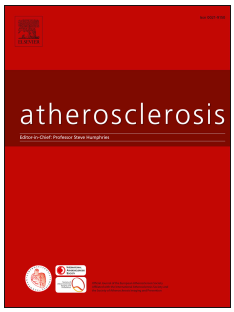

Association of adverse pregnancy outcomes with cardiovascular risk profiles in later life – current insights from the Hamburg City Health Study (HCHS)

Elisabeth Unger, Nataliya Makarova, Katrin Borof, Patricia Schlieker, Carla V. Reinbold, Ghazal Aarabi, Stefan Blankenberg, Christina Magnussen, Christian-Alexander Behrendt, Birgit-Christiane Zyriax, Renate B. Schnabel

PII: S0021-9150(24)01094-3

DOI: https://doi.org/10.1016/j.atherosclerosis.2024.118526

Reference: ATH 118526

To appear in: *Atherosclerosis*

Received Date: 16 November 2023

Revised Date: 9 May 2024

Accepted Date: 18 June 2024

Please cite this article as: Unger E, Makarova N, Borof K, Schlieker P, Reinbold CV, Aarabi G, Blankenberg S, Magnussen C, Behrendt C-A, Zyriax B-C, Schnabel RB, Association of adverse pregnancy outcomes with cardiovascular risk profiles in later life – current insights from the Hamburg City Health Study (HCHS) *Atherosclerosis*, https://doi.org/10.1016/j.atherosclerosis.2024.118526.

Authors' contributions

EU. and N.M. contributed to conceptualization, investigation, methodology, data curation, formal analysis, visualization and writing – original and revised draft. B.C.Z. and R.B.S. contributed to conceptualization, investigation, methodology, project administration, formal analysis, supervision, validation and writing – review & editing. K.B., P.S., C.V.R. and G.A. contributed to data curation, formal analysis, validation, visualization and writing - review & editing. C.A.B. and C.M. contributed to data curation and validation, methodology as well as reviewing and editing. S.B. contributed to project administration, supervision, investigation and methodology.

All listed authors gave final approval and agree to be accountable for all aspects of the presented research work ensuring integrity and accuracy.

Adverse pregnancy outcomes and cardiovascular risk profiles in later life

n=10,000
45-74 years

n= 5,108 women

n=1,970 women reported on pregnancy

Ø 63 years

Hamburg City Health Study

Gestational hypertension (8.7%)

- BMI ↑
- Smoking ↑
- Hypertension ↑
- Septal diameter ↑
- LV-mass index ↑
- Myocardial infarction ↑

Gestational weight gain >20kg (18%)

- BMI ↑
- Smoking ↑
- Left atrial volume index ↓
- Stroke ↑

Gestational diabetes (2.4%)

- Diabetes mellitus ↑

Weight gain >20kg + birth weight >4kg (2.9%)

- Left atrial strain ↓
- Carotid intima-media thickness ↑

Fetal birth weight >4kg (14%)

- BMI ↑
- Hypertension ↑
- Heart rate ↓
- p wave duration ↑
- Mitral E/E‘ ratio ↑
- Carotid intima-media thickness ↑

Fetal birth weight <2.5kg (10%)

- Mitral E/E‘ ratio ↑
- Diastolic Dysfunction ↑
- Carotid intima-media thickness ↓

1) Title page

Association of adverse pregnancy outcomes with cardiovascular risk profiles in later life – current insights from the Hamburg City Health Study (HCHS)

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Target journal: Atherosclerosis
Words: 3988 (excluding the title, author names/affiliations, abstract, keywords, figures/tables and references)
Number of tables: 3
Number of figures: 3
Supplement: 3 tables, 6 figures

Previous Presentation: Part of this work was presented at the Congress of the German Cardiac Society (talk) and the Congress of the European Society of Cardiology 2023 (poster).

2) Abstract

Background and aims

Adverse pregnancy outcomes (APO) have been related to increased cardiovascular (CV) risk and mortality in later life. Underlying pathomechanisms for the development of CV disease in these women are not yet fully understood. In this study, we aimed to investigate the relationship between APO and individual CV risk profiles in later life.

Methods

We used cross-sectional data from 10,000 participants enrolled in the Hamburg City Health Study (HCHS). We analysed self-reported APO, CV risk factors and health status, including biomarkers, electrocardiogram, echocardiography and vascular ultrasound. To examine associations, Wilcoxon rank sum test and Pearson's χ^2-test were performed. Multivariable-adjusted regression models were calculated to determine associations.

Results

N=1,970 women who reported pregnancies were included. Median age was 63 years, 8.7% reported gestational hypertension (gHTN), 18% excessive weight gain and 2.4 % gestational diabetes. Ten percent had delivered newborns with birth weight <2.5 kg, 14% newborns with birth weight >4 kg. In multivariable-adjusted models, significant associations between APO, CV risk profiles and cardiac remodeling were identified. gHTN correlated with higher BMI (Beta 1.68, CI 95% 0.86 – 2.50; p <0.001), hypertension (OR 4.58, CI 95% 2.79 – 7.86; p <0.001), left ventricular remodeling (e.g. left ventricular mass index (Beta 4.46, CI 95% 1.05 – 7.87; p=0.010)) and myocardial infarction (OR 3.27, CI 95% 0.94 – 10.07; p=0.046).

Conclusions

In this population-based sample, APO were associated with CV risk profiles and cardiac remodeling in later life, suggesting early manifestations of future CV risk during pregnancy. Prospective data is needed for individual risk stratification in women with APO.

Words: 248

Keywords: cardiovascular risk profiles; adverse pregnancy outcomes; gestational hypertension; cross-sectional

3) Abbreviations

ABI	Ankle-brachial index
APO	Adverse pregnancy outcomes
CIMT	Carotid intima media thickness
dBP	Diastolic blood pressure
EGWG	Excessive gestational weight gain
gDM	Gestational diabetes mellitus
gHTN	Gestational hypertension
$HbA1_c$	Glycated hemoglobin c
HCHS	Hamburg City Health Study
HDP	Hypertensive disorders of pregnancy
HLP	Hyperlipoproteinaemia
HTN	Hypertension
IVSD	Interventricular septal thickness at end diastole
LAEF	Left atrial ejection fraction
LAS	Left atrial strain
LAVI	Left atrial volume index
LDL-C	Low density lipoprotein cholesterol
LVEF	Left ventricular ejection fraction
LVMI	Left-ventricular mass index
OR	Odds ratio
sBP	Systolic blood pressure
T2DM	Type 2 diabetes mellitus

4) Introduction

Pregnancy is a complex physiological process resulting in significant metabolic and hormonal changes that may have both immediate and long-term effects on the cardiovascular (CV) health of women. [1–3] Data suggest the stagnation of mortality from coronary heart disease in younger and middle-aged women, contrary to the overall global trend, resulting in a growing scientific and clinical focus on the reproductive period for further insights into female cardiovascular risk and chances for preventative action. [4–8] In recent years, there has been a worrying trend towards deteriorating maternal health with rising incidences of gestational hypertension (gHTN) and gestational diabetes (gDM) as well as increasing co-occurrence of multiple adverse pregnancy outcomes [9,10]. The United States have seen a relative increase rate of 78% in gestational diabetes mellitus over a decade, attributed mainly to a sedentary lifestyle, rising (pre)obesity and advanced maternal age - with similar trends in Europe. [9,11–14] In patients with gDM, the risk of developing Type 2 diabetes mellitus is 7-fold increased with high risk for subsequent atherosclerotic cardiovascular disease. [15,16] In the global north, nearly half of all pregnancies are affected by excessive gestational weight gain (>20kg) with higher rates in high-income countries and higher prevalence of classical cardiovascular risk factors such as hypertension and elevated BMI in later life. [17,18] Classical cardiovascular risk factors such as hypertension and higher BMI are more prevalent in women with excessive gestational weight gain, although data is controversial with regard to future maternal cardiovascular health, likewise for women that gave birth to infants with high birth weight. [8,10,19–21] Low fetal birth weight, an important marker for overall maternal and fetal health during pregnancy, was identified as an independent risk factor for future maternal atherosclerotic cardiovascular disease [10,22]. The most common medical disorder during pregnancy, gestational hypertension, affects up to 15% of all pregnant women worldwide.[4] gHTN is a well-established risk factor for chronic hypertension, early left ventricular remodeling, cardiovascular disease, and - even in the absence of chronic hypertension - premature cardiovascular mortality, a cascade often referred to as accelerated cardiovascular ageing. [16–19]

Rationale of the study

Several adverse pregnancy outcomes such as gestational hypertension (gHTN), gestational diabetes (gDM), excessive gestational weight gain (EGWG) or fetal birth weight at the extremes have been identified as potential contributors to maternal cardiovascular risk in later life. [4] Although there is distinct data on echocardiographic changes for women with a history of hypertensive diseases of pregnancy, comparatively little is known on specific clinical or echocardiographic phenotypes for other individual or co-occurring adverse pregnancy outcomes. [24] In our study, we examined women from the general population with a history of adverse pregnancy outcomes (APO) across a broad, radiation-free cardiovascular assessment for phenotyping in later life to facilitate future tailored preventative strategies.

5) Methods

Study design and cohort selection

The Hamburg City Health Study (HCHS) is a large, single-centre, population-based cohort study enrolling participants from the metropolitan region of Hamburg, Germany. It aims to identify risk factors for major chronic diseases and developing risk-prediction models in an older urban cohort. [27] Between 02/2016 and 11/2018, 10,000 random participants aged 45-74 years were included into the study with quality-controlled baseline data available for further analysis. N= 5,108 (51%) were women. 1,970 women reported pregnancies history and therefore met inclusion criteria for this study. 475 reported no history of pregnancy. 2663 women provided no information with respect to their pregnancy history. The local ethics committee of the Landesaerztekammer

Hamburg (Medical Association of Hamburg, PV5131) approved the study protocol and all participants gave informed consent. The study is registered at ClinicalTrial.gov (NCT03934957).

Study proceedings

Upon inclusion, participants underwent a broad baseline assessment at a single dedicated study centre, self-reporting on lifestyle, medical and family history among other items on questionnaires. Routine bloodwork, cardiac biomarkers as well as echocardiography and vascular ultrasound were obtained. For the assessment of medication, study participants were asked to bring a list of prescribed medication at their baseline visit.

A 12-lead electrocardiogram (ECG) was acquired from each participant under resting conditions using eletonic interval durations. Further ECG analyses, i.e. rhythm and atrioventricular conduction, and quality control was conducted by trained physicians. Ankle-brachial-index (ABI) and blood pressure were measured after 5 minutes of rest in a supine position. Blood samples were drawn under fasting conditions. Laboratory measurements included biomarkers such as N-terminal pro-B-type natriuretic peptide (NT-proBNP; immunoassay by Alere NT-proBNP for ARCHITECT, Abbott Diagnostics), glycated hemoglobin (HbA1C) and high-sensitivity Troponin I (Architect i2000, Abbott, Green Oaks, Illinois, USA). Lipid quantification (e.g. total cholesterol) and derived LDL-Cholesterol as estimated by the Friedewald formula were obtained. Diabetes mellitus was defined as the intake of antidiabetic medication, a fasting glucose >126 mg/dL, a non-fasting glucose >200 mg/dL or self-reported diabetes. Hypertension was defined as a resting systolic blood pressure >140 mmHg/ diastolic blood pressure >90 mmHg upon inclusion, use of antihypertensive drugs or self-reported hypertension. Dyslipidaemia was defined as an LDL/HDL ratio of > 3.5 or lipid-lowering medication use.

Reproductive history

In the form of standardized questionnaires, the women reported general information about their reproductive history. With respect to their pregnancy history, the women reported whether they had ever been pregnant and whether they had suffered any adverse maternal or fetal outcomes of past pregnancies that included gestational hypertension, gestational diabetes mellitus without a previous diagnosis of diabetes mellitus, excessive gestational weight gain (defined as a weight gain of >20kg), high (>4kg) and low (<2.5kg) fetal birth weight.

Echocardiography and vascular ultrasound

Participants underwent standardized transthoracic echocardiography performed and interpreted by dedicated research sonographers and trained physicians using state-of-the-art cardiac ultrasound equipment (Siemens Acuson SC2000 Prime, Siemens Healthineers, Erlangen, Germany). Quality control was performed by clinicians blinded to the participants' medical history. We used standardized 2D echocardiographic methods for LV chamber quantification according to international guidelines. [28] Left ventricular and atrial ejection fraction were calculated by Simpson's biplane method of summation of discs. [28] Diastolic function was assessed by pulsed wave Doppler of the mitral inflow (E/A ratio) and tissue Doppler of the septal and lateral mitral annulus (E/E' ratio).[29] Maximum tricuspid regurgitation pressure gradient was calculated using pulse-wave doppler profiles. For strain analyses, a 2D speckle-tracking technique was performed using commercially available software for postprocessing (ACUSON SC2000 Version 4.0, syngo® SC2000 workplace, Siemens Healthineers, Erlangen, Germany), left atrial global peak strain was averaged from the left and right left atrial wall and roof. [30] Biplane left ventricular ejection fraction was not measured in 893 participants due to suboptimal image quality. LA strain was not measured in 1,113 participants due to lack of dedicated imaging or quality.

