

Hypertensive Disorders of Pregnancy and Adult Offspring Cardiometabolic Outcomes: A Systematic Review and Meta-analysis



Thoulass, Janine¹; Robertson, Lynn¹; Denadai, Lucas¹; Black, Corri¹; Crilly, Michael¹; Iversen, Lisa²; Scott, Neil¹; Hannaford, Philip Christopher²

¹ Chronic Disease Research Group, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK, AB25 2ZD;

² Academic Primary Care, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK, AB25 2ZD

Background

- Hypertensive disorders of pregnancy affect up to 8% of pregnancies.¹
- They include eclampsia, pre-eclampsia, gestational hypertension, pre-existing chronic hypertension and pre-eclampsia superimposed on chronic hypertension.
- Previous systematic reviews have shown that the offspring of women with pre-eclampsia have increased BP and BMI in childhood and early adulthood.^{2,3}
- Less is known about the later life consequences.

Aim

To systematically review the association between maternal hypertensive disorders of pregnancy and cardiovascular risk factors and disease in adult offspring.

Methods

INCLUSION CRITERIA

Types of study: Observational epidemiological studies

Types of participant: Offspring aged at least 18 years at last follow up

Types of exposure: In utero exposure to any maternal hypertensive disorder of pregnancy

Types of outcome: The primary outcome was cardiovascular disease (cerebrovascular disease or coronary heart disease). Secondary outcomes were cardiometabolic factors associated with cardiovascular risk (blood pressure, body mass, glucose metabolism, lipids) and all cause mortality

SEARCH METHODS

- Medline, EMBASE and CINAHL, bibliographies of included studies
- No language restrictions
- Quality appraisal was done using the Newcastle Ottawa Scale
- Meta-analysis used a fixed effects approach

Results

- 8 cohort studies were included in the review (fig 1&2)
- Key quality issues included definition of hypertensive disorders of pregnancy, characterisation of comparison groups and completeness of follow-up

