School of Life Course and Population Sciences

Maternal obesity and offspring cardiovascular remodelling – the effect of preconception and antenatal lifestyle interventions: a systematic review

Samuel J Burden,[1] **Rahaf Alshehri**,[2] **Pablo Lamata**,[3] **Lucilla Poston**,[1] **Paul D Taylor** [1]

1 Department of Women and Children's Health, School of Life Course and Population Sciences, King's College London, United Kingdom; 2 Cardiovascular Medicine and Science Research, School of Cardiovascular and Metabolic Medicine & Sciences, King's College London, United Kingdom. 3 Biomedical Engineering, School of Biomedical Engineering & Imaging Sciences, King's College London, United Kingdom.

Background

- Cardiovascular disease may have origins in preconception, *in utero*, and early infancy.
- Maternal obesity is associated with cardiovascular remodelling in children (Fig. 1) and adverse cardiovascular outcomes in adulthood.[1-5]
- Preconception or antenatal lifestyle interventions in women with obesity may prevent child cardiovascular remodelling.

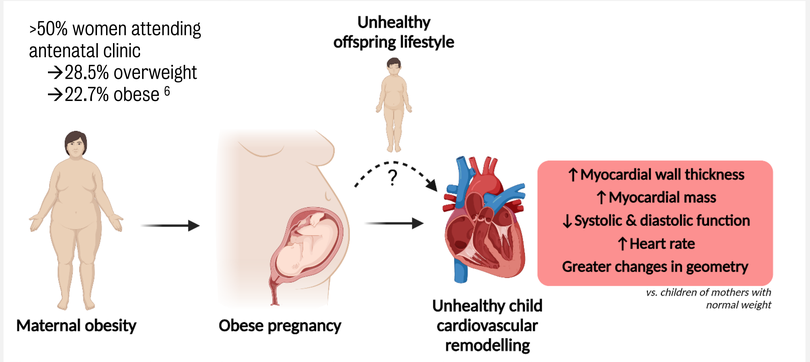

Fig 1. The impact of maternal obesity on child cardiovascular remodelling.

Aims: To systematically review and determine whether preconception or antenatal lifestyle interventions in women with obesity can limit offspring cardiovascular remodelling and identify knowledge gaps for future study.

Methods

PubMed.gov & Embase → rayyan

PROSPERO (CRD42023454762)

Inclusion

- Preconception or antenatal lifestyle (diet and/or physical activity) RCT in women with overweight or obesity. Offspring of any age (paediatric or adult).
- Cardiac structure; cardiac function (systolic and diastolic function); heart rate and heart rate variability; arterial stiffness and arterial thickness (e.g. pulse-wave velocity); blood pressure.

Exclusion

- RCTs focussed on women with normal weight. Or utilising nutritional supplements or drugs.
- Fetal cardiovascular remodelling.
- Cardiometabolic health and other aspects of offspring health.
- Reviews, case reports, animal studies, published in grey literature, conference or meeting abstracts, not written in English.

Risk of bias: Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (NHLBI).

- Q3 replaced with Q7 from NHLBI Quality Assessment of Case-Control Studies → better reflected sampling from an established cohort.
- Recruitment or randomisation bias assessed by Q2.4, Q5.4, and Q5.5 from the ROBINS-I tool and domain 1 of the RoB 2 tool, respectively.

British Heart Foundation
SP/F/21/150013

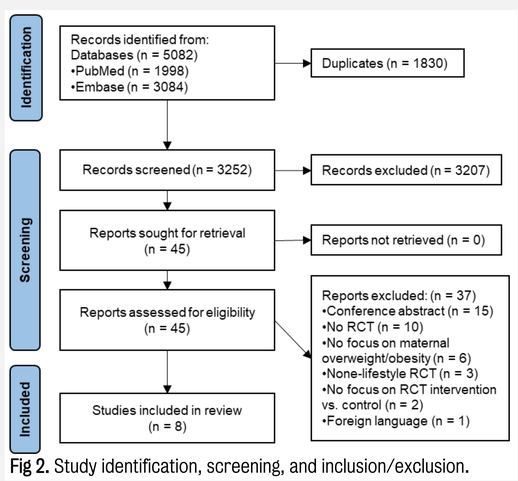

Fig 2. Study identification, screening, and inclusion/exclusion.

Conclusions

- Some evidence that preconception/antenatal lifestyle interventions in women with obesity can limit offspring cardiac remodelling (Fig. 3).
- Supports findings in animals (changes in cardiac structure and function but no difference in blood pressure).[15]
- Statistical shape modelling provides novel insights into cardiac remodelling where standard metrics cannot.
- Should these findings be confirmed in larger follow-up studies of older offspring, relevant public health strategies to improve the cardiovascular health of the next generation would be warranted.

Mechanisms (?)