Vascular ultrasound was conducted using a Siemens SC2000® with a 7.5 MHz linear array transducer. B-Mode sonography was used to measure carotid intima-media thickness (CIMT), values were obtained three times in a

longitudinal view of the left and right common carotid artery >1cm proximal to the carotid bulbus, and mean values were calculated. Plaques were defined as a circumscribed focal thickening of the intima-media > 1.5 mm and measured in the common and proximal internal carotid artery.

Statistical analysis

The participants' baseline characteristics were presented overall and individually for self-reported maternal or fetal complications of pregnancy (**table 1**). Categorical variables were listed as percentages (%), continuous variables as median with interquartile ranges ($25^{th}/75^{th}$ quartile). Aside from descriptive statistics, we carried out Wilcoxon rank sum test and Pearson's χ^2-test to examine associations between APO and cardiovascular risk factors as well as potential indicators of subclinical cardiovascular disease (**table 2**). To determine correlations, we applied regression models adjusted for classical CV risk factors (age, BMI, type II diabetes mellitus, hypertension, dyslipidaemia and smoking (**table 3**)) to complete cases. Of note, when testing for correlations with traditional CV risk factors, the model was adjusted to avoid correcting for the studied risk factor (see **table 3**). A p-value of 0.05 was taken as a standard for significance and confidence intervals set at 95% for the expected range of the true odds ratio. Results were displayed in a Venn' diagram for distribution of APO, boxplots and a graphical abstract (see **figures 1-3**). To account for multiple testing, adjusted p-values were calculated according to Benjamini and Hochberg.[31] A principal component analysis was performed for a better understanding of the underlying variances within the data (see **Supplement figure 6**). Statistical analyses were carried out using R version 4.1.0.

6) Results

Study population

The median age was 63 years. 19% were currently smoking and had dyslipidaemia, 59% had hypertension and 33% metabolic syndrome. Overall, total cholesterol was slightly elevated, Troponin I and NTproBNP were within reference range (see **table 1** for baseline data). The prevalence of adverse pregnancy outcomes is listed in table 2. The most common cardiovascular disease was atrial fibrillation (5.2%), either diagnosed by 12-channel resting ECG upon inclusion or self-reported. 31% of participants used antihypertensive medication. Left ventricular ejection fraction was found to preserved, 16% had diastolic dysfunction. 29% of all participants had carotid stenosis or plaques on vascular ultrasound (36 vs. 28%; p=0.037).

Adverse pregnancy outcomes

Gestational hypertension

When compared with non-hypertensive pregnancies, women with gestational hypertension had higher BMI (27.3 vs. 25.0 kg/m^2, p <0.001), more hypertension (85 vs. 55%.; p <0.001) and dyslipidaemia (27% vs. 18% p=0.006). They were more likely to take antihypertensive or lipid-lowering medication (table 2). Elevated BMI, arterial hypertension and elevated systolic blood pressure upon inclusion were confirmed to be significantly associated with a history of gestational hypertension in our regression model after adjustment for classical CVRF (**table 3**). Biomarkers $HbA1_c$, high-sensitive Troponin I and NTproBNP were elevated in this group when compared to non-hypertensive pregnancies. We found indicators of left ventricular remodeling in this cohort as interventricular septum diameter (IVSD), relative wall thickness (RWT) and left ventricular mass index (LVMI) were elevated and mitral inflow (E/A) was lower. After adjustment, HTN was significantly associated with left ventricular remodeling (IVSD (Beta 0.43 [CI 95% 0.16 – 0.70]; p <0.002) and LVMI (Beta 4.46 [CI 95% 1.05 – 7.87]: p=0.010) in our regression model (see **Supplement table 1** for an additional regression model). LA strain showed a tendency to be lower with borderline statistical significance (41% vs. 38%; p=0.056). P-wave duration on ECG was longer (114

vs. 112ms; p=0.043). With respect to vascular disease, these women had lower ABI (0.99 vs. 1.02; p=0.014) and more often carotid plaques or stenosis (36 vs. 28% vs.; p=0.037).

Gestational diabetes

Women who reported gestational diabetes (n=45; 2.4%) were younger than those with normoglycemic pregnancies. These women had a higher prevalence of diabetes mellitus in later life (33% vs. 5,8%, p <0.001), with higher $HbA1_c$ and more often use of antidiabetic medication (3.1% vs. 20%; p <0.001), however, total cholesterol (203 vs 213mg/dl; p=0.018) and LDL-C (114 vs. 122mg/dl; p=0.084) were lower in this group. Regression models reaffirmed the association of gDM with T2DM in later life (OR 10.82 [CI 95% 4.55 – 25.23]; p <0.001), independent of other classical risk factors. Systolic (122 vs. 134 mmHg; p=0.006) and diastolic (78 vs. 81 mmHg p=0.042) blood pressure was even lower without difference in use of antihypertensive medication. With respect to vascular alterations, ABI was not significantly elevated and carotid intima-media thickness (CIMT; 0.74 vs 0.7mm; p=0.032) was in fact lower.

Excessive gestational weight gain

Women who reported excessive gestational weight gain had higher BMI in later life (28.5 vs. 24.8kg/m^2; p <0.001), higher prevalence of diabetes mellitus (10 vs. 5.8%; p=0.005) and were more likely to smoke at baseline (26 vs. 18%; p <0.001). Regression analyses confirmed an association with higher BMI (Beta 3.57 [CI 95% 2.97 – 4.16]; p <0.001) and higher smoking rates. Surprisingly, total cholesterol was slightly lower (208 vs. 215mg/dl; p<0.037) when compared with women reporting non-excessive gestational weight gain, albeit no evident difference in lipid-lowering medication. Antidiabetic medication intake was more common (6.8 vs 2.9%; p <0.001) without differences in $HbA1_c$. On echocardiography, there were signs of left ventricular remodeling with higher IVSD (9.71 vs. 9.39mm; p=0.003) and LVMI, albeit changes were less pronounced than in women with HDP. Our regression model showed that this cohort was more likely to have a lower left-atrial volume index (Beta -0.66 [CI 95% [-1.32 – 0.00]; p=0.049).

High fetal birth weight

In women reporting elevated fetal birth weight (>4kg) in their offspring, we observed higher BMI (26.1 vs. 25.1 kg/m^2; p=0.003), which was confirmed by regression analysis (Beta 1.22 [CI 95% 0.55 – 1.89]; p <0.001). While there was no difference in use of antihypertensive medication, arterial hypertension was found to be less prevalent (52 vs. 59 %; p=0.044), also represented by the regression model. We also saw slower heart rates (Beta -1.74 [CI 95% 3.48 – 0.00]; p=0.050), longer p-wave durations, lower E/e' and higher carotid intima-media thickness (OR 0.03 [CI 95% 0.01 – 0.04]; p=0.001) in this group. We observed an overlap of women who reported excessive gestational weight gain and high fetal birth weight (2.9%; n=57).

Low fetal birth weight

In women who reported low fetal birth weight (<2.5kg), no significant correlations were found with cardiovascular risk profiles, medication use or biomarkers. On ECG, PQ interval was longer (164 vs. 160ms; p=0.031) and heart rate was slower (64 vs. 66bpm, p=0.019). Lower fetal birth weight was associated with elevated E/e' (Beta 0.69 [CI 95% (0.31 – 1.07)]; p <0.001) and left ventricular diastolic dysfunction in our regression model, as indicated by correlation analyses. In this cohort, carotid intima-media thickness was significantly lower (OR -0.02 [CI 95% -0.04 – 0.00]; p=0.041).

For analyses regarding women that reported both, excessive gestational weight gain and high fetal birth weight, please see **supplement table 2.** In this group, we found carotid intima-media thickness to be higher (Beta 0.05 (95% CI 0.01 – 0.08); p=0.006) and LA strain to be reduced (Beta -9.79(95% CI -17.69 – -1.89); p=0.015).

With respect to manifest cardiovascular disease, a history of gHTN correlated with myocardial infarction in later life, while excessive gestational weight gain was significantly associated with stroke in our cohort (**table 3 and supplement table 3**). Adjusted p-values according to Benjamini-Hochberg are shown in **supplement table 4 &5.**

7) Discussion

Our cross-sectional observational study of women with a history of pregnancy from an urban European population had three main findings:

1) Reported adverse pregnancy outcomes were associated with overall higher burden of classical cardiovascular risk factors, subclinical and manifest cardiovascular disease in later life;
2) APO were associated with echocardiographic evidence of cardiac remodeling and
3) we found heterogenous phenotypes of risk profiles and (sub)clinical cardiovascular disease in women with APO (see figure 1 graphical abstract).

We observed a complex picture of risk constellations and cardiovascular changes in later life among women with different APO. The identified prevalence of gestational hypertension in this cohort (8.7%) was within the range of 6-15% as reported by previous studies. Gestational hypertension was associated with left ventricular remodeling with early signs of concentric hypertrophy independent of classical CV risk factors in accordance with previously published data. Previous analyses suggested that gestational hypertension itself mediates left-ventricular remodeling and its progression to cardiovascular disease and heart failure, which is common in women with a history of gHTN in later life. [32] Left atrial involvement as an early manifestation of diastolic dysfunction was suggested by a mild tendency towards lower LA strain when comparing gHTN to normotensive pregnancies. LA strain is an emerging indicator of LA stiffness and dysfunction when other established parameters are not yet altered. [33] LA strain measurements are independent of structural or volume-dependent alterations of other heart chambers or valves, contrary to surrogates for left ventricular filling pressures such as E/A or E/e'; hence, strain was proposed as an additional parameter for quantification of diastolic dysfunction. [34] However, in our cohort, only 44% of images were eligible for strain analyses due to suboptimal image quality or lack of images which may have weakened the aforementioned correlations, while conventional surrogate parameters for atrial dysfunction were still normal, supposedly due to an early stage of disease. A correlation between gestational hypertension and carotid plaques or stenosis was not confirmed by regression analyses corrected for classical CV risk, potentially due to sample size. Carotid artery disease, being highly prevalent in the population sample and worldwide, was found to be more pronounced in women with a history of preeclampsia/eclampsia in previous studies, entities that may be underreported in this population sample. [17, 34–36] All in all, our data supports the hypothesis of accelerated cardiovascular aging among women with gestational hypertension as our findings of LV remodeling were distinct and independent of classical cardiovascular risk factors in later life. [4,26,39]

The results for women who reported gestational diabetes were less pronounced than estimated. Prevalence of gDM was lower in our cohort than commonly reported in epidemiological studies suggesting potentially undetected gDM among our participants. [11,13,14] This hypothesis is supported by the fact that this subgroup was younger than the general cohort (58 years (25th,75th quartile 52,66) vs. 63 years (56,70)), indicating false-negatives and underappreciation of the disease in pregnancies before that time. Supposedly, a number of pregnancies took place 4 or even 5 decades ago in the absence of a routine screening for gDM, which was

established in Germany in 2012. [11,15] Some authors described an increase of 75% in prevalence of gDM when applying modern diagnostic criteria, which may have strengthened our analyses. [11]

The picture of general health in women with gestational weight gain >20kg was heterogeneous. In our regression model, EGWG was associated with elevated BMI and smoking in later life. This may indicate a clustering of unhealthy behaviours or the potential use of smoking as weight control. [40] A previously described association with arterial hypertension and dyslipidaemia could not be confirmed in this cohort. [20] We hypothesize that women with elevated BMI, an overt cardiovascular risk factor easily to diagnose, are potentially being selected for preventative and therapeutic measures more alertly, e.g. treatment of diabetes mellitus with beneficial effects on lipid status and blood pressure. Regression analyses of echocardiographic data showed a correlation with lower left atrial volume index; in this cohort, normal or indeed altered atrial volumes may be masked due to a systemic underestimation of left atrial enlargement when indexing the left atrium to body surface area in (pre)obese individuals. [41]

Women reporting high fetal birth weight were more likely to develop higher BMI while being less prone to arterial hypertension or type II diabetes mellitus while displaying slower heart rate (HR), longer p-wave durations and lower E/e' on echocardiography. P-wave durations >120ms correlates with myocardial fibrosis, atrial fibrillation, and cardiac death, assuming (electrical) left atrial impairment, so that our findings may herald early signs of atrial cardiomyopathy in this group in the absence of elevated estimated left ventricular filling pressures.[42] Low fetal birth weight was related to remodeling that affected primarily left ventricular diastolic function (e.g. higher E/e', diastolic dysfunction). Carotid artery disease was not more common among these subjects, suggesting a primary affection of smaller vascular beds (e.g. coronary microvascular dysfunction) or processes such as underlying myocardial fibrosis. [43]

To identify individual risk constellations, we investigated the reporting of more than one APO. Aside from an overlap of excessive gestational weight gain and elevated fetal birth weight, we found no clustering suitable for further statistical analyses, potentially due to sample size. Reporting both APO was associated with indicators of subclinical carotid artery disease and atrial cardiomyopathy. The presence of multiple APO has previously been shown to contribute to a higher risk for atherosclerotic cardiovascular disease, as they may share an underlying pathomechanism; therefore, taking a dedicated reproductive history is an imperative consideration when assessing CV risk in females later life. [10] The timing for preventative intervention remains challenging in these women. The concept of a fourth trimester after women experienced adverse pregnancy outcomes was proposed to create a window for awareness of cardiovascular risk in these women and facilitate the transition into a systematic preventative follow-up. [44–46] Preliminary data showed that an even stronger link between obstetrics and preventative medicine is required for optimal patient education for women with adverse pregnancy outcomes. [47] Clarifying the potentially severe implications for future CV risk profiles and disease to patients based on their pregnancy history may facilitate the transition to preventative medical counselling postpartum and awareness for female cardiovascular disease in later life.

