Age at Menarche and Pregnancy and Perinatal Outcomes: triangulating evidence from multivariable regression and Mendelian randomization analyses

Elisabeth Aiton

University of Bristol, United Kingdom

25th September 2024

Supervised by Professor Abigail Fraser and Dr Amy Taylor

MRC Integrative Epidemiology Unit

University of BRISTOL

wellcome

WCE

WORLD CONGRESS OF EPIDEMIOLOGY 2024

Background

- Onset of puberty has been decreasing since the 1900s
- Attributed to improved nutrition
- Earlier age at menarche has been associated with increased risks of adverse pregnancy outcomes, such as preterm birth and gestational hypertension

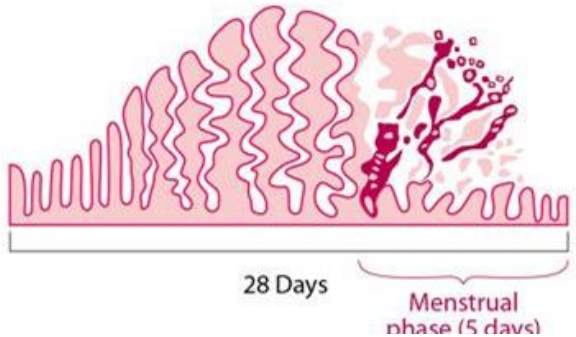
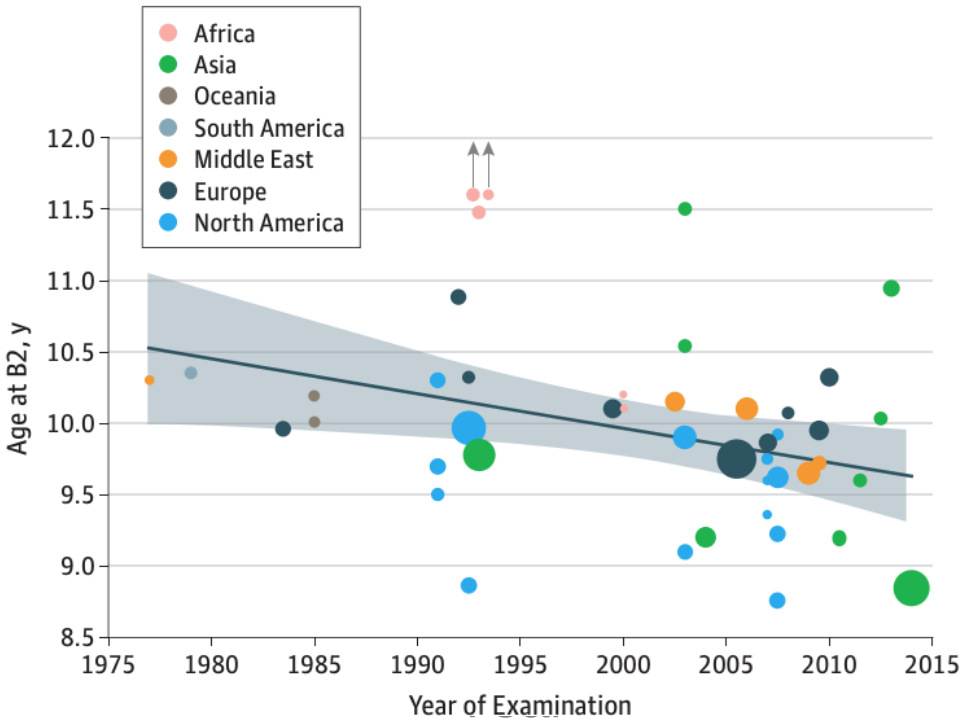