Figure 1 Results of search strategy

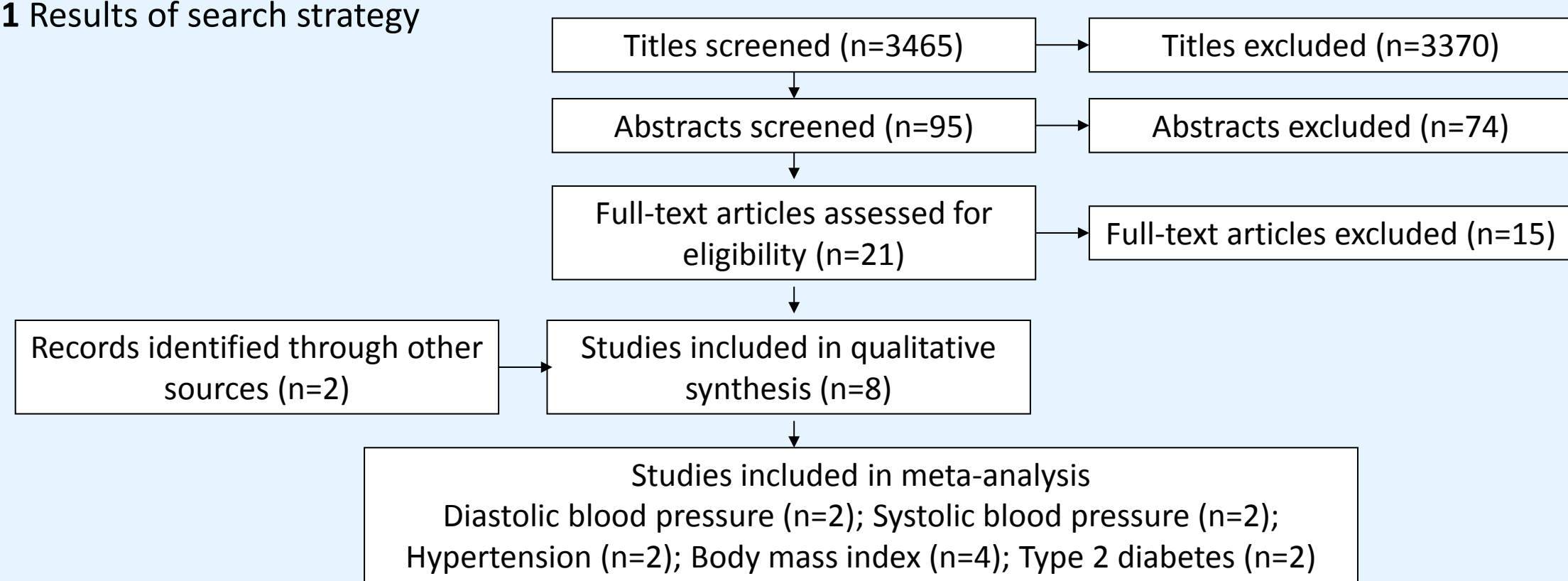


Figure 2 Study characteristics

Author	DOB	Age at follow-up	Offspring inclusion criteria	Exposure group(s)	Outcomes	Newcastle Ottawa Scale
Kajantie 2009 ⁴	1934-44	59-69y	Singleton offspring	(1) Severe pre-eclampsia (2) Pre-eclampsia (3) Gestational hypertension	Coronary heart disease Stroke Hypertension	S5/C2/O2
Lazdam 2010 ⁵	1982-85	22-26y	Preterm offspring	(1) Gestational hypertension	Blood pressure Body mass index Fasting glucose Lipids	S4/C2/O2
Libby 2006 ⁶	1952-58	45-51y	Type 1 DM excluded	(1) Pre-eclampsia and eclampsia	Type 2 diabetes	S5/C2/O2
Mamun 2012 ⁷	1981-83	21y	All offspring	(1) Hypertensive disorders of pregnancy	Blood pressure Body mass index	S5/C2/O2
Mogren 2001 ⁸	1955-66	31-41y	All offspring	(1) Pre-eclampsia or hypertension during pregnancy	Blood pressure Body mass index Lipids	S4/C2/O3
Palmsten 2010 ⁹	1959-66	34-44y	All offspring	(1) Pregnancy-related hypertension	Hypertension	S5/C2/O1
Ros 2001 ¹⁰	1973-78	20-25y	Female offspring	(1) Mild pre-eclampsia (2) Severe pre-eclampsia	Body mass index	S5/C2/O1
Thomas 2007 ¹¹	1958	45y	Type 1 DM excluded	(1) Pre-eclampsia	Body mass index Glycosylated haemoglobin Type 2 diabetes	S5/C2/O2

CARDIOVASCULAR

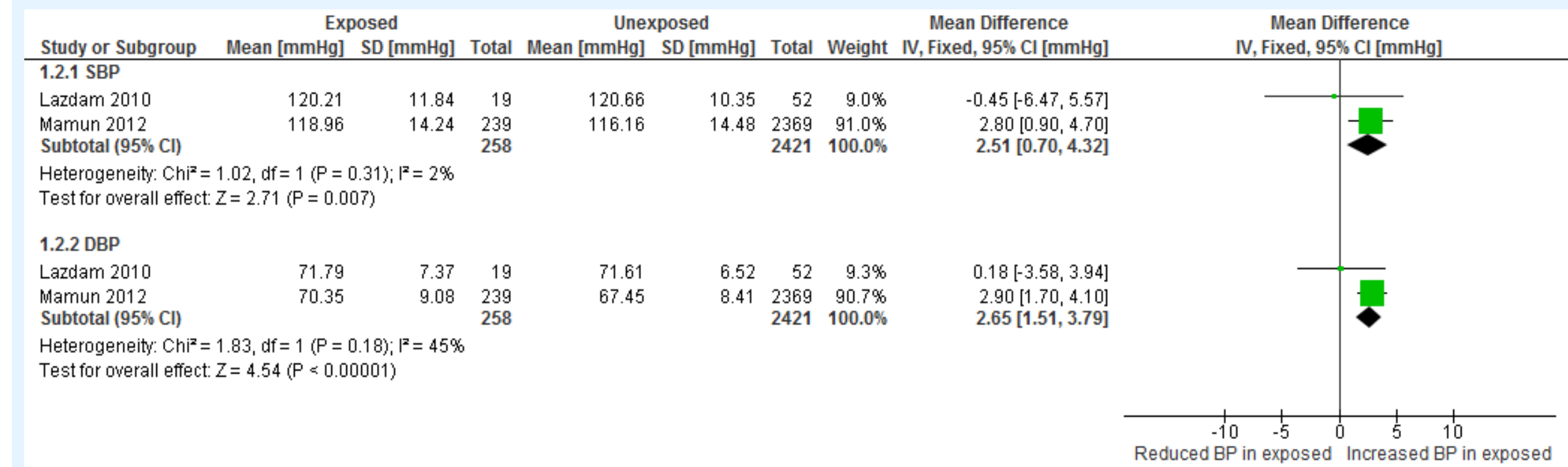
Coronary heart disease (one study): No statistically significant increases in risk in adult offspring exposed to maternal pre-eclampsia or gestational hypertension.⁴

Stroke (one study): Statistically significant increases in risk in adult offspring exposed to maternal gestational hypertension and severe pre-eclampsia, but not non-severe pre-eclampsia.⁴