Limitations

The participants of the HCHS represent a middle-aged, largely urban population sample in the metropolitan region of Hamburg in northern Germany. Lifestyles as well as the accessibility of healthcare and preventive programmes vary considerably in the urban vs. the rural setting and these disparities may lead to a lack of generalizability of the data presented here. The cross-sectional nature of the analyses does not allow deduction of causalities with respect to the observed associations. However, our current findings will be the basis for future

studies. Overall, the data presented here has to be regarded as hypothesis-generating. Moreover, reduced power of this study due to sample size may have hindered the identification of smaller, previously described associations, e.g. for gestational diabetes. Suboptimal image quality limited echocardiographic data availability (e.g. 30% missingness of E/e'). Our data is partially based on self-reported health status and APO from questionnaires, which may be prone to recall bias. Although the questionnaires did not systematically obtain information about number, duration, further outcomes (e.g. resulting in a live birth) or point in time of previous pregnancies, we can assume that the reported complications of pregnancy occurred decades ago with different diagnostic algorithms and definitions of diseases. Current definitions of APO, especially gestational hypertension and diabetes, might have resulted in a higher prevalence and potentially stronger associations. On the other hand, the clearly limited and potentially biased information on questionnaires may be regarded as representative of obtaining a patient history during consultations with healthcare providers and could therefore represent a contemporary real-world setting.

8) Conclusions

In this study, we found that a history of adverse pregnancy outcomes was common among urban females between 45-74 years. These women had a higher burden of classical cardiovascular risk factors, subclinical and manifest cardiovascular disease in later life, indicating early manifestation during pregnancy. Depending on the reported previous adverse pregnancy outcome, we found miscellaneous clinical phenotypes of risk patterns and disease. Including questions about complications of pregnancy while history-taking may lead to the detection of less-overt individual risk constellations in women in later life. Ultimately, a history of adverse pregnancy outcomes may be relevant for personalized risk assessment, individualised preventative strategies and timing of potential therapeutic interventions to prevent hard cardiovascular outcomes in women in later life. This hypothesis, however, needs to be tested in future, prospective research.

Highlights

- A history of previous adverse pregnancy outcomes was a common finding in a middle-aged urban female population
- Women with APO had more pronounced CV risk profiles and disease, possibly triggered or aggravated during pregnancy
- A history of gestational hypertension was associated with left ventricular remodeling and myocardial infarction
- Weight gain>20kg and birth weight>4kg corelated with lower left-atrial strain and higher carotid intima-media thickness
- A history of APO may indicate women in a community at increased risk of adverse cardiovascular outcomes in later life

9) Conflicts of interest and financial support

All participating institutes and departments from the University Medical Center Hamburg-Eppendorf contribute with scaled budgets to the overall funding of the Hamburg City Health Study (HCHS). Moreover, HCHS has received funding from the Innovative medicine initiative (IMI) under Grant No. 116074 (European public-private-partnership), Fondation Leducq (Grant Number 16 CVD 03), euCanSHare (Grant Agreement No. 825903-euCanSHare H2020) and the Deutsche Forschungsgemeinschaft (DFG project Grant TH1106/5-1; AA93/2-1). The HCHS is further supported by Joachim Herz Foundation; Deutsche Gesetzliche Unfallversicherung (DGUV); Deutsches Krebsforschungszentrum (DKFZ); Deutsches Zentrum für Herz-Kreislauf-Forschung (DZHK); Deutsche Stiftung für Herzforschung; Seefried Stiftung; Bayer; Amgen, Novartis; Schiller; Siemens; Topcon, Unilever and by

donations from the "Förderverein zur Förderung der HCHS e.V.", and TePe® (2014). Sponsor funding has in no way influenced the content, conclusions or management of this study.
E.U., K.B., G.A. and C.A.B. have not received any project related funding.
N.M. reports personal fees from Abbott Laboratories, outside the submitted work.
CM receives study-specific funding from the German Center for Cardiovascular Research (DZHK; Promotion of women scientists' programme; *FKZ 81X3710112*), the *Deutsche Stiftung für Herzforschung*, the *Dr. Rolf M. Schwiete Stiftung*, NDD, and Loewenstein *Medical* unrelated to the current work. CM has received speaker fees from AstraZeneca, Novartis, Boehringer Ingelheim/Lilly, Bayer, Pfizer, Sanofi, Aventis, Apontis, Abbott outside this work. CM has participated in a Boehringer Ingelheim heart failure advisory board.
S.B. is supported by the Innovative medicine initiative (IMI) under Grant No. 116074, the Fondation Leducq under Grant Number 16 CVD 03, Siemens, Bayer, Astra Zeneca, Deutsche Gesetzliche Unfallversicherung (DGUV) and Novartis for project related analyses.
B.C.Z. has received an unrestricted project-related funding from BASF and Unilever for implementing a food frequency questionnaire into the interviews of the Hamburg City Health Study and reports fees from Jenapharm GmbH and BESINS Heathcare for lectures outside this work.
R.B.S has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme under the grant agreement No 648131, from the European Union's Horizon 2020 research and innovation programme under the grant agreement No 847770 (AFFECT-EU) and German Center for Cardiovascular Research (DZHK e.V.) (81Z1710103 and 81Z0710114); German Ministry of Research and Education (BMBF 01ZX1408A) and ERACoSysMed3 (031L0239). Wolfgang Seefried project funding German Heart Foundation. R.B.S has received lecture fees and advisory board fees from BMS/Pfizer and Bayer outside this work.
E.U., N.M., K.B., P.S., C.V.R, G.A, C.M., C.A.B, S.B, B.C.Z. and R.B.S. report no conflicts of interest.

10) Authors' contributions

EU. and N.M. contributed to conceptualization, investigation, methodology, data curation, formal analysis, visualization and writing – original and revised draft. B.C.Z. and R.B.S. contributed to conceptualization, investigation, methodology, project administration, formal analysis, supervision, validation and writing – review & editing. K.B., P.S., C.V.R. and G.A. contributed to data curation, formal analysis, validation, visualization and writing - review & editing. C.A.B. and C.M. contributed to data curation and validation, methodology as well as reviewing and editing. S.B. contributed to project administration, supervision, investigation and methodology. All listed authors gave final approval and agree to be accountable for all aspects of the presented research work ensuring integrity and accuracy.

Availability of data statement

The data underlying this article are available in the article and in its online supplementary material.

11) Acknowledgements

The authors are obliged to all participants in the Hamburg City Health Study, cooperating institutes, partners, patrons and the Deanery of the University Medical Center Hamburg-Eppendorf for supporting the HCHS. We acknowledge the vital contribution of the scientific staff at the Population Health Research Department for the conduction of the study and thank them for their efforts. The publication has been approved by the Steering Board of the Hamburg City Health Study.

12) References

1. Sattar N, Greer IA. Pregnancy complications and maternal cardiovascular risk: opportunities for intervention and screening? *BMJ* 2002;**325**:157–60.

2. Neiger R. Long-Term Effects of Pregnancy Complications on Maternal Health: A Review. *J Clin Med* 2017;**6**, DOI: 10.3390/JCM6080076.
3. Wang MC, Freaney PM, Perak AM *et al.* Association of pre-pregnancy cardiovascular risk factor burden with adverse maternal and offspring outcomes. *Eur J Prev Cardiol* 2022;**29**:E156–8.
4. O'Kelly AC, Michos ED, Shufelt CL *et al.* Pregnancy and Reproductive Risk Factors for Cardiovascular Disease in Women. *Circ Res* 2022;**130**:652–72.
5. Virani SS, Alonso A, Aparicio HJ *et al.* Heart Disease and Stroke Statistics - 2021 Update: A Report From the American Heart Association. *Circulation* 2021;**143**:E254–743.
6. Wilmot KA, O'Flaherty M, Capewell S *et al.* Coronary heart disease mortality declines in the United States from 1979 through 2011: Evidence for stagnation in young adults, especially women. *Circulation* 2015;**132**:997–1002.
7. Garcia M, Mulvagh SL, Merz CNB *et al.* Cardiovascular disease in women: Clinical perspectives. *Circ Res* 2016;**118**:1273–93.
8. Bonamy AKE, Parikh NI, Cnattingius S *et al.* Birth characteristics and subsequent risks of maternal cardiovascular disease: Effects of gestational age and fetal growth. *Circulation* 2011;**124**:2839–46.
9. Venkatesh KK, Lynch CD, Powe CE *et al.* Risk of Adverse Pregnancy Outcomes Among Pregnant Individuals With Gestational Diabetes by Race and Ethnicity in the United States, 2014-2020. *JAMA* 2022;**327**:1356–67.
10. Søndergaard MM, Hlatky MA, Stefanick ML *et al.* Association of Adverse Pregnancy Outcomes With Risk of Atherosclerotic Cardiovascular Disease in Postmenopausal Women. *JAMA Cardiol* 2020;**5**:1390–8.
11. Saeedi M, Cao Y, Fadl H *et al.* Increasing prevalence of gestational diabetes mellitus when implementing the IADPSG criteria: A systematic review and meta-analysis. *Diabetes Res Clin Pract* 2021;**172**:108642.
12. Cameron NA, Petito LC, Shah NS *et al.* Association of Birth Year of Pregnant Individuals With Trends in Hypertensive Disorders of Pregnancy in the United States, 1995-2019. *JAMA Netw Open* 2022;**5**:e2228093–e2228093.
13. Zhou T, Du S, Sun D *et al.* Prevalence and Trends in Gestational Diabetes Mellitus Among Women in the United States, 2006–2017: A Population-Based Study. *Front Endocrinol (Lausanne)* 2022;**13**:868094.
14. Reitzle L, Schmidt C, Heidemann C *et al.* Gestational diabetes in Germany: Development of screening participation and prevalence. *Journal of Health Monitoring* 2021;**6**:3–18.
15. Vrachnis N, Augoulea A, Iliodromiti Z *et al.* Previous gestational diabetes mellitus and markers of cardiovascular risk. *Int J Endocrinol* 2012;**2012**, DOI: 10.1155/2012/458610.
16. Bellamy L, Casas JP, Hingorani AD *et al.* Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *The Lancet* 2009;**373**:1773–9.
17. Deputy NP, Sharma AJ, Kim SY *et al.* Prevalence and Characteristics Associated With Gestational Weight Gain Adequacy. *Obstetrics and gynecology* 2015;**125**:773.
18. Santos S, Voerman E, Amiano P *et al.* Impact of maternal body mass index and gestational weight gain on pregnancy complications: an individual participant data meta-analysis of European, North American and Australian cohorts. *BJOG* 2019;**126**:984–95.
19. Hutchins F, El Khoudary SR, Catov J *et al.* Excessive Gestational Weight Gain and Long-Term Maternal Cardiovascular Risk Profile: The Study of Women's Health Across the Nation. *J Womens Health* 2022;**31**:808–18.
20. Holland ML, Groth SW, Kitzman HJ. Gestational Weight Gain and Health Outcomes 18 Years Later in Urban Black Women. *Matern Child Health J* 2015;**19**:2261.