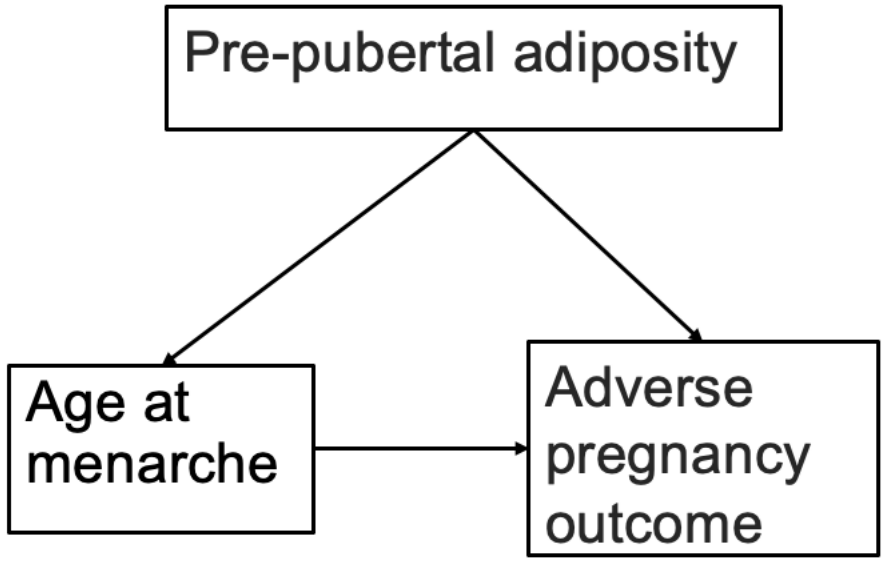
Figure 2. Secular Changes in Age at Onset of Tanner Breast Stage 2 (B2) From 1977 to 2013 Around the World According to Year of Study



Eckert-Lind et al., 2020

Research question

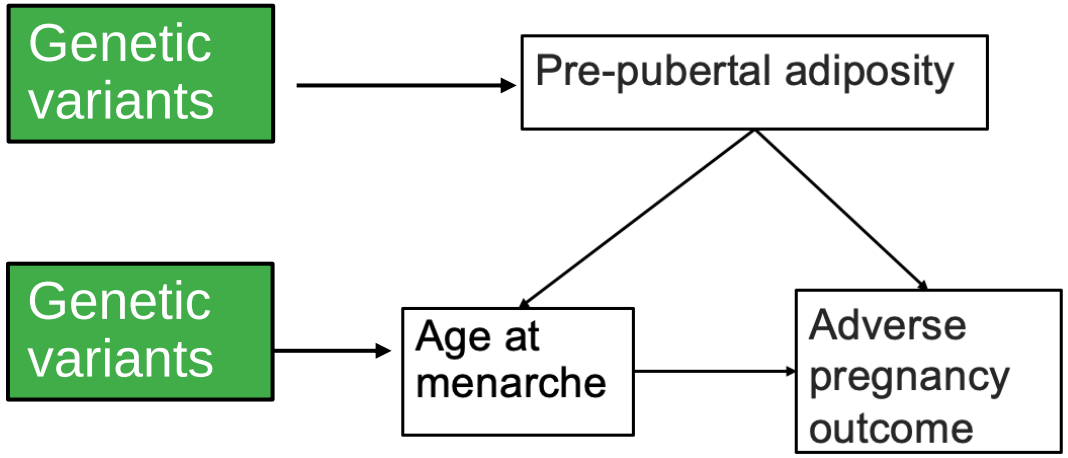
Does an earlier age at menarche cause adverse pregnancy outcomes, after accounting for adiposity?



