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# INPLASY

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# Maternal bisphenols exposure and thyroid function in children: a systematic review and meta-analysis

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#### ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 May 2024 and was last updated on 28 May 2024.

## **INTRODUCTION**

Review question / Objective This study aims to explore the associations of prenatal exposure to bisphenols with thyroid function in newborns and early childhood, with particular focuses on the sex-dependent, exposure level, and matrix effects.

**Condition being studied** The disease, condition, or healthcare domain being studied in the systematic review is the impact of prenatal bisphenol exposure on thyroid function in newborns and early childhood. Bisphenol compounds, such as BPA, BPF, BPS, BPAF, and TCBPA, are known endocrine disruptors that have been linked to alterations in thyroid hormone levels. Thyroid hormones play a crucial role in the regulation of metabolism, growth, and development, making any disruption in their levels potentially harmful, especially during critical periods of prenatal and early childhood development. This systematic review aims to assess the association between prenatal bisphenol exposure and thyroid function in order to better understand the potential health risks and inform public health policies and interventions.

## **METHODS**

**Participant or population** Pregnant women with prenatal exposure to bisphenols and their offspring(newborn or children).

**Intervention** Maternal prenatal exposure to bisphenols like BPA, BPF, BPS, BPAF, and TCBPA.

Comparator Non-exposed control group.

Study designs to be included Cohort study.

**Eligibility criteria** Studies were included if they (i) focused on prenatal bisphenols (BPs) exposure like (BPA, BPF, BPS, BPAF, and TCBPA and children's thyroid function presented by thyroid hormone metric including TSH, TT3, TT4, FT3, and FT4) ; (ii)

detected BPs from maternal blood, urine, amniotic fluid (AF), or umbilical cord blood samples; (iii) quantified measured the correlation between BP concentrations and TH levels in children. Studies were excluded if they were reviews, animal studies, conference abstracts, lectures, literature, or editorial materials.

Information sources Electronic databases.

**Main outcome(s)** The main outcome of the review is the association between prenatal bisphenol exposure (BPA, BPF, BPS, BPAF, TCBPA) and thyroid hormone levels in newborns and early childhood. The specific thyroid hormones of interest include thyroid stimulating hormone (TSH), total tri-iodothyronine (TT3), total thyroxine (TT4), free tri-iothyronine (FT3), and free thyroxine (FT4). These outcomes were measured using blood or urine samples collected from newborns and children during the prenatal period and early childhood.

Additional outcome(s) The sex-dependent, exposure level, and matrix effects between prenatal exposure to BPs and thyroid function in newborns and early childhood.

Quality assessment / Risk of bias analysis Funnel plots and Egger's linear regression method will be used to check publication bias, and the quality of each eligible study was assessed using the Newcastle Ottawa Scale (NOS).

**Strategy of data synthesis** The effect sizes of eligible studies will be synthesized using coefficients from multivariable regression models, alongside their 95% confidence intervals (CIs).

Heterogeneity among studies was assessed using the I^2 statistic, with  $I^2 \ge 50\%$  indicating considerable heterogeneity and necessitating a random-effects model. Conversely, a fixed-effects model was applied for  $I^2 < 50\%$ . Forest plots were employed to visually depict the results of the metaanalysis. Results were visually represented through forest plots, and subgroup analyses were conducted to explore the sex-specific effects. To ascertain the stability of the results, sensitivity analyses were performed. The data acquisition and analysis processes were conducted utilizing Stata 16.0 software.

**Subgroup analysis** Planned investigation of subgroups in the systematic review will include the following factors: different types of thyroid hormones (e.g., TSH, TT3, TT4, FT3, FT4), sex differences (boy vs. girl), levels of bisphenol exposure (low, moderate, high), and matrix (serum

vs. urine). The planned analytic approach for these subgroup analyses will involve conducting separate meta-analyses for each subgroup to assess the specific effects of prenatal bisphenol exposure on thyroid function.

**Sensitivity analysis** The stability of the results was evaluated by the one-by-one elimination method.

Country(ies) involved China; Tanzania.

**Keywords** Bisphenols, Prenatal exposure, Children, Thyroid function, Meta-analysis.

## **Contributions of each author**

Author 1 - Jiani Liu. Author 2 - Min Tian. Author 3 - Haiyue Qin. Author 4 - Danrong Chen. Author 5 - Sabitina Mrisho Mzava. Author 6 - Xu Wang. Author 7 - Francis Manyori Bigambo.

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