21. Li CY, Chen HF, Sung FC *et al.* Offspring birth weight and parental cardiovascular mortality. *Int J Epidemiol* 2010;**39**:1082–90.
22. Rich-Edwards JW, Fraser A, Lawlor DA *et al.* Pregnancy Characteristics and Women's Future Cardiovascular Health: An Underused Opportunity to Improve Women's Health? *Epidemiol Rev* 2014;**36**:57–70.
23. Boucheron P, Lailler G, Moutengou E *et al.* Hypertensive disorders of pregnancy and onset of chronic hypertension in France: the nationwide CONCEPTION study. *Eur Heart J* 2021, DOI: 10.1093/EURHEARTJ/EHAB686.
24. Countouris ME, Villanueva FS, Berlacher KL *et al.* Association of Hypertensive Disorders of Pregnancy With Left Ventricular Remodeling Later in Life. *J Am Coll Cardiol* 2021;**77**:1057–68.
25. Wang YX, Arvizu M, Rich-Edwards JW *et al.* Hypertensive Disorders of Pregnancy and Subsequent Risk of Premature Mortality. *J Am Coll Cardiol* 2021;**77**:1302–12.
26. Honigberg MC, Zekavat SM, Aragam K *et al.* Long-Term Cardiovascular Risk in Women With Hypertension During Pregnancy. *J Am Coll Cardiol* 2019;**74**:2743–54.
27. Jagodzinski A, Johansen C, Koch-Gromus U *et al.* Rationale and Design of the Hamburg City Health Study. *Eur J Epidemiol* 2020;**35**:169–81.
28. Lang RM, Badano LP, Victor MA *et al.* Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Journal of the American Society of Echocardiography* 2015;**28**:1-39.e14.
29. Nagueh SF, Smiseth OA, Appleton CP *et al.* Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Journal of the American Society of Echocardiography* 2016;**29**:277–314.
30. Badano LP, Kolias TJ, Muraru D *et al.* Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *Eur Heart J Cardiovasc Imaging* 2018;**19**:591–600.
31. Jafari M, Ansari-Pour N. Why, when and how to adjust your P values? *Cell J* 2019;**20**:604–7.
32. Mantel Ä, Sandström A, Faxén J *et al.* Pregnancy-Induced Hypertensive Disorder and Risks of Future Ischemic and Nonischemic Heart Failure. *Heart Fail* 2023;**11**:1216–28.
33. Mandoli GE, Sisti N, Mondillo S *et al.* Left atrial strain in left ventricular diastolic dysfunction: have we finally found the missing piece of the puzzle? *Heart Fail Rev* 2020;**25**:409–17.
34. Frydas A, Morris DA, Belyavskiy E *et al.* Left atrial strain as sensitive marker of left ventricular diastolic dysfunction in heart failure. *ESC Heart Fail* 2020;**7**:1956.
35. Countouris ME, Villanueva FS, Berlacher KL *et al.* Association of Hypertensive Disorders of Pregnancy With Left Ventricular Remodeling Later in Life. *J Am Coll Cardiol* 2021;**77**:1057–68.
36. Bokslag A, Franssen C, Alma LJ *et al.* Early-onset preeclampsia predisposes to preclinical diastolic left ventricular dysfunction in the fifth decade of life: An observational study. *PLoS One* 2018;**13**:e0198908.
37. Garovic VD, Milic NM, Weissgerber TL *et al.* Carotid Artery Intima-Media Thickness and Subclinical Atherosclerosis in Women With Remote Histories of Preeclampsia: Results From a Rochester Epidemiology Project-Based Study and Meta-analysis. *Mayo Clin Proc* 2017;**92**:1328–40.
38. Behrendt CA, Thomalla G, Rimmele DL *et al.* Editor's Choice - Prevalence of Peripheral Arterial Disease, Abdominal Aortic Aneurysm, and Risk Factors in the Hamburg City Health Study: A Cross Sectional Analysis. *Eur J Vasc Endovasc Surg* 2023;**65**:590–8.

552 39. Michael C. Honigberg MM, Jowell AR. Accelerated Coronary Atherosclerosis After Preeclampsia:
553 Seeing Is Believing∗. *J Am Coll Cardiol* 2022;**79**:2322–4.
554 40. Wee CC, Rigotti NA, Davis RB *et al.* Relationship Between Smoking and Weight Control Efforts
555 Among Adults in the United States. *Arch Intern Med* 2001;**161**:546–50.
556 41. Azzari F, Krsticevic L, Dionne N *et al.* Evaluation of left atrial volume in obesity. How indexation by
557 body surface compares to indexation by height. *Eur Heart J Cardiovasc Imaging* 2021;**22**, DOI:
558 10.1093/EHJCI/JEAA356.014.
559 42. Kabutoya T, Kario K. P-wave changes as an index of hypertensive organ damage and a predictor of
560 cardiovascular events: can the P wave be used to assess atrial reverse remodeling? *Hypertension*
561 *Research 2022 45:8* 2022;**45**:1400–3.
562 43. Hong D, Lee SH, Shin D *et al.* Prognostic Impact of Cardiac Diastolic Function and Coronary
563 Microvascular Function on Cardiovascular Death. *J Am Heart Assoc* 2023;**12**:27690.
564 44. Newstead J, von Dadelszen P, Magee LA. Preeclampsia and future cardiovascular risk. *Expert Rev*
565 *Cardiovasc Ther* 2007;**5**:283–94.
566 45. Parsonage WA, Zentner D, Lust K *et al.* Heart Disease and Pregnancy: The Need for a Twenty-First
567 Century Approach to Care. *Heart Lung Circ* 2021;**30**:45–51.
568 46. McIntyre HD, Kapur A, Divakar H *et al.* Gestational Diabetes Mellitus-Innovative Approach to
569 Prediction, Diagnosis, Management, and Prevention of Future NCD-Mother and Offspring. *Front*
570 *Endocrinol (Lausanne)* 2020;**11**, DOI: 10.3389/FENDO.2020.614533.
571 47. Chan SE, Nowik CM, Pudwell J *et al.* Standardized Postpartum Follow-Up for Women with
572 Pregnancy Complications: Barriers to Access and Perceptions of Maternal Cardiovascular Risk. *J Obstet*
573 *Gynaecol Can* 2021;**43**:746–55.
574
575 **13) Figure legends**

576 Table 1: Clinical baseline characteristics, electrocardiographic, echocardiographic and vascular ultrasound data;
577 Median (25^{th}/75^{th} quartile) for continuous, n (%) for categorical variables; *Smoking:* current smoking upon
578 inclusion*; HbA*1_c: Glycated hemoglobin A1c; NTproBNP: N-terminal prohormone of brain natriuretic peptide;
579 ACEi: Angiotensin-converting-enzyme inhibitors; ARI: Angiotensin-receptor inhibitors; TR PGmax: maximum
580 tricuspid regurgitation pressure gradient
581
582 Table 2: Baseline characteristics of women in our cohort with adverse pregnancy outcomes vs. those without.
583 Median (25^{th}/75^{th} quartile) for continuous, n (%) for categorical variables. Pearson's χ^2-test /Wilcoxon rank sum
584 test **| Bold font: p <0.05**; *Smoking:* current smoking upon inclusion*; sBP*: systolic blood pressure; *dBP*: diastolic
585 blood pressure; BMI: Body-mass index; $HbA1_c$: Glycated hemoglobin A1c: LDL-C: Low-density lipoprotein
586 cholesterol; NTproBNP: N-terminal prohormone of brain natriuretic peptide; LVEF [%]: Left ventricular ejection
587 fraction; IVSD [mm]: Interventricular septal end diastole; RWT: relative wall thickness (2x posterior wall
588 thicknes/ left ventricular diastolic diameter; LVMI [g/m^2]: left-ventricular mass index (Left ventricular
589 mass/Body Surface Area); LAVI [mL/m^2]: left atrial volume index (Left atrial volume/Body Surface Area); LAEF
590 [%]: left atrial ejection fraction; LA strain [%]: left atrial strain; ABI: Ankle-brachial index; CIMT[mm]: Carotid
591 intima-media thickness
592 Table 3: Demographic characteristics and electrocardiographic, echocardiographic and vascular parameters in
593 women with adverse pregnancy outcomes gestational hypertension, gestational diabetes, excessive gestational
594 weight gain, high (>4kg) and low (<2.5kg) fetal birth weight vs. in those without APO– multivariate regression
595 models; †: adjusted for age, type II diabetes mellitus, hypertension, dyslipidaemia, smoking | **Bold font: p**
596 **<0.05**; BP_{sys}: systolic blood pressure; BP_{dia}: diastolic blood pressure; Body mass index (weight/$height^2$); $HbA1_c$:
597 Glycated hemoglobin A1c: LDL-C: Low-density lipoprotein cholesterol; NTproBNP: N-terminal prohormone of
598 brain natriuretic peptide; IVSD [mm]: Interventricular septal thickness at end diastole; Relative Wall Thickness
599 (2x posterior wall thicknes/ left ventricular diastolic diameter); LVMI [g/m^2]: left-ventricular mass index (Left

ventricular mass/Body Surface Area); LAVI [mL/m^2]: Left atrial volume index (Left atrial volume/Body Surface Area); ABI: Ankle-brachial index; CIMT[mm]: Carotid intima-media thickness

Figure 1: Graphical abstract - Correlations of adverse pregnancy outcomes with cardiovascular risk profiles and manifest disease in later life determined by a multivariable regression model ($p < 0.05$)

Figure 2: Overlapping adverse pregnancy outcomes; n=57 women reported both, elevated fetal birth weight and excessive gestational weight gain (Venn diagram)

Figure 3: Women with a history of gestational hypertension and indicators of left-ventricular remodeling: left ventricular mass index (LVMI; g/m^2) and interventricular septum end-diastole (IVSD; mm); Box plots

14) Figures and Tables

Baseline characteristics	**n=1,970**
Age [yrs]	63.0 (56.0,70.0)
Female	1,970 (100%)
Education	
medium	1,119 (58%)
higher	665 (35%)
Body mass index [kg/m^2]	25.3 (22.7,28.8)
Current Smoking	377 (19%)
Hypertension	1,133 (59%)
Blood $pressure_{sys}$ [mmHg]	133.5 (121.0,147.0)
Blood $pressure_{dias}$ [mmHg]	80.5 (74.5,87.0)
Metabolic syndrome	600 (33%)
Diabetes	127 (6.8%)
Dyslipidaemia	361 (19%)
$HbA1_c$ [%]	5.5 (5.3,5.8)
Total cholesterol [mg/dl]	213.0 (188.0,241.0)
LDL cholesterol [mg/dl]	122.0 (98.0,146.0)
Troponin I [pg/ml]	1.7 (1.1,2.6)
NTproBNP [pg/ml]	93.0 (56.0,158.0)
Medication	
Antihypertensive medication	603 (31%)
ACEi and ARI	370 (19%)
Calcium channel blocker	128 (6.6%)
Beta blockers	310 (16%)
Diuretics	46 (2.4%)
Oral antidiabetics	72 (3.7%)
Lipid lowering medication	282 (15%)
Antithrombotic medication	222 (12%)
Complications of pregnancy	
Gestational hypertension	158 (8.7%)
Gestational diabetes mellitus	45 (2.4%)
Excessive gestational weight gain [>20 kg]	332 (18%)

High fetal birth weight [>4000 g]	258 (14%)
Low fetal birth weight [<2500 g]	190 (10%)
Excessive weight gain & high fetal birth weight	57 (2.9%)
History of cardiovascular disease	
Myocardial infarction	25 (1.3%)
Stroke	58 (3.0%)
Heart Failure	75 (3.8%)
Atrial fibrillation	96 (5.2%)
ECG parameters	
Heart rate [bpm]	66.0 (59.0,73.0)
RR interval [ms]	910.0 (818.0,1,011.0)
PQ interval [ms]	160.0 (146.0,176.0)
P duration [ms]	112.0 (104.0,122.0)
QRS duration [ms]	90.0 (84.0,96.0)
QT_c (Bazett) [ms]	424.0 (411.0,438.0)
Echocardiography	
Left ventricular ejection fraction [%]	59.6 (56.6,62.9)
Interventricular septum thickness [mm]	9.4 (8.6,10.4)
Relative wall thickness	0.4 (0.3,0.4)
Left ventricular mass [g]	134.7 (116.4,156.5)
Left ventricular mass index (LVMI) [g/m^2]	76.6 (67.3,87.9)
E/A	0.9 (0.8,1.2)
E/e' mean	7.5 (6.4,8.9)
TR PGmax [mmHg]	21.8 (19.5,25.6)
Diastolic Dysfunction	197 (16%)
Left atrial volume index (LAVI) [mL/m^2]	26.2 (24.5,28.0)
Left atrial ejection fraction [%]	46.8 (38.9,52.7)
Left atrial strain [%]	40.4 (31.8,51.5)
Vascular parameters	
Ankle-brachial index mean	1.0 (0.9,1.1)
Carotid intima-media thickness [mm]	0.7 (0.7,0.8)
Carotid plaques/stenosis	549 (29%)
Right carotid plaque	394 (21%)