Methods

Mendelian Randomization

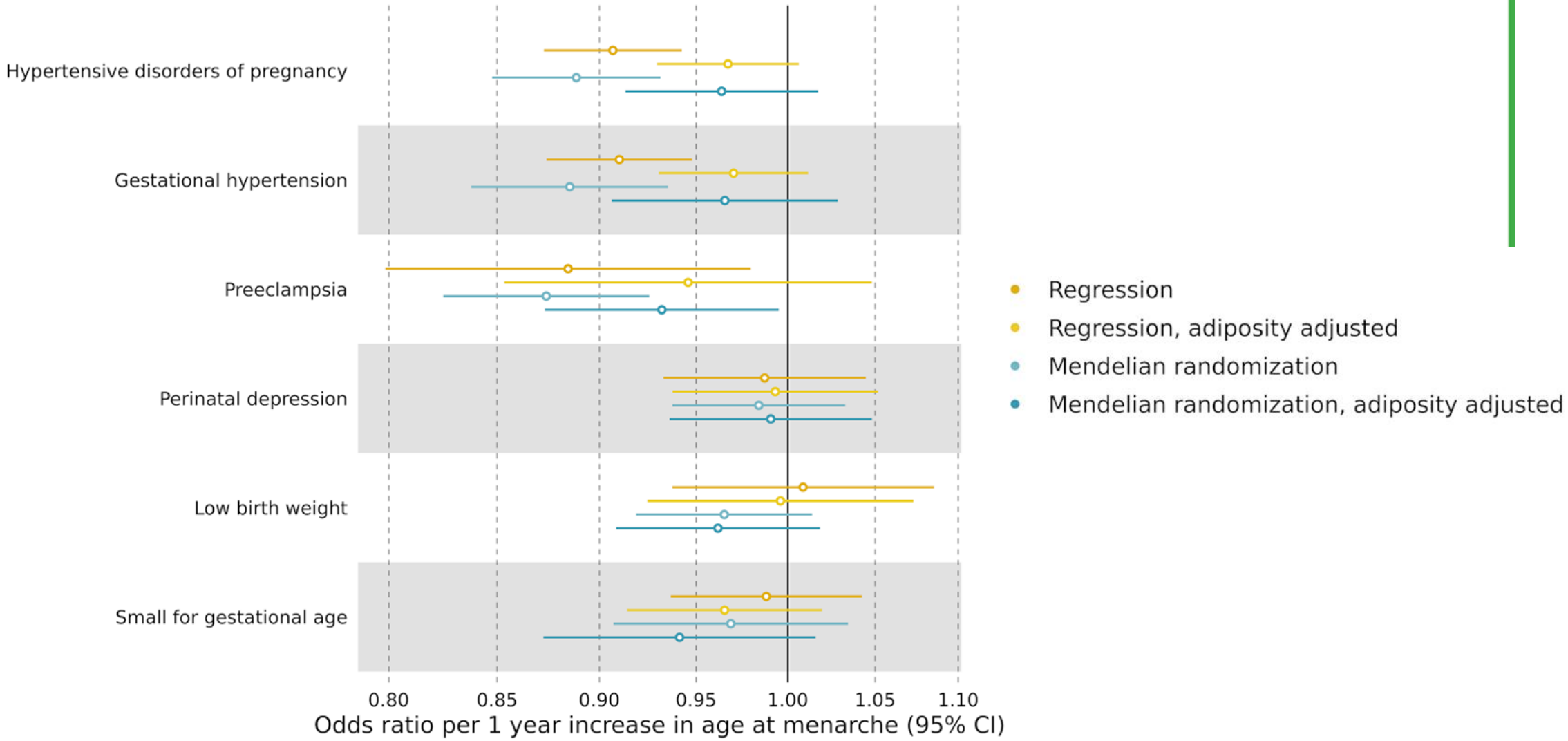
- Two models, one adjusted for adiposity
- Genetic variants associated with exposure used as instrumental variables
- Sample sizes n = 85,000 to n = 646,000
- Sensitivity analysis adjusting for fetal genetic inheritance