- Maternal insulin and/or leptin resistance, lipids, lipoproteins
- Reduced sympathetic and increased parasympathetic drive
- Epigenetics / genetics
- Shared lifestyle
- ???

Results

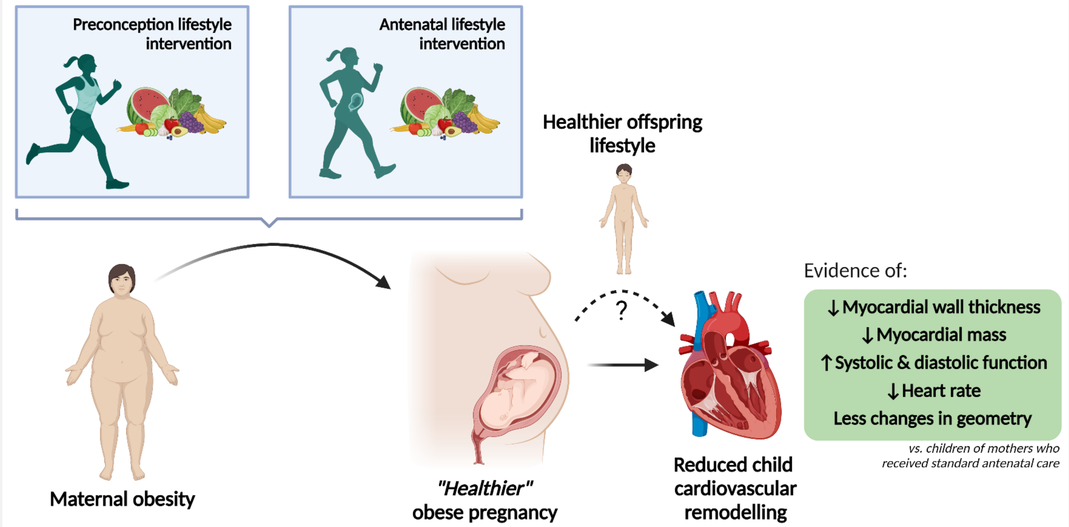

Fig 3. The protective effect of preconception and antenatal lifestyle interventions on child cardiovascular remodelling.

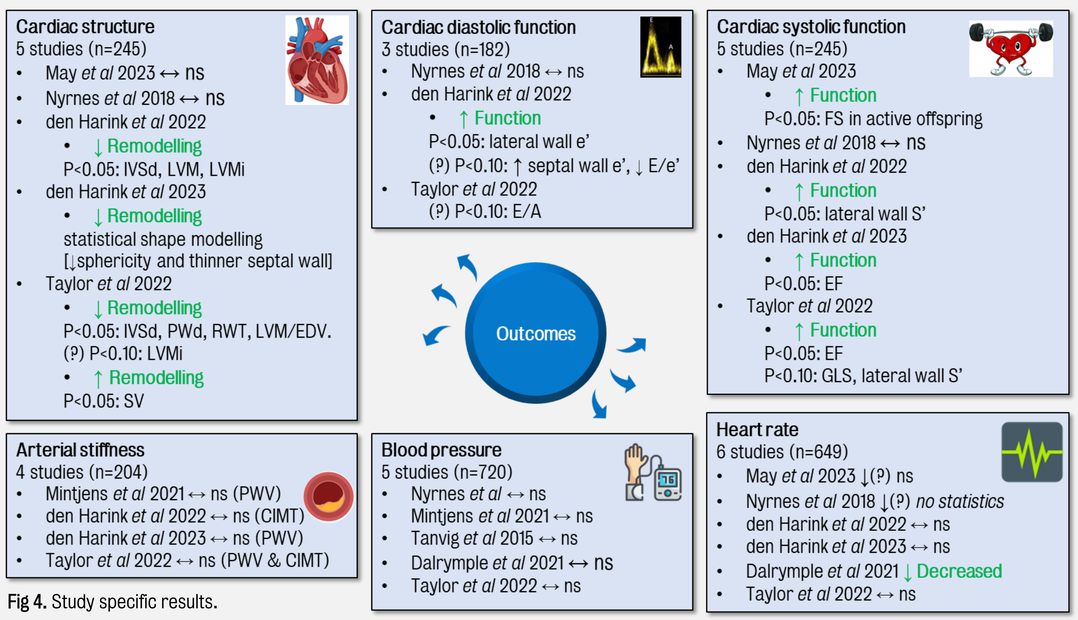

Fig 4. Study specific results.

5 RCTs, 8 follow-ups. *ENHANCED* → May *et al* 2023 [7]; *ETIP* → Nyrnes *et al* 2018 [8]; *Lifestyle* → Mintjens *et al* 2021 [9], den Harink *et al* 2022 [10], den Harink *et al* 2023 [11]; *LiP* → Tanvig *et al* 2015 [12]; *UPBEAT* → Dalrymple *et al* 2021 [13], Taylor *et al* 2022.[14]

There was evidence of reduced cardiac remodelling, with reduced interventricular septal wall thickness commonly reported. Some studies identified improved systolic and diastolic function and reductions in heart rate. There were no differences in blood pressure or arterial stiffness measures. A high loss to follow up was a common limitation. There were no studies >7 years-old.