Table 1: Clinical baseline characteristics, electrocardiographic, echocardiographic and vascular ultrasound data; Median ($25^{th}/75^{th}$ quartile) for continuous, n (%) for categorical variables; *Smoking:* current smoking upon inclusion; $HbA1_c$: Glycated hemoglobin A1c; NTproBNP: N-terminal prohormone of brain natriuretic peptide; ACEi: Angiotensin-converting-enzyme inhibitors; ARI: Angiotensin-receptor inhibitors; TR PGmax: maximum tricuspid regurgitation pressure gradient

Characteristic	Gestational hypertension	p-value	Gestational diabetes	p-value	Excessive gestational weight gain	p-value	High fetal birth weight	p-value	Low fetal birth weight	p-value
BMI [kg/m2]	**27.3 (23.9, 32.8)**	**<0.001**	24.8 (23.3, 30.3)	0.7	**28.5 (24.8, 33.6)**	**<0.001**	**26.1 (23.2, 29.9)**	**0.003**	25.3 (22.6, 28.2)	0.5
Diabetes	15 (9.9%)	0.07	**14 (33%)**	**<0.001**	**31 (10%)**	**0.005**	16 (6.7%)	>0.9	14 (7.7%)	0.6
Current smoking	27 (17%)	0.5	8 (18%)	0.8	**85 (26%)**	**<0.001**	50 (20%)	0.8	42 (22%)	0.2
Hypertension	**133 (85%)**	**<0.001**	20 (45%)	0.082	201 (61%)	0.2	**131 (52%)**	**0.04**	109 (59%)	>0.9
Dyslipidaemia	**41 (27%)**	**0.006**	9 (21%)	0.7	63 (21%)	0.5	49 (20%)	0.4	35 (19%)	0.8
sBP ***[mmHg]***	**138 (127, 152)**	**<0.001**	**122 (117, 138)**	**0.006**	132 (121, 146)	0.3	**130 (120, 144)**	**0.02**	134 (121, 148)	0.4
dBP ***[mmHg]***	**82 (77, 88)**	**0.023**	**78 (73, 83)**	**0.042**	81 (75, 87)	0.5	**79 (73, 86)**	**0.017**	81 (74, 86)	0.5
HbA1c [%]	**5.60 (5.30, 5.90)**	**0.006**	**5.70 (5.32, 6.50)**	**0.004**	5.50 (5.30, 5.80)	0.5	5.50 (5.30, 5.80)	0.4	5.50 (5.20, 5.70)	0.14
Total cholesterol [mg/dl]	208 (183, 240)	0.2	**203 (179, 220)**	**0.018**	**208 (183, 240)**	**0.037**	214 (185, 238)	0.7	209 (185, 239)	0.3
LDL-C [mg/dl]	120 (98, 145)	0.7	114 (101, 135)	0.084	119 (98, 147)	0.6	122 (98, 145)	>0.9	116 (94, 142)	0.075
Troponin I [pg/ml]	**2.00 (1.40, 3.10)**	**<0.001**	1.70 (1.10, 2.70)	0.6	1.80 (1.20, 2.50)	0.2	1.70 (1.20, 2.50)	0.7	1.70 (1.20, 2.55)	>0.9
NTproBNP [pg/ml]	**104 (61, 194)**	**0.023**	74 (56, 114)	0.10	89 (51, 148)	0.2	89 (54, 151)	0.8	87 (58, 193)	0.8
Medication										
Antihypertensive	**94 (60%)**	**<0.001**	13 (29%)	0.7	111 (34%)	0.10	76 (30%)	0.8	61 (33%)	0.6
Antidiabetic	8 (5.1%)	0.2	**9 (20%)**	**<0.001**	**22 (6.8%)**	**<0.001**	9 (3.6%)	>0.9	8 (4.3%)	0.6
Lipid lowering	**32 (20%)**	**0.024**	9 (20%)	0.3	46 (14%)	>0.9	38 (15%)	0.6	26 (14%)	>0.9
ECG										
Heart rate [bpm]	67 (60, 74)	0.2	66 (60, 70)	>0.9	66 (59, 75)	0.7	66 (59, 73)	0.4	**64 (57, 72)**	**0.019**
RR interval [ms]	894 (810, 1,004)	0.2	909 (854, 1,008)	>0.9	912 (804, 1,022)	0.7	914 (824, 1,017)	0.4	**940 (837, 1,059)**	**0.019**
PQ interval [ms]	162 (146, 178)	0.5	158 (148, 178)	0.8	158 (146, 174)	0.7	163 (148, 180)	0.07	**164 (148, 180)**	**0.031**
P duration [ms]	**114 (106, 126)**	**0.043**	110 (102, 122)	0.4	112 (104, 124)	0.4	**114 (106, 124)**	**0.014**	114 (106, 124)	0.2
QRS duration [ms]	90 (84, 96)	>0.9	92 (80, 98)	0.8	90 (84, 96)	0.3	90 (84, 96)	>0.9	90 (84, 96)	0.3
$QT_{cBazett}$ ***[ms]***	426 (412, 439)	0.2	419 (406, 432)	0.12	425 (412, 438)	0.3	426 (413, 438)	0.3	423 (411, 439)	>0.9
Echocardiography										
LVEF [%]	59.4 (56.0, 63.1)	0.8	57.4 (56.6, 59.5)	0.13	59.3 (56.6, 62.8)	0.7	58.9 (56.4, 62.3)	0.2	60.5 (57.0, 63.3)	0.13

IVSD [mm]	**10.13 (9.13, 11.05)**	**<0.001**	9.47 (8.43, 10.28)	0.7	**9.71 (8.78, 10.55)**	**0.003**	9.49 (8.61, 10.33)	>0.9	9.43 (8.50, 10.35)	0.7
RWT	**0.39 (0.35, 0.44)**	**0.012**	0.36 (0.33, 0.44)	0.7	0.38 (0.34, 0.43)	0.9	0.37 (0.34, 0.41)	0.2	0.38 (0.34, 0.42)	0.4
LVMI [g/m²]	**81 (71, 96)**	**0.002**	72 (65, 90)	0.5	**78 (69, 90)**	**0.035**	75 (68, 88)	0.5	77 (66, 94)	0.6
E/A	0.86 (0.72, 1.12)	0.006	1.00 (0.80, 1.34)	0.3	0.93 (0.76, 1.13)	0.11	0.94 (0.77, 1.21)	0.8	0.94 (0.80, 1.12)	0.9
E/e' mean	7.82 (6.66, 9.35)	0.07	7.54 (6.75, 8.58)	0.8	7.36 (6.36, 8.97)	0.9	**7.21 (5.86, 8.12)**	**<0.001**	**7.79 (6.64, 9.78)**	**0.011**
Diastolic Dysfunction	20 (21%)	0.08	4 (16%)	>0.9	32 (16%)	0.8	21 (13%)	0.3	**30 (24%)**	**0.011**
LAVI [mL/m²]	26.58 (24.86, 28.20)	0.4	25.75 (24.93, 27.06)	0.4	26.34 (24.27, 27.74)	0.6	26.74 (25.43, 28.34)	0.069	26.55 (24.86, 28.51)	0.2
LAEF [%]	47 (45, 49)	0.8	58 (58, 58)	0.2	48 (42, 52)	0.5	49 (46, 55)	0.13	47 (37, 50)	0.2
LA strain [%]	38 (30, 48)	0.06	39 (31, 56)	>0.9	39 (31, 47)	0.10	39 (32, 49)	0.6	40 (28, 49)	0.4
Vascular parameters										
ABI mean	**0.99 (0.91, 1.07)**	**0.014**	1.03 (0.94, 1.11)	0.6	1.00 (0.94, 1.08)	0.3	1.02 (0.94, 1.11)	0.7	1.00 (0.93, 1.09)	0.2
CIMT [mm]	0.74 (0.67, 0.84)	0.5	**0.70 (0.64, 0.78)**	**0.032**	0.74 (0.68, 0.83)	0.4	**0.75 (0.69, 0.85)**	**0.013**	**0.72 (0.66, 0.81)**	**0.049**
Carotid plaques/stenosis	**55 (36%)**	**0.037**	16 (37%)	0.2	85 (27%)	0.4	67 (28%)	0.6	54 (30%)	0.7

Table 2: Baseline characteristics of women in our cohort with adverse pregnancy outcomes (APO) vs. those without APO; Median (25^{th}/75^{th} quartile) for continuous, n (%) for categorical variables. Pearson's χ^2-test /Wilcoxon rank sum test | **Bold font: p <0.05**; *Smoking:* current smoking upon inclusion*; sBP*: systolic blood pressure; *dBP*: diastolic blood pressure; BMI: Body-mass index; $HbA1_c$: Glycated hemoglobin $A1_c$: LDL-C: Low-density lipoprotein cholesterol; NTproBNP: N-terminal prohormone of brain natriuretic peptide; LVEF [%]: Left ventricular ejection fraction; IVSD [mm]: Interventricular septal end diastole; RWT: relative wall thickness (2x posterior wall thicknes/ left ventricular diastolic diameter; LVMI [g/m^2]: left-ventricular mass index (Left ventricular mass/Body Surface Area); LAVI [mL/m^2]: left atrial volume index (Left atrial volume/Body Surface Area); LAEF [%]: left atrial ejection fraction; LA strain [%]: left atrial strain; ABI: Ankle-brachial index; CIMT[mm]: Carotid intima-media thickness

Table 3: Demographic characteristics and electrocardiographic, echocardiographic and vascular parameters in women with adverse pregnancy outcomes gestational hypertension, gestational diabetes, excessive gestational weight gain, high (>4kg) and low (<2.5kg) fetal birth weight vs. those without (APO) – multivariable regression models; †: adjusted for age, type II diabetes mellitus, hypertension, dyslipidaemia, smoking | **Bold font: p <0.05**; *Smoking:* current smoking upon inclusion*; sBP*: systolic blood pressure; *dBPT:* diastolic blood pressure; Body mass index (weight/$height^2$); $HbA1_c$: Glycated hemoglobin $A1_c$: LDL-C: Low-density lipoprotein cholesterol; NTproBNP: N-terminal prohormone of brain natriuretic peptide; IVSD [mm]: Interventricular septal thickness at end diastole; Relative Wall Thickness (2x posterior wall thicknes/ left ventricular diastolic diameter); LVMI [g/m^2]: left-ventricular mass index (Left ventricular mass/Body Surface Area); LAVI [mL/m^2]: Left atrial volume index (Left atrial volume/Body Surface Area); ABI: Ankle-brachial index; CIMT[mm]: Carotid intima-media thickness