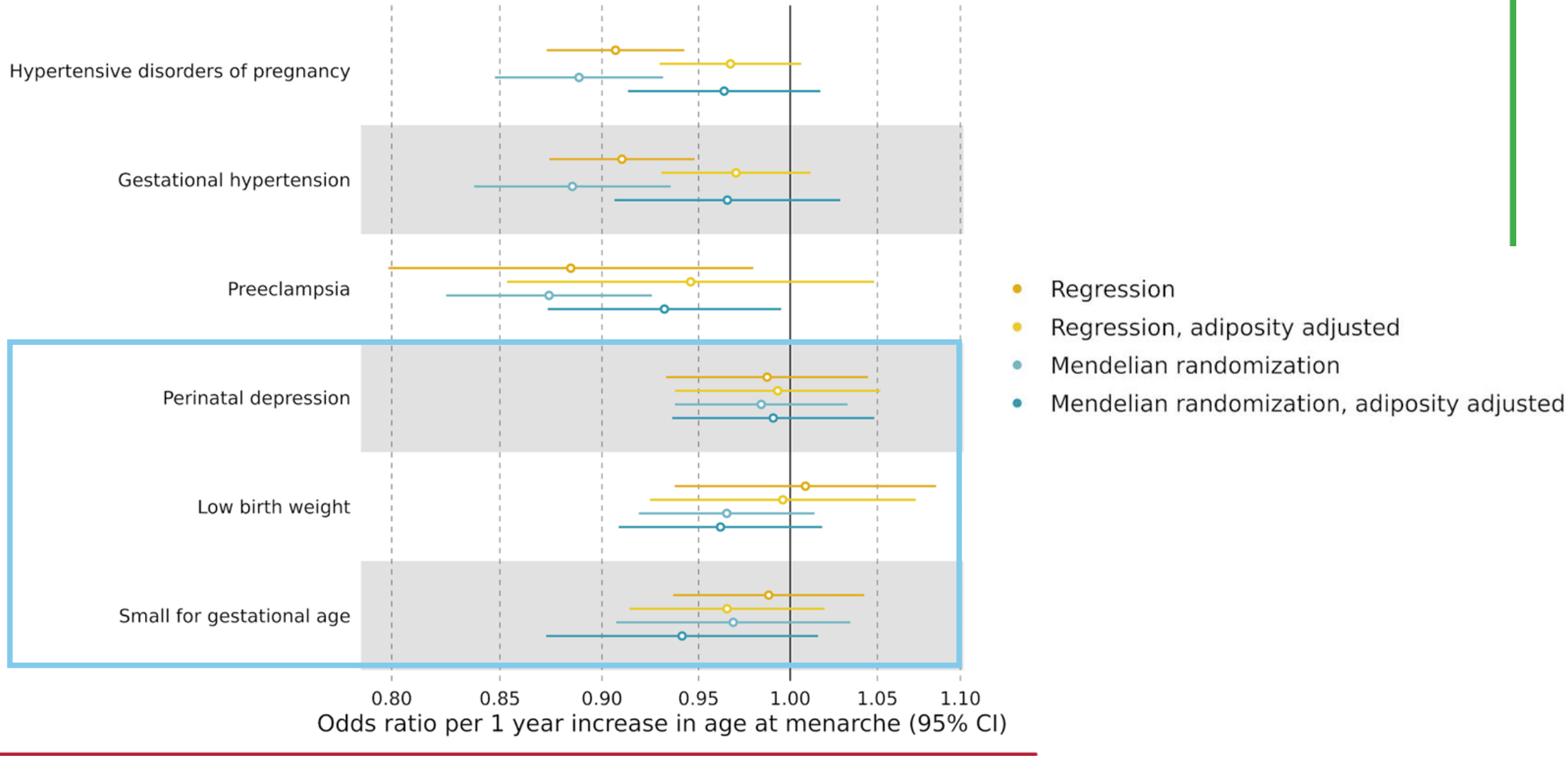
Multivariable regression

- Two models, one adjusted for adiposity
- UK birth cohort: Avon Longitudinal Study of Parents and Children (ALSPAC)
- n = 9,441
- Self-reported age at menarche
- Pregnancy outcomes from maternity records
- Pre-pregnancy BMI as a proxy for pre-pubertal adiposity
- Both models adjusted for education, ethnicity, age, parity, offspring sex