BLOOD PRESSURE

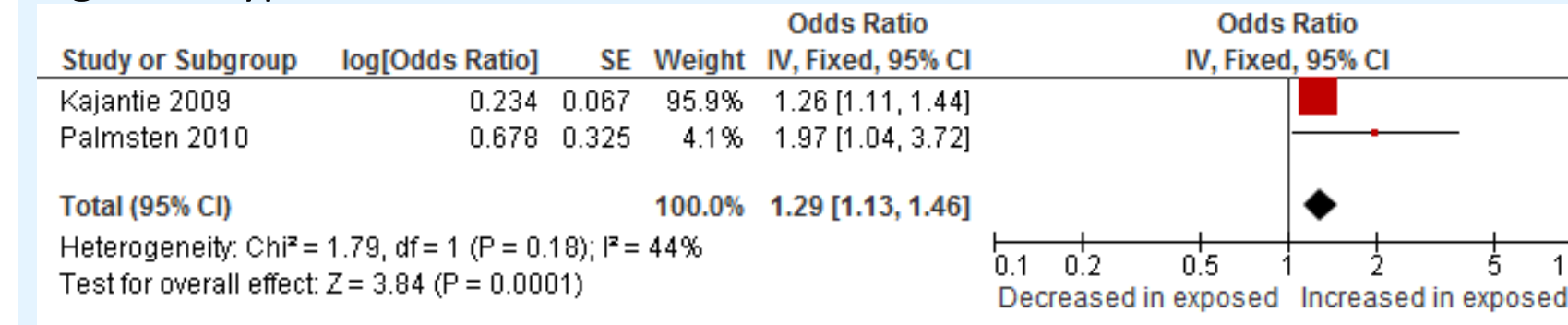
Blood pressure (three studies): Meta-analysis of two studies showed statistically significant increases in both systolic and diastolic blood pressure (fig 3)^{5,7}. A third study showed a statistically significant increase in risk of elevated blood pressure in adult offspring exposed to maternal hypertensive disorders of pregnancy.⁸

Figure 3 Blood pressure



Hypertension (two studies): Meta-analysis showed a statistically significant increased risk of hypertension (fig 4).^{4,9}

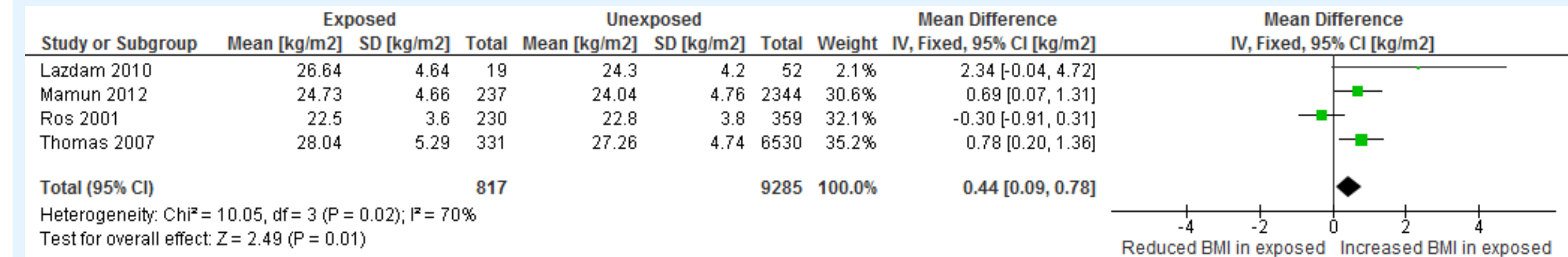
Figure 4 Hypertension



BODY MASS

Body mass index (five studies): Meta-analysis of four studies showed a statistically significant increase in BMI (fig 5)^{5,7,10,11}. A fifth study showed a statistically significant increase in risk of overweight and obesity in adult offspring exposed to maternal hypertensive disorders of pregnancy.⁸

Figure 5 Body Mass Index



GLUCOSE METABOLISM

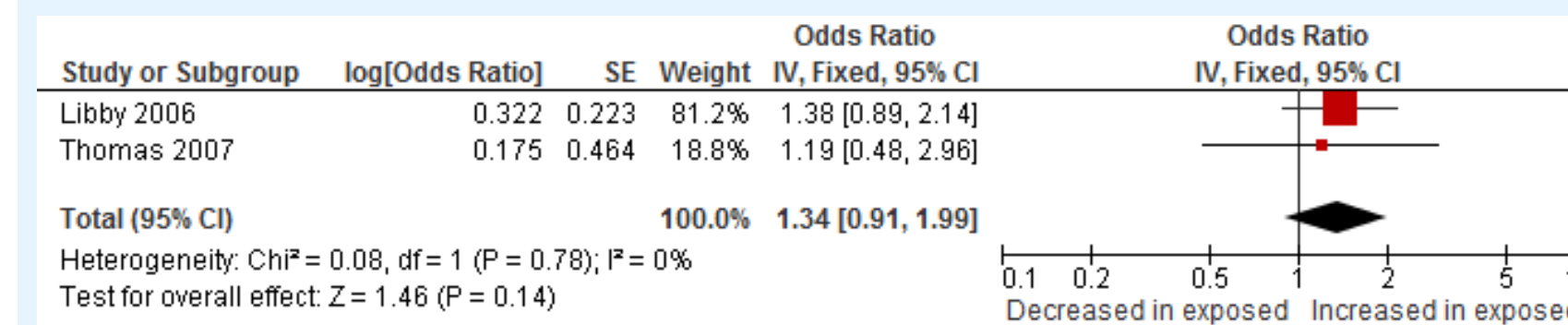
Fasting glucose (one study): No statistically significant differences in adult offspring exposed to maternal hypertensive disorders of pregnancy.⁵