Mulitvariable regression models†

	Gestational hypertension		**Gestational diabetes**		**Excessive weight gain**		**High birth weight**		**Low fetal birth weight**	
Parameters	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
Body mass index [kg/m2]	**1.68 (0.86 – 2.50)**	**<0.001**	0.23 (-1.31 – 1.77)	0.77	**3.57 (2.97 – 4.16)**	**<0.001**	**1.22 (0.55 – 1.89)**	**<0.001**	-0.47 (-1.24 – 0.29)	0.22
Diabetes	0.86 (0.41 – 1.66)	0.66	**10.82 (4.55 – 25.23)**	**<0.001**	1.16 (0.66 – 1.98)	0.60	0.77 (0.39 – 1.42)	0.43	1.40 (0.70 – 2.61)	0.31
Current smoking	0.74 (0.43 – 1.19)	0.23	0.61 (0.23 – 1.41)	0.29	**1.57 (1.13 – 2.18)**	**0.007**	0.99 (0.68 – 1.42)	0.97	1.08 (0.71 – 1.60)	0.72
Hypertension	**4.58 (2.79 – 7.86)**	**<0.001**	0.51 (0.23 – 1.13)	0.01	0.98 (0.72 – 1.35)	0.92	**0.66 (0.48 – 0.91)**	**0.010**	1.08 (0.75 – 1.56)	0.69
Dyslipidaemia	1.12 (0.72 – 1.72)	0.60	0.78 (0.29 – 1.89)	0.60	0.86 (0.59 – 1.25)	0.44	1.01 (0.67 – 1.49)	0.96	1.11 (0.71 – 1.70)	0.64
sBP [mmHg]	**6.34 (3.18 – 9.51)**	**<0.001**	-5.56 (-11.39 – 0.27)	0.06	-0.82 (-3.29 – 1.64)	0.51	**-2.78 (-5.34 – -0.22)**	**0.034**	2.32 (-0.58 – 5.21)	0.12
dBP [mmHg]	1.28 (-0.41 – 2.97)	0.14	-2.89 (-5.98 – 0.19)	0.07	-0.58 (-1.89 – 0.72)	0.38	**-1.88 (-3.23 – -0.53)**	**0.006**	-0.57 (-2.11 – 0.96)	0.46
HbA1c [%]	-0.01 (-0.08 – 0.07)	0.88	0.03 (-0.10 – 0.16)	0.7	-0.04 (-0.10 – 0.01)	0.13	-0.04 (-0.09 – 0.02)	0.23	-0.05 (-0.12 – 0.01)	0.11
Total cholesterol [mg/dl]	-3.25 (-10.30 – 3.79)	0.37	-10.76 (-23.65 – 2.13)	0.10	-1.14 (-6.55 – 4.28)	0.68	-0.76 (-6.37 – 4.85)	0.79	-2.35 (-8.74 – 4.04)	0.47
LDL-C [mg/dl]	-2.17 (-8.70 – 4.36)	0.51	-7.70 (-19.74 – 4.35)	0.21	-0.45 (-5.45 – 4.55)	0.86	-0.75 (-5.94 – 4.45)	0.78	-4.35 (-10.30 – 1.59)	0.15
Troponin I [pg/ml]	-0.02 (-0.58 – 0.54)	0.93	-0.20 (-1.20 – 0.80)	0.70	0.18 (-0.25 – 0.61)	0.41	-0.22 (-0.67 – 0.22)	0.33	0.06 (-0.45 – 0.56)	0.83
NTproBNP [pg/ml]	5.94 (-32.87 – 44.75)	0.76	-30.44 (-101.89 – 41.00)	0.40	21.72 (-8.10 – 51.54)	0.15	17.60 (-14.69 – 49.89)	0.29	0.68 (-35.57 – 36.94)	0.97
Heart rate [bpm]	-0.91 (-3.05 – 1.22)	0.40	0.51 (-3.39 – 4.40)	0.80	-0.98 (-2.63 – 0.68)	0.25	**-1.74 (-3.48 – -0.00)**	**0.050**	-1.52 (-3.48 – 0.44)	0.13
RR interval [ms]	9.84 (-16.58 – 36.25)	0.47	-11.40 (-59.71 – 36.90)	0.64	13.63 (-6.82 – 34.09)	0.19	18.79 (-2.78 – 40.35)	0.09	23.82 (-0.55 – 48.19)	0.06
PQ interval [ms]	-0.48 (-5.63 – 4.67)	0.85	1.88 (-7.72 – 11.49)	0.70	-2.92 (-6.93 – 1.08)	0.15	2.14 (-2.14 – 6.42)	0.33	4.73 (-0.06 – 9.52)	0.05
P duration [ms]	2.61 (-0.78 – 6.01)	0.13	-0.24 (-6.60 – 6.12)	0.94	-0.93 (-3.60 – 1.74)	0.50	**3.17 (0.35 – 5.98)**	**0.027**	2.80 (-0.37 – 5.96)	0.08
QRS [ms]	-1.31 (-3.49 – 0.87)	0.24	-2.17 (-6.13 – 1.78)	0.28	0.91 (-0.75 – 2.56)	0.28	-0.03 (-1.79 – 1.73)	0.97	0.79 (-1.19 – 2.77)	0.43
QTc (Bazett) [ms]	-1.77 (-5.65 – 2.12)	0.37	-5.67 (-12.71 – 1.36)	0.11	1.27 (-1.72 – 4.26)	0.41	1.01 (-2.15 – 4.16)	0.53	1.22 (-2.34 – 4.77)	0.50
Left ventricular ejection fraction [%]	0.12 (-1.01 – 1.24)	0.84	-0.70 (-2.90 – 1.50)	0.53	0.39 (-0.46 – 1.24)	0.37	-0.22 (-1.11 – 0.66)	0.62	0.65 (-0.34 – 1.64)	0.20
IVSD [mm]	**0.43 (0.16 – 0.70)**	**0.002**	-0.08 (-0.56 – 0.41)	0.76	0.08 (-0.13 – 0.29)	0.47	-0.00 (-0.22 – 0.22)	0.99	0.13 (-0.12 – 0.38)	0.30
Relative wall thickness	0.01 (-0.01 – 0.02)	0.46	-0.01 (-0.03 – 0.02)	0.63	0.00 (-0.01 – 0.01)	0.58	-0.00 (-0.01 – 0.01)	0.51	0.01 (-0.01 – 0.02)	0.24
Left ventricular mass index [g/m^2]	**4.46 (1.05 – 7.87)**	**0.010**	0.57 (-5.19 – 6.34)	0.85	1.74 (-0.83 – 4.30)	0.18	0.28 (-2.38 – 2.94)	0.83	2.37 (-0.63 – 5.38)	0.12
E/A	-0.04 (-0.11 – 0.03)	0.25	0.04 (-0.08 – 0.16)	0.50	-0.04 (-0.09 – 0.01)	0.09	-0.00 (-0.05 – 0.05)	0.98	-0.03 (-0.09 – 0.03)	0.33
E/e'	0.06 (-0.35 – 0.48)	0.76	0.11 (-0.66 – 0.88)	0.78	-0.06 (-0.38 – 0.26)	0.71	**-0.40 (-0.72 – -0.07)**	**0.017**	**0.69 (0.31 – 1.07)**	**<0.001**
Diastolic Dysfunction	1.22 (0.65 – 2.18)	0.52	0.97 (0.21 – 3.28)	0.96	0.99 (0.58 – 1.64)	0.96	0.82 (0.45 – 1.42)	0.49	**2.19 (1.30 – 3.60)**	**0.002**
Left atrial volume index [ml/m^2]	0.04 (-0.78 – 0.86)	0.93	-0.62 (-1.96 – 0.73)	0.37	**-0.66 (-1.32 – -0.00)**	**0.049**	0.52 (-0.12 – 1.17)	0.11	0.50 (-0.21 – 1.21)	0.17
Left atrial ejection fraction [%]	4.75 (-0.83 – 10.34)	0.10	7.59 (-11.89 – 27.08)	0.44	1.63 (-3.28 – 6.53)	0.51	3.59 (-2.01 – 9.19)	0.21	0.11 (-4.79 – 5.00)	0.97
Left atrial strain [%]	-2.52 (-6.76 – 1.72)	0.24	0.67 (-6.69 – 8.03)	0.86	-2.83 (-6.06 – 0.40)	0.09	-1.08 (-4.42 – 2.26)	0.53	-1.98 (-5.61 – 1.65)	0.28
ABI mean	-0.02 (-0.05 – 0.00)	0.05	0.03 (-0.02 – 0.08)	0.18	0.96 (0.68 – 1.34)	0.80	0.92 (0.64 – 1.32)	0.67	-0.02 (-0.04 – 0.01)	0.14
Carotid intima-media thickness [mm]	-0.01 (-0.03 – 0.01)	0.26	-0.01 (-0.05 – 0.02)	0.47	0.01 (-0.01 – 0.02)	0.26	**0.03 (0.01 – 0.04)**	**0.001**	**-0.02 (-0.04 – -0.00)**	**0.046**
Carotid plaques/stenosis	1.23 (0.81 – 1.84)	0.32	1.70 (0.76 – 3.65)	0.18	-0.01 (-0.03 – 0.01)	0.19	0.00 (-0.02 – 0.02)	0.68	0.98 (0.66 – 1.45)	0.93
Myocardial infarction	**3.27 (0.94 – 10.07)**	**0.046**								
Stroke					**2.20 (1.00 – 4.62)**	**0.042**				

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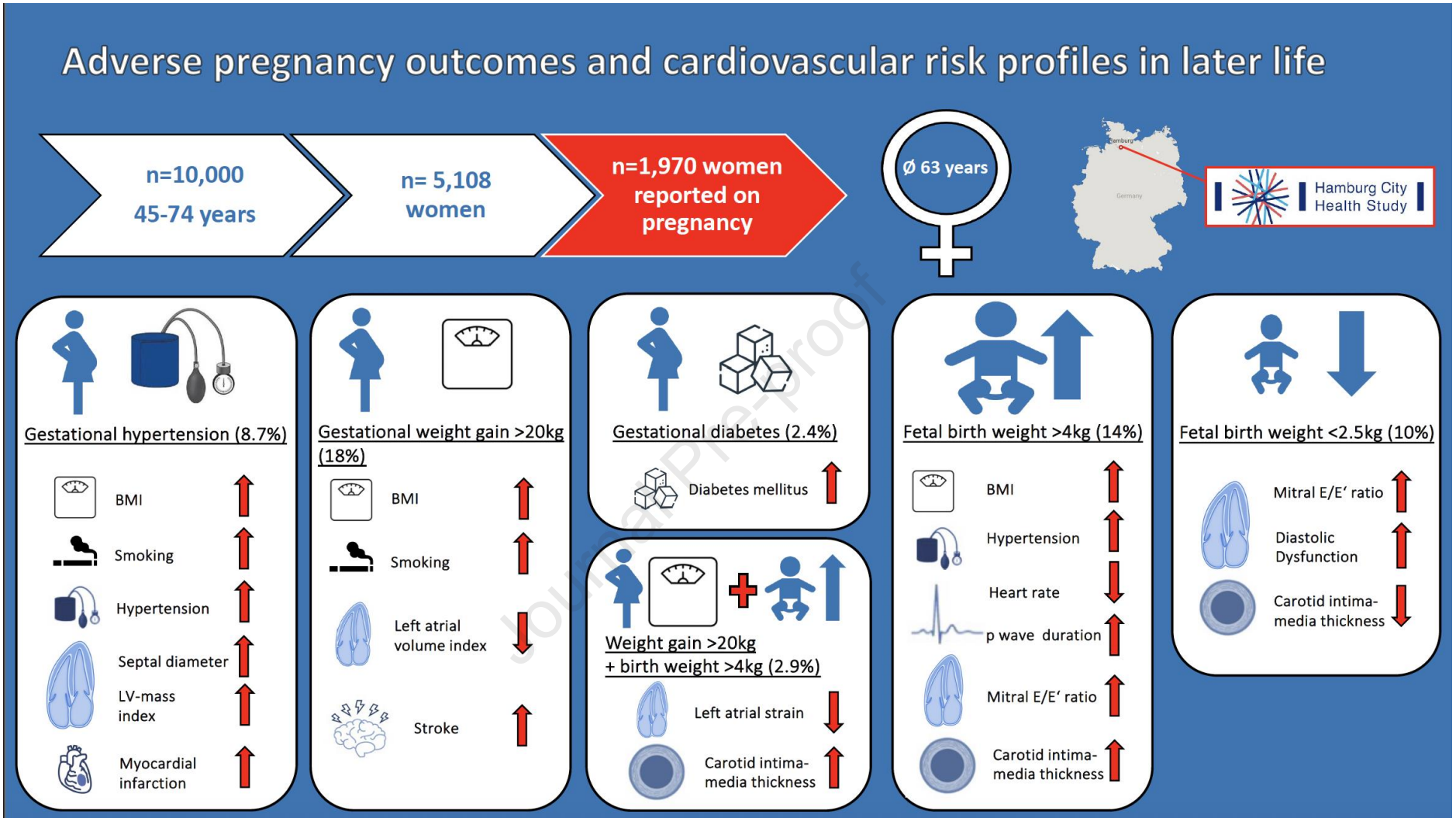


Figure 1: Graphical abstract - Correlations of adverse pregnancy outcomes with cardiovascular risk profiles and manifest disease in later life determined by a multivariable regression model (p <0.05)

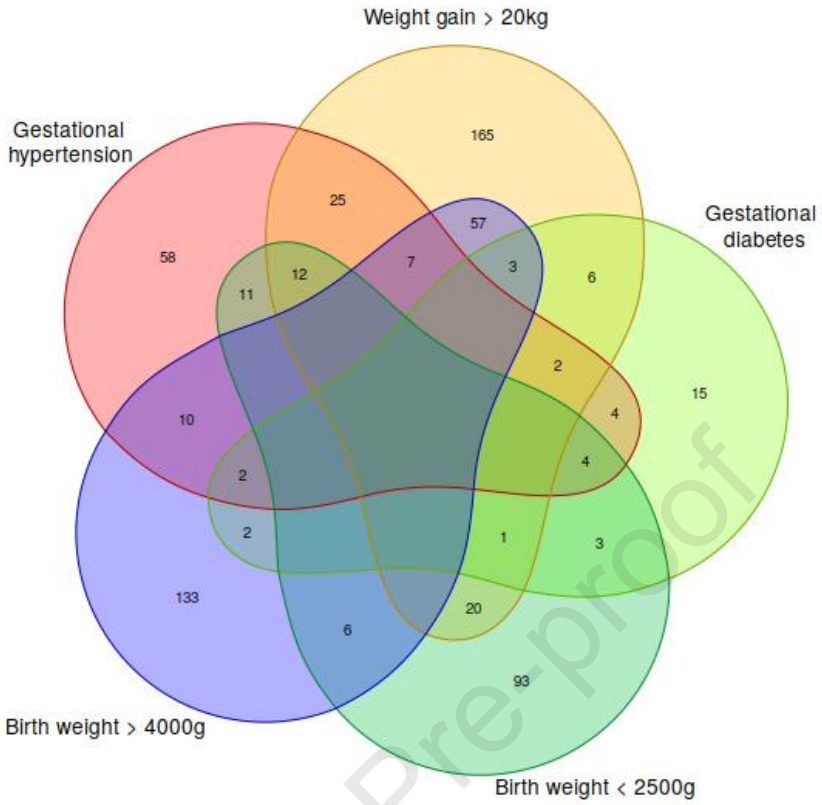


Figure 2: Venn diagram of overlapping adverse pregnancy outcomes; n=57 women reported both, elevated fetal birth weight and excessive gestational weight gain