Table 2. Study characteristics

Study	Summary	Quality
May *et al* 2023	Antenatal exercise; n=18 with obesity (n=140 randomised); 4-5 weeks postnatal; echocardiography and heart rate; split into "active" or "quiet" states with only n=3 in some groups.	Fair
Nyrnes *et al* 2018	Antenatal exercise; n=53 (n=91 randomised); 1-3 days and 6-8 weeks postnatal; echocardiography, blood pressure, and heart rate; adherence to the intervention was only 50%.	Fair
Mintjens *et al* 2021	Preconception diet and exercise; n=43 (n=577 randomised); 3-6 years-old; blood pressure, pulse-wave velocity; 10.5% of control group lost >5% body weight in first six-months, whilst only 43% of intervention group achieved this overall.	Fair
den Harink *et al* 2022	n=60 (n=577 randomised); echocardiography, heart rate, and carotid ultrasound; *Otherwise the same as Mintjens et al 2021.*	Fair
den Harink *et al* 2023	n=49 (n=577 randomised); cardiac MRI & heart rate; *Otherwise the same as Mintjens et al 2021.*	Fair
Tanvig *et al* 2015	Antenatal diet and exercise; n=150 (n=360 randomised); blood pressure; 2.5-3.2 years-old.	Fair
Dalrymple *et al* 2021	Antenatal diet and exercise; n=404 (n=1555 randomised); 3 years-old; blood pressure & heart rate; only study to account for missing data.	Fair
Taylor *et al* 2022	Antenatal diet and exercise; n=70 (n=1555 randomised); 3 years-old; echocardiography, carotid ultrasound, pulse-wave velocity, blood pressure, heart rate variability; only study to account for notable confounding variables in all analyses, <10% of the original cohort was studied.	Fair

ICONSB · bio RENDER · DOHaD International Society for Developmental Origins of Health and Disease

Dr. Samuel J Burden, PhD
Research Associate
Dept. Women & Children's Health, School of Life Course and Population Sciences, King's College London

References
1. Kankowski L et al. The Impact of Maternal Obesity on Offspring Cardiovascular Health: A Systematic Literature Review. Front Endocrinol (Lausanne) 2022.
2. den Harink T et al. Maternal obesity in pregnancy and children's cardiac function and structure: A systematic review [...]. PLoS One 2022.
3. Kereliuk SM et al. Recent Experimental Studies of Maternal Obesity, Diabetes during Pregnancy and the Developmental Origins [...]. Int J Mol Sci 2022.
4. Razaz N et al. Maternal obesity and risk of cardiovascular diseases in offspring: a population-based cohort and [...]. Lancet Diabetes Endocrinol 2020.
5. Reynolds RM, Allan KM, Raja EA, et al. Maternal obesity during pregnancy and premature mortality from cardiovascular [...]. BMJ 2013.
6. NMPA Project Team. National Maternity and Perinatal Audit: Clinical Report 2022. In. London: RCOG; 2017.
7. May LE et al. Influence of Supervised Maternal Aerobic Exercise during Pregnancy on 1-Month-Old Neonatal Cardiac Function [...]. Med Sci Sports Exerc 2023.
8. Nyrnes SA et al. Cardiac function in newborns of obese women and the effect of exercise during pregnancy. A randomized controlled trial. PLoS One 2018.
9. Mintjens S et al. The Effects of a Preconception Lifestyle Intervention on Childhood Cardiometabolic Health-Follow-Up of a Randomized Controlled Trial. Cells 2021.
10. den Harink T et al. Preconception lifestyle intervention in women with obesity and echocardiographic indices of cardiovascular health[...]. Int J Obes (Lond) 2022.
11. den Harink T et al. A preconception lifestyle intervention in women with obesity and cardiovascular health in their children. Pediatr Res 2023.
12. Tanvig M et al. Effects of lifestyle intervention in pregnancy and anthropometrics at birth on offspring metabolic profile at 2.8 years [...]. J Clin Endocrinol Metab 2015.
13. Dalrymple KV et al. Adiposity and cardiovascular outcomes in three-year-old children of participants in UPBEAT, an RCT of a complex [...]. Pediatr Obes 2021.
14. Taylor PD et al. Lifestyle intervention in obese pregnancy and cardiac remodelling in 3-year olds: children of the UPBEAT RCT. Int J Obes (Lond) 2022.
15. Beeson JH et al. Maternal exercise intervention in obese pregnancy improves the cardiovascular health of the adult male offspring. Mol Metab 2018.