

With the pilot search string, we obtain 297 hits after duplicate screening (29/09/2020).
We selected 150 publications of which: 82 were epidemiological studies and 68 animal studies.
The data extraction parameters were applied to the full text. The frequency of different EDCs that appeared in the publications analysed is given in Table 3.

Table 3. Summarized results from the pilot study.

Chemicals	Epidemiological studies	Mammalian model studies
Pesticides	24	25
Phenols (Bisphenol A, Triclosan)	18	11
Phthalates	19	3
Perfluorinated compounds	11	0
Flame retardants (BPDE, BDE)	12	6
PCBs	9	5
Metals	9	3
Dioxins	3	1
Parabens	5	0