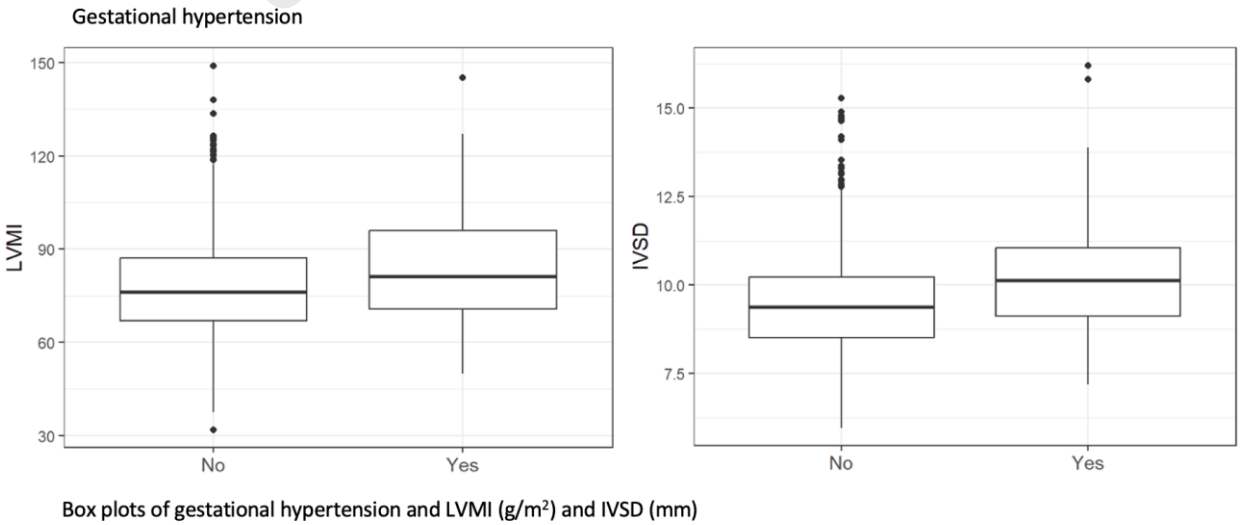


Figure 3: Women with a history of gestational hypertension and indicators of left-ventricular remodeling: left ventricular mass index (LVMI; g/m^2) and interventricular septum end-diastole (IVSD; mm); Box plots

15) Supplement

Supp. Table 1	**gHTN - Model 1†**		**gDM - Model 1†**		**EGWG - Model 1†**		**Fetal Birth weight >4kg - Model 1†**		**Fetal Birth weight <2,5kg - Model 1†**	
Parameters	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Body mass index [kg/m2]	**1.68 (0.86 – 2.50)**	**<0.001**	0.12 (-1.43 – 1.66)	0.88	**3.62 (3.03 – 4.21)**	**<0.001**	**1.20 (0.53 – 1.87)**	**<0.001**	-0.44	0.26
Diabetes	0.83 (0.41 – 1.58)	0.59	**10.20 (4.34 – 23.37)**	**<0.001**	1.17 (0.68 – 1.95)	0.56	0.75 (0.38 – 1.37)	0.38	1.41	0.29
Currently smoking	0.74 (0.44 – 1.20)	0.25	0.61 (0.22 – 1.40)	0.28	**1.55 (1.11 – 2.13)**	**0.008**	1.00 (0.68 – 1.42)	0.98	1.12	0.59
Hypertension	**4.64 (2.82 – 7.95)**	**<0.001**	0.50 (0.23 – 1.10)	0.09	0.97 (0.71 – 1.32)	0.83	**0.66 (0.48 – 0.90)**	**0.010**	1.09	0.66
Dyslipidaemia	1.09 (0.70 – 1.66)	0.71	0.76 (0.29 – 1.83)	0.56	0.93 (0.64 – 1.34)	0.72	1.03 (0.69 – 1.51)	0.89	1.13	0.59
BP_{sys} [mmHg]	**6.41 (3.25 – 9.57)**	**<0.001**	-5.50 (-11.33 – 0.34)	0.07	-1.09 (-3.54 – 1.36)	0.38	**-2.81 (-5.37 – -0.25)**	**0.031**	2.04	0.17
Bp_{dias} [mmHg]	1.32 (-0.37 – 3.02)	0.13	-2.78 (-5.87 – 0.31)	0.08	-0.71 (-2.01 – 0.59)	0.29	**-1.89 (-3.24 – -0.54)**	**0.006**	-0.60	0.45
HbA1c [%]	-0.01 (-0.08 – 0.06)	0.76	0.02 (-0.12 – 0.15)	0.81	-0.04 (-0.09 – 0.02)	0.19	-0.04 (-0.10 – 0.02)	0.21	-0.05 (-0.12 – 0.01)	0.11
Total cholesterol [mg/dl]	-3.92 (-11.05 – 3.21)	0.28	-10.68 (-23.72 – 2.35)	0.11	-0.44 (-5.88 – 5.00)	0.87	1.20 (-6.88 – 4.47)	0.68	-1.27 (-7.72 – 5.19)	0.70
LDL-C [mg/dl]	-2.48 (-9.08 – 4.11)	0.46	-7.18 (-19.34 – 4.98)	0.25	0.37 (-4.66 – 5.40)	0.89	-0.94 (-6.19 – 4.31)	0.73	3.02 (-9.01 – 2.97)	0.32
Troponin I [pg/ml]	-0.02 (-0.58 – 0.54)	0.94	-0.22 (-1.22 – 0.78)	0.66	0.18 (-0.25 – 0.61)	0.40	-0.23 (-0.67 – 0.22)	0.32	0.04 (-0.47 – 0.54)	0.89
NTproBNP [pg/ml]	5.71 (-33.01 – 44.43)	0.77	-31.69 (-103.02 – 39.65)	0.38	21.90 (-7.69 – 51.49)	0.15	17.97 (-14.23 – 50.17)	0.27	0.20 (-36.30 – 35.89)	0.99
Heart rate [bpm]	-0.99 (-3.13 – 1.14)	0.36	0.31 (-3.59 – 4.21)	0.88	0.86 (-2.51 – 0.78)	0.30	**-1.82 (-3.56 – -0.08)**	**0.040**	-1.52 (-3.47 – 0.44)	0.13
RR interval [ms]	10.51 (-15.93 – 36.95)	0.44	-9.58 (-57.89 – 38.74)	0.7	12.58 (-7.80 – 32.97)	0.23	19.73 (-1.81 – 41.27)	0.07	23.56 (-0.76 – 47.87)	0.06
PQ interval [ms]	-0.45 (-5.60 – 4.70)	0.86	2.21 (-7.40 – 11.83)	0.65	-3.12 (-7.11 – 0.86)	0.13	2.34 (-1.93 – 6.61)	0.28	4.74 (-0.04 – 9.51)	0.05
P duration [ms]	2.58 (-0.83 – 5.98)	0.14	-0.22 (-6.59 – 6.15)	0.95	-1.12 (-3.78 – 1.54)	0.41	**3.27 (0.46 – 6.08)**	**0.023**	2.69 (-0.46 – 5.85)	0.10
QRS [ms]	-1.25 (-3.47 – 0.97)	0.27	-2.27 (-6.30 – 1.76)	0.27	0.85 (-0.81 – 2.51)	0.31	-0.04 (-1.83 – 1.75)	0.97	0.60 (-1.41 – 2.62)	0.56
QTc (Bazett) [ms]	-1.87 (-5.76 – 2.02)	0.35	-6.08 (-13.12 – 0.96)	0.09	1.22 (-1.76 – 4.19)	0.42	1.07 (-2.09 – 4.23)	0.51	0.95 (-2.60 – 4.50)	0.6
Left ventricular ejection fraction [%]	0.10 (-1.01 – 1.22)	0.86	-0.71 (-2.90 – 1.48)	0.53	0.36 (-0.48 – 1.19)	0.40	-0.23 (-1.12 – 0.65)	0.60	0.65 (-0.33 – 1.64)	0.19
IVSD [mm]	**0.40 (0.14 – 0.67)**	**0.003**	-0.09 (-0.58 – 0.40)	0.72	0.11 (-0.10 – 0.31)	0.32	0.01 (-0.21 – 0.22)	0.95	0.11 (-0.14 – 0.36)	0.39
Relative wall thickness	0.00 (-0.01 – 0.02)	0.55	-0.01 (-0.03 – 0.02)	0.6	0.00 (-0.01 – 0.02)	0.40	-0.00 (-0.01 – 0.01)	0.52	0.01 (-0.01 – 0.02)	0.27
Left ventricular mass index [g/m^2]	**4.29 (0.88 – 7.71)**	**0.014**	0.40 (-5.38 – 6.17)	0.89	1.95 (-0.61 – 4.50)	0.14	0.32 (-2.35 – 2.99)	0.82	2.01 (-0.99 – 5.01)	0.19
E/A	-0.04 (-0.11 – 0.03)	0.25	0.04 (-0.08 – 0.16)	0.48	-0.04 (-0.09 – 0.01)	0.1	-0.00 (-0.05 – 0.05)	0.96	-0.03 (-0.09 – 0.03)	0.3
E/e'	0.02 (-0.39 – 0.44)	0.91	0.05 (-0.72 – 0.82)	0.91	-0.04 (-0.35 – 0.28)	0.82	**-0.39 (-0.72 – -0.06)**	**0.019**	**0.66 (0.28 – 1.03)**	**0.001**
Diastolic Dysfunction	1.13 (0.60 – 2.01)	0.70	0.95 (0.21 – 3.16)	0.94	1.04 (0.61 – 1.72)	0.88	0.84 (0.47 – 1.45)	0.56	**2.10 (1.26 – 3.44)**	**0.004**
Left atrial volume index [ml/m^2]	0.07 (-0.76 – 0.90)	0.87	-0.44 (-1.81 – 0.92)	0.52	**-0.67 (-1.33 – -0.01)**	**0.047**	0.54 (-0.12 – 1.19)	0.11	0.62 (-0.10 – 1.34)	0.09
Left atrial ejection fraction [%]	4.54 (-1.01 – 10.09)	0.11	7.49 (-12.03 – 27.01)	0.45	1.71 (-3.04 – 6.47)	0.48	3.80 (-1.77 – 9.37)	0.18	0.56 (-4.16 – 5.28)	0.82
Left atrial strain [%]	-2.57 (-6.80 – 1.67)	0.24	0.21 (-7.15 – 7.57)	0.96	-3.06 (-6.27 – 0.15)	0.06	-1.12 (-4.46 – 2.22)	0.51	-2.05 (-5.66 – 1.56)	0.27
ABI mean	-0.02 (-0.05 – 0.00)	0.06	0.04 (-0.01 – 0.09)	0.17	-0.01 (-0.03 – 0.01)	0.22	0.00 (-0.02 – 0.02)	0.79	-0.02 (-0.04 – 0.01)	0.14
Carotid intima-media thickness [mm]	-0.01 (-0.03 – 0.01)	0.25	-0.02 (-0.05 – 0.02)	0.41	0.01 (-0.01 – 0.02)	0.26	**0.03 (0.01 – 0.04)**	**0.001**	**-0.02 (-0.04 – -0.00)**	**0.041**
Carotid plaques/stenosis	1.19 (0.80 – 1.77)	0.39	1.55 (0.70 – 3.27)	0.26	1.00 (0.71 – 1.39)	0.99	0.93 (0.65 – 1.32)	0.69	1.02 (0.68 – 1.49)	0.94