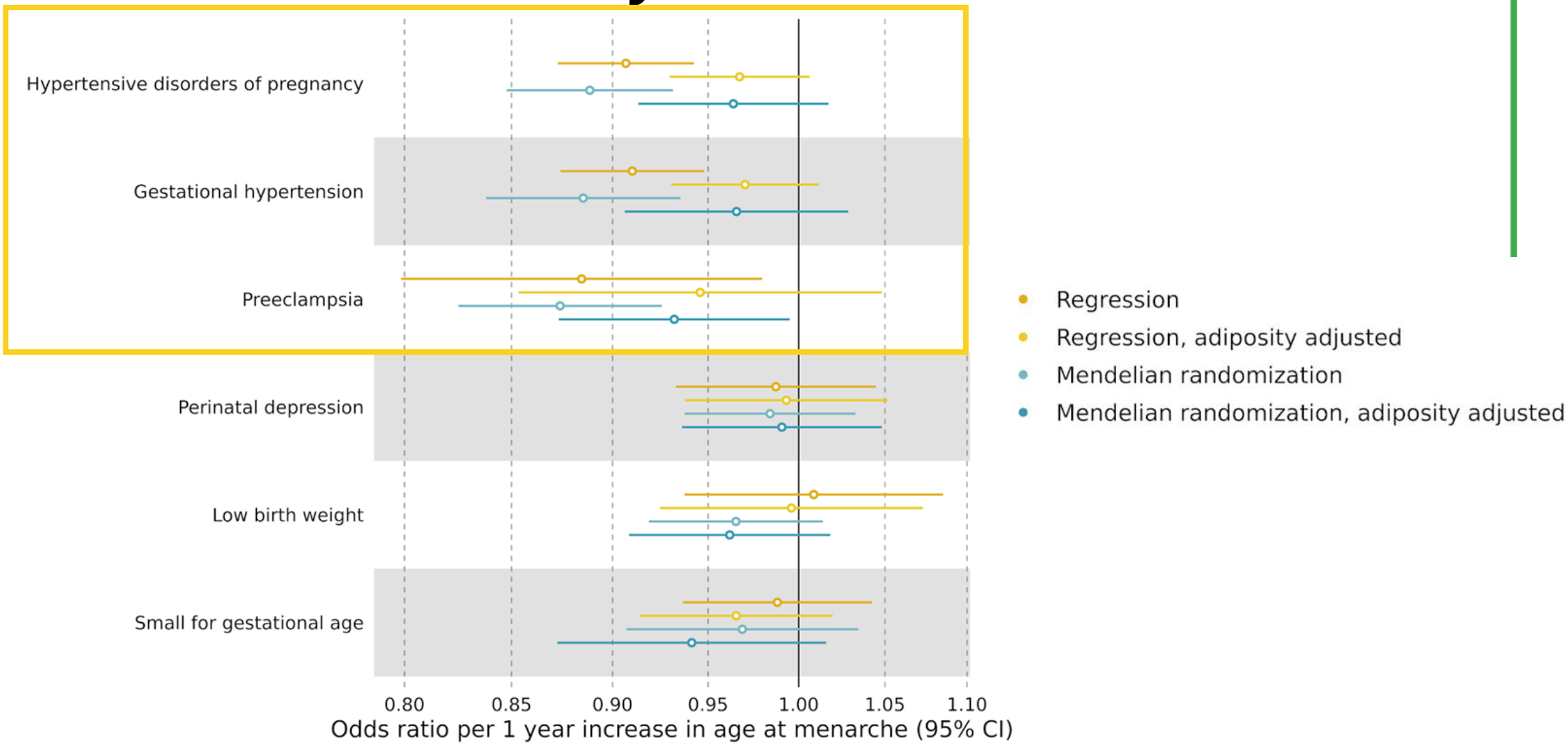
Results: Main analysis



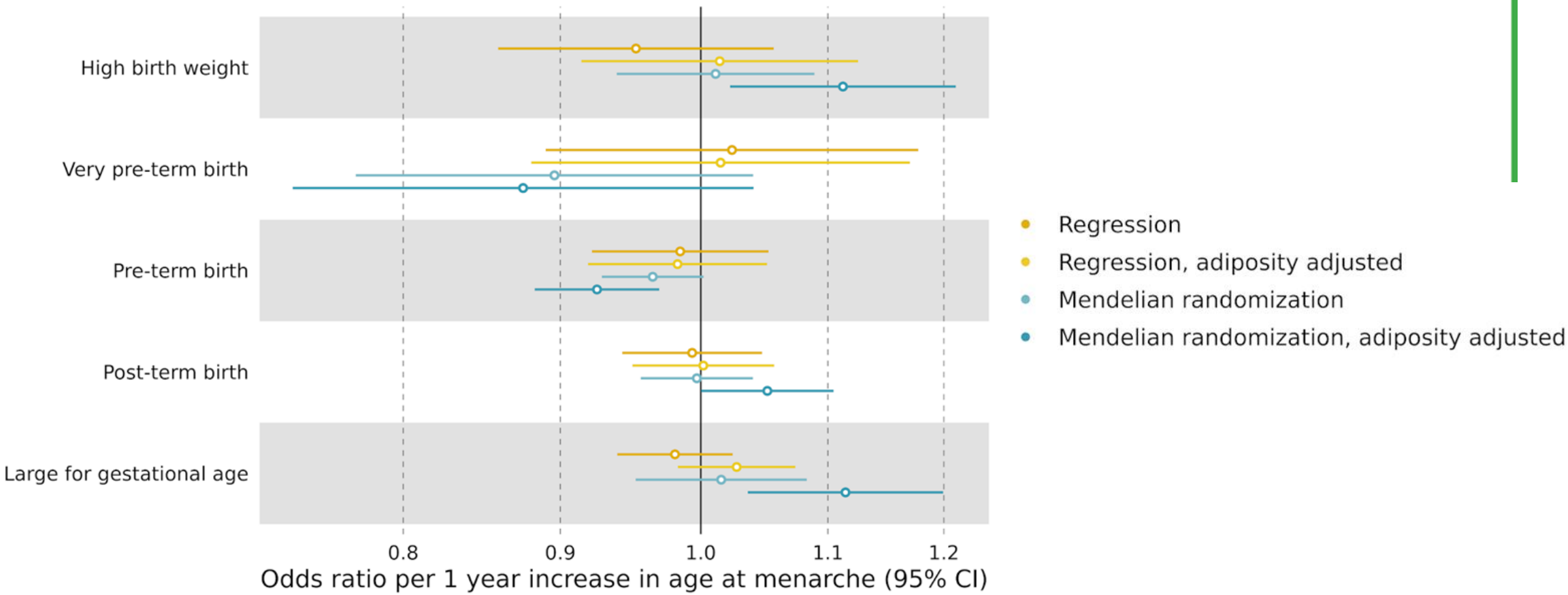
Results: Main analysis



Results: Main analysis

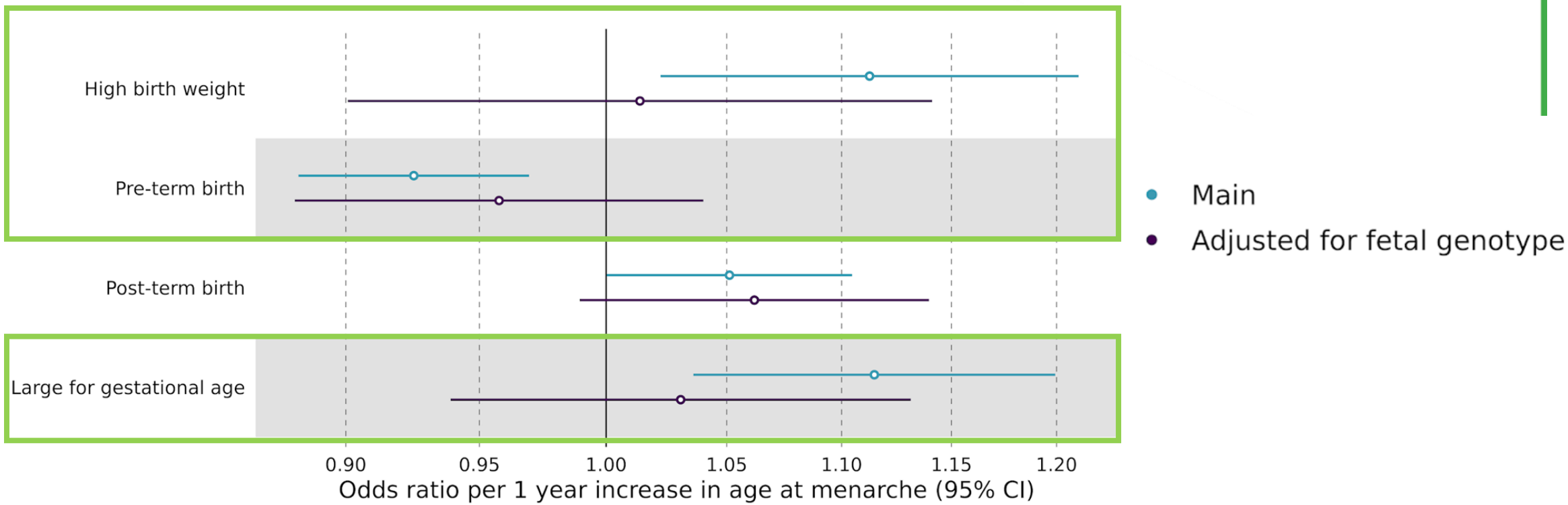


Results: Main analysis



Sensitivity analysis adjusting for fetal genotype

- Mendelian randomization, adiposity adjusted model



Discussion

Finding	Outcomes	Strength of evidence
Age at menarche not causally associated with… 	Perinatal depression, low birthweight, small for gestational age	Strong, both approaches agreed
Causal effect driven by adiposity 	Hypertensive disorders of pregnancy	Strong, both approaches agreed
Causally related to age at menarche, **only after** adiposity adjustment 	High birthweight, preterm birth, large for gestational age Post-term birth	Only in Mendelian randomization Attenuated when fetal genotype accounted for

Thank you! 👋

MRC Integrative Epidemiology Unit

University of BRISTOL

MR PREG collaboration in Bristol

- Amy Taylor
- Abi Fraser
- Deborah Lawlor
- Carolina Borges
- Qian Yang
- Jevvy Huang
- Gemma Clayton
- Hara Chatzigeorgiou
- Nancy McBride
- Tom Bond
- Ana Goncalves Soares
- Peiyuan Huang

e.aiton@bristol.ac.uk
Twitter: @lizzy_aiton

WCE
WORLD CONGRESS OF EPIDEMIOLOGY 2024