Glycosylated haemoglobin (one study): Statistically significant increase in adult offspring exposed to maternal pre-eclampsia.¹¹

Glycosylated haemoglobin and type 2 diabetes (one study): Statistically significant increase in adult offspring exposed to maternal pre-eclampsia.¹¹

Type 2 diabetes (two studies): Meta-analysis showed no statistically significant increase in risk in adult offspring exposed to maternal hypertensive disorders of pregnancy (fig 6).^{6,11}

Figure 6 Type 2 diabetes



LIPIDS

Total cholesterol (two studies): No evidence of significant differences in adult offspring exposed to maternal hypertensive disorders of pregnancy.^{5,8}

Discussion and conclusion

LIMITATIONS

- A limited number of studies was available.

IMPLICATIONS

- Adult offspring exposed to maternal hypertensive disorders of pregnancy appear to have adverse cardiovascular risk changes.
- This supports the hypothesis that adult offspring exposed to maternal hypertensive disorders in pregnancy have a risk of clinical cardiometabolic events later in life, including hypertension and stroke.

FUTURE AREAS OF RESEARCH

- What is the strength, specificity, timing and attributable risk of any associations so that high-risk individuals can be identified?
- Do such individuals benefit from earlier monitoring and intervention?

This project was funded by NHS Grampian Endowment Funding

References: 1. Roberts JM, Pearson G, Cutler J, Lindheimer M. Summary of the NHLBI working group on research on hypertension during pregnancy. *Hypertension*. 2003;41(3):437-445. 2. Ferreira I, Peeters LL, Stehouwer CDA. Preeclampsia and increased blood pressure in the offspring: Meta-analysis and critical review of the evidence. *J Hypertens*. 2009;27(10):1955-1959. 3. Davis EF, Lazdam M, Lewandowski AJ, et al. Cardiovascular risk factors in children and young adults born to preeclamptic pregnancies: A systematic review. *Pediatrics*. 2012; 129(6):e1552-e1561. 4. Kajantie E, Eriksson JG, Osmond C, Thornburg K, Barker DJ. Pre-eclampsia is associated with increased risk of stroke in the adult offspring: The Helsinki birth cohort study. *Stroke*. 2009;40(4):1176-1180. 5. Lazdam M, De La Horra A, Pitcher A, et al. Elevated blood pressure in offspring born premature to hypertensive pregnancy: Is endothelial dysfunction the underlying vascular mechanism?. *Hypertension*. 2010;56(1):159-165. 6. Libby G, Murphy DJ, McEwan NF, et al. Pre-eclampsia and the later development of type 2 diabetes in mothers and their children: An intergenerational study from the Walker cohort. *Diabetologia*. 2007;50(3):523-530. 7. Mamun AA, Kinarivala MK, O'Callaghan M, Williams G, Najman J, Callaway L. Does hypertensive disorder of pregnancy predict offspring blood pressure at 21 years evidence from a birth cohort study. *J Hum Hypertens*. 2012;26(5):288-294. 8. Mogren I, Hogberg U, Stegmayr B, Lindahl B, Stenlund H. Fetal exposure, heredity and risk indicators for cardiovascular disease in a Swedish welfare cohort. *Int J Epidemiol*. 2001;30(4):853-862. 9. Palmsten K, Buka SL, Michels KB. Maternal pregnancy-related hypertension and risk for hypertension in offspring later in life. *Obstet Gynecol*. 2010;116(4):858-864. 10. Ros HS, Lichtenstein P, Ekblom A, Cnattingius S. Tall or short? twenty years after preeclampsia exposure in utero: Comparisons of final height, body mass index, waist-to-hip ratio, and age at menarche among women, exposed and unexposed to preeclampsia during fetal life. *Pediatr Res*. 2001;49(6):763-769. 11. Thomas C, Hypponen E, Power C. Prenatal exposures and glucose metabolism in adulthood: Are effects mediated through birth weight and adiposity?. *Diabetes Care*. 2007;30(4):918-924.