

Background

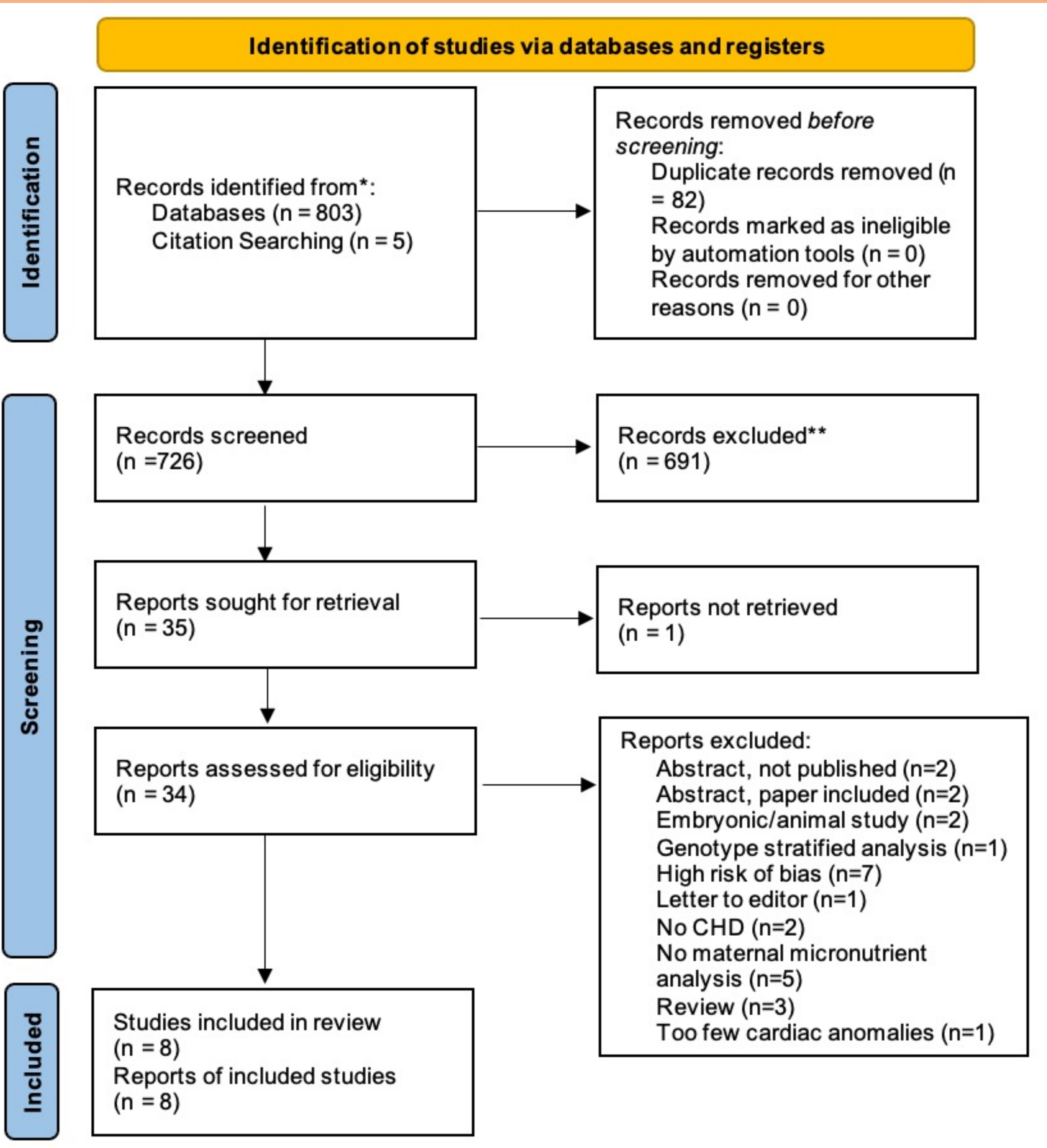
- Congenital anomalies affect ~2% of pregnancies, congenital heart disease (CHD) is the most common.
- Understanding of aetiology is limited.
- Micronutrients are essential vitamins and trace elements with roles in developmental biology.
- RCOG and NICE recommend vitamin and micronutrient supplementation in pregnancy. Meta-analysis suggests folate supplementation reduces CHD.
- No systematic assessment of maternal micronutrient levels or deficiency.

Review Question

- Do maternal micronutrient deficiencies increase the risk of fetal CHD?

Methods

- PROSPERO: CRD42021276699
- *Population* – Biological mothers; *Exposure* – Mothers with micronutrient deficiency; *Comparator* – Mothers without micronutrient deficiency; *Outcome* – Fetus/Child with CHD.
- Observational studies (all case-control).
- Systematic literature search of MEDLINE, EMBASE and Cochrane Library.
- Two authors independently screened titles and abstracts and performed data extraction.
- SIGN risk of bias assessment.
- Narrative synthesis due to heterogeneity.
- PRISMA Guidelines followed.



Study Characteristics

- 8 studies included.
- Data from 2427 pregnancies, 1199 offspring with CHD.
- 8 micronutrients assessed across studies.
- Blood (7) or hair (1) samples.
- Samples in pregnancy (2), postnatally (4), not reported (2).

Micronutrient	Manuscript (s)	Results
Vitamin D	Dilli et al.	↓ Vit D cases vs. controls; no OR for deficiency
	Koster et al.	↓ Vit D cases vs. controls; ↑ aOR CHD vit D deficiency
	Mokhtar et al.	↓ Vit D cases vs. controls; ↔ aOR CHD vit D deficiency
Ferritin	Yang et al.	↓ Ferritin cases vs. controls; no OR for deficiency
Copper	Hu et al.	↑ Copper cases vs. controls; ↔ aOR CHD copper deficiency
	Ou et al.	↓ Copper cases vs. controls; ↔ aOR CHD copper deficiency
Selenium	Ou et al.	↓ Selenium cases vs. control; ↑ OR CHD selenium deficiency
Zinc	Dilli et al.	↑ Zinc cases vs. controls; no OR for deficiency
	Hu et al.	↔ Zinc cases vs. controls; ↔ aOR CHD zinc deficiency
Vitamin A	Dilli et al.	↔ Vit A cases vs. controls; no OR for deficiency
Vitamin B12	Dilli et al.	↔ Vit B12 cases vs. controls; no OR for deficiency
	Verkleij-Hagoort et al.	↔ Vit B12 cases vs. controls; ↔ aOR CHD Vit B12 deficiency
	Hobbs et al.	↔ Vit B12 cases vs. controls; no OR for deficiency
Folate	Dilli et al.	↔ Vit Folate cases vs. controls; no OR for deficiency
	Verkleij-Hagoort et al.	↔ Vit Folate cases vs. controls; ↔ aOR CHD folate deficiency
	Hobbs et al.	↔ Vit Folate cases vs. controls; no OR for deficiency

Conclusions

- Not enough evidence to confidently determine if maternal micronutrient deficiency increases the risk of CHD in offspring.
- Small sample sizes, heterogenous study designs, contradictory findings.
- No standardized definitions of deficiency utilized across studies.
- Varying confounders accounted for in studies.

The Future

- Prospective cohort study recruiting mothers and fetuses in 2nd/3rd trimester with maternal, diagnosis, outcome and surgical data alongside biosamples.
- Surgical-PEARL Study commenced May 2022 (<https://www.isrctn.com/ISRCTN12557586>).
- Please contact authors to collaborate.