Supp. Table 1: Demographic characteristics and electrocardiographic, echocardiographic and vascular parameters in women with adverse pregnancy outcomes gestational hypertension (gHTN), gestational diabetes (gDM), excessive gestational weight gain (EGWG), high (>4kg) and low (<2.5kg) fetal birth weight vs. those without – regression models; Model 1†: adjusted for age, BMI, type II diabetes mellitus, hypertension| **Bold font: p <0.05**; *Smoking:* current smoking upon inclusion*; BP_{sys}*: systolic blood pressure; BP_{dia}: diastolic blood pressure; Body mass index (weight/height^2); $HbA1_c$: Glycated hemoglobin $A1_c$: LDL-C: Low-density lipoprotein cholesterol; NTproBNP: N-terminal prohormone of brain natriuretic peptide; IVSD [mm]: Interventricular septal thickness at end diastole; Relative Wall Thickness (2x posterior wall thicknes/ left ventricular diastolic diameter); LVMI [g/m^2]: left-ventricular mass index (Left ventricular mass/Body Surface Area); LAVI [mL/m^2]: Left atrial volume index (Left atrial volume/Body Surface Area); ABI: Ankle-brachial index; CIMT[mm]: Carotid intima-media thickness

Supp. Table 2	**EGWG + Birth weight >4kg; Model 1†**		**EGWG + Birth weight >4kg; Model 2‡**	
Parameters	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
HbA1c [%]	0.01 (-0.13 – 0.11)	0.84	-0.01 (-0.12 – 0.11)	0.93
Total cholesterol [mg/dl]	-4.79 (-16.29 – 6.72)	0.42	-4.85 (-16.20 – 6.50)	0.40
LDL-C [mg/dl]	-3.85 (-14.44 – 6.73)	0.48	-4.08 (-14.55 – 6.39)	0.45
Troponin I [pg/ml]	0.85 (-0.03 – 1.74)	0.06	0.86 (-0.03 – 1.74)	0.06
NTproBNP [pg/ml]	52.20 (-12.11 – 116.51)	0.11	54.09 (-10.27 – 118.44)	0.1
Heart rate [bpm]	-1.45 (-4.91 – 2.02)	0.41	-1.36 (-4.82 – 2.10)	0.44
RR interval [ms]	25.90 (-17.08 – 68.88)	0.24	25.23 (-17.70 – 68.16)	0.25
PQ interval [ms]	3.94 (-4.57 – 12.45)	0.36	3.75 (-4.75 – 12.25)	0.39
P duration [ms]	3.17 (-2.40 – 8.75)	0.26	3.07 (-2.49 – 8.64)	0.28
QRS [ms]	1.06 (-2.51 – 4.62)	0.56	0.99 (-2.50 – 4.49)	0.58
QTc (Bazett) [ms]	5.93 (-0.39 – 12.24)	0.07	6.07 (-0.24 – 12.37)	0.06
Left ventricular ejection fraction [%]	-0.04 (-1.79 – 1.72)	0.97	-0.04 (-1.80 – 1.73)	0.97
IVSD [mm]	0.25 (-0.21 – 0.70)	0.28	0.22 (-0.23 – 0.67)	0.33
Relative wall thickness	-0.00 (-0.03 – 0.02)	0.78	-0.00 (-0.03 – 0.02)	0.73
Left ventricular mass index [g/m^2]	3.64 (-1.70 – 8.98)	0.18	3.41 (-1.91 – 8.73)	0.21
E/A	-0.08 (-0.18 – 0.02)	0.16	-0.08 (-0.18 – 0.02)	0.13
E/e'	-0.24 (-0.91 – 0.43)	0.49	-0.25 (-0.91 – 0.42)	0.47
Diastolic Dysfunction	1.14 (0.32 – 3.19)	0.82	1.05 (0.29 – 3.00)	0.93
Left atrial volume index [ml/m^2]	0.20 (-1.24 – 1.64)	0.78	0.19 (-1.24 – 1.62)	0.79
Left atrial ejection fraction [%]	2.17 (-7.77 – 12.11)	0.67	1.24 (-8.86 – 11.33)	0.81
Left atrial strain [%]	**-9.81 (-17.73 – -1.89)**	**0.02**	**-9.79 (-17.69 – -1.89)**	**0.015**
ABI mean	0.01 (-0.03 – 0.05)	0.54	0.01 (-0.03 – 0.05)	0.54
Carotid intima-media thickness [mm]	**0.05 (0.01 – 0.08)**	**0.007**	**0.05 (0.01 – 0.08)**	**0.006**
Carotid plaques/stenosis	1.14 (0.53 – 2.27)	0.73	1.17 (0.54 – 2.36)	0.67

Supp. Table 2: Demographic characteristics and electrocardiographic, echocardiographic and vascular parameters in women with adverse pregnancy outcomes excessive gestational weight gain (EGWG) and high fetal birth weight vs. those without – regression models: Model 1†: adjusted for age, BMI, diabetes, hypertension; Model 2‡: adjusted for age, BMI, type II diabetes mellitus, hypertension, dyslipidaemia, smoking | **Bold font: p <0.05**; BP_{sys}: systolic blood pressure; BP_{dia}: diastolic blood pressure; Body mass index (weight/height^2); $HbA1_c$: Glycated hemoglobin $A1_c$: LDL-C: Low-density lipoprotein cholesterol; NTproBNP: N-terminal prohormone of brain natriuretic peptide; IVSD [mm]: Interventricular septal thickness at end diastole; Relative Wall Thickness (2x posterior wall thicknes/ left ventricular diastolic diameter); LVMI [g/m^2]: left-ventricular mass index (Left ventricular mass/Body Surface Area); LAVI [mL/m^2]: Left atrial volume index (Left atrial volume/Body Surface Area); ABI: Ankle-brachial index; CIMT[mm]: Carotid intima-media thickness

		Model 1†		Model 2‡	
APO	**Manifest CV disease**	**Odds Ratio (CI 95%)**	p-value	**Odds Ratio (CI 95%)**	p-value
gHTN	Myocardial infarction	**3.06 (0.95 – 8.54)**	**0.042**	**3.27 (0.94 – 10.07)**	**0.046**
	Stroke	0.18 (0.01 – 0.87)	0.1	0.17 (0.01 – 0.83)	0.09
	Heart failure	1.78 (0.84 – 3.52)	0.1	1.78 (0.83 – 3.55)	0.12
	Atrial fibrillation	1.31 (0.62 – 2.54)	0.44	1.32 (0.62 – 2.59)	0.44
gDM	Myocardial infarction	2.15 (0.11 – 13.42)	0.5	3.06 (0.15 – 21.43)	0.33
	Stroke	0.00 (0.00 – 519337.13)	0.98	0.00 (0.00 – 8446499380863.99)	0.99
	Heart failure	0.00 (0.00 – 2396.98)	0.98	0.00 (0.00 – 1919.51)	0.98
	Atrial fibrillation	0.00 (0.00 – 1781.21)	0.98	0.00 (0.00 – 1645.77)	0.98
Weight gain >20kg	Myocardial infarction	1.13 (0.25 – 3.61)	0.85	1.06 (0.23 – 3.53)	0.93
	Stroke	**2.14 (0.98 – 4.41)**	**0.046**	**2.20 (1.00 – 4.62)**	**0.042**
	Heart failure	1.71 (0.85 – 3.29)	0.12	1.59 (0.78 – 3.09)	0.18
	Atrial fibrillation	1.26 (0.66 – 2.31)	0.47	1.23 (0.63 – 2.30)	0.52
Birth weight >4kg	Myocardial infarction	0.81 (0.13 – 2.90)	0.78	0.67 (0.10 – 2.57)	0.61
	Stroke	0.46 (0.11 – 1.30)	0.20	0.46 (0.11 – 1.31)	0.21
	Heart failure	0.89 (0.36 – 1.90)	0.78	0.84 (0.33 – 1.81)	0.67
	Atrial fibrillation	0.81 (0.36 – 1.61)	0.57	0.85 (0.38 – 1.71)	0.67

Supp. Table 3: Manifest cardiovascular disease in women with adverse pregnancy outcomes (APO) gestational hypertension (gHTN), gestational diabetes (gDM), excessive gestational weight gain (EGWG) or high (>4kg) fetal birth weight vs. those without - regressions models. Model 1†: adjusted for age, BMI, diabetes, hypertension; Model 2‡: adjusted for age, BMI, type II diabetes mellitus, hypertension, dyslipidaemia, smoking | **Bold font: p <0.05**

Supplement table 4

Mulitvariable regression models†									
	Gestational hypertension			**Gestational diabetes**			**Excessive weight gain**		
Parameters	Odds ratio (95% CI)	p-value	p adjust	Odds ratio (95% CI)	p-value	p adjust	Odds ratio (95% CI)	p-value	p adjust
Body mass index [kg/m2]	**1.68 (0.86 – 2.50)**	**<0.001**	**<0.001**	0.23 (-1.31 – 1.77)	0.77	0.77	**3.57 (2.97 – 4.16)**	**<0.001**	**<0.001**
Diabetes	0.86 (0.41 – 1.66)	0.66	0.66	**10.82 (4.55 – 25.23)**	**<0.001**	**<0.001**	1.16 (0.66 – 1.98)	0.60	0.60
Current smoking	0.74 (0.43 – 1.19)	0.23	0.40	0.61 (0.23 – 1.41)	0.29	0.40	**1.57 (1.13 – 2.18)**	**0.007**	**0.01**
Hypertension ***	**4.58 (2.79 – 7.86)**	**<0.001**	**<0.001**	0.51 (0.23 – 1.13)	0.10	0.14	0.98 (0.72 – 1.35)	0.92	0.92
Dyslipidaemia ***	1.12 (0.72 – 1.72)	0.60	0.60	0.78 (0.29 – 1.89)	0.60	0.59	0.86 (0.59 – 1.25)	0.44	0.44
sBP [mmHg]	**6.34 (3.18 – 9.51)**	**<0.001**	**<0.001**	-5.56 (-11.39 – 0.27)	0.06	0.09	-0.82 (-3.29 – 1.64)	0.51	0.60
dBP [mmHg]	1.28 (-0.41 – 2.97)	0.14	0.19	-2.89 (-5.98 – 0.19)	0.07	0.09	-0.58 (-1.89 – 0.72)	0.38	0.53
HbA1c [%]	-0.01 (-0.08 – 0.07)	0.88	0.88	0.03 (-0.10 – 0.16)	0.68	0.68	-0.04 (-0.10 – 0.01)	0.13	0.15
Total cholesterol [mg/dl]	-3.25 (-10.30 – 3.79)	0.37	0.49	-10.76 (-23.65 – 2.13)	0.10	0.16	-1.14 (-6.55 – 4.28)	0.68	0.68
LDL-C [mg/dl]	-2.17 (-8.70 – 4.36)	0.51	0.64	-7.70 (-19.74 – 4.35)	0.21	0.28	-0.45 (-5.45 – 4.55)	0.86	0.97
Troponin I [pg/ml]	-0.02 (-0.58 – 0.54)	0.93	0.93	-0.20 (-1.20 – 0.80)	0.70	0.80	0.18 (-0.25 – 0.61)	0.41	0.47
NTproBNP [pg/ml]	5.94 (-32.87 – 44.75)	0.76	0.76	-30.44 (-101.89 – 41.00)	0.40	0.46	21.72 (-8.10 – 51.54)	0.15	0.20
Heart rate [bpm]	-0.91 (-3.05 – 1.22)	0.40	0.49	0.51 (-3.39 – 4.40)	0.80	0.80	-0.98 (-2.63 – 0.68)	0.25	0.33
RR interval [ms]	9.84 (-16.58 – 36.25)	0.47	0.53	-11.40 (-59.71 – 36.90)	0.64	0.74	13.63 (-6.82 – 34.09)	0.19	0.26
PQ interval [ms]	-0.48 (-5.63 – 4.67)	0.85	0.85	1.88 (-7.72 – 11.49)	0.70	0.80	-2.92 (-6.93 – 1.08)	0.15	0.30
P duration [ms]	2.61 (-0.78 – 6.01)	0.13	0.18	-0.24 (-6.60 – 6.12)	0.94	0.94	-0.93 (-3.60 – 1.74)	0.50	0.63
QRS [ms]	-1.31 (-3.49 – 0.87)	0.24	0.35	-2.17 (-6.13 – 1.78)	0.28	0.32	0.91 (-0.75 – 2.56)	0.28	0.45
QTc (Bazett) [ms]	-1.77 (-5.65 – 2.12)	0.37	0.50	-5.67 (-12.71 – 1.36)	0.11	0.18	1.27 (-1.72 – 4.26)	0.41	0.54
Left ventricular ejection fraction [%]	0.12 (-1.01 – 1.24)	0.84	0.84	-0.70 (-2.90 – 1.50)	0.53	0.53	0.39 (-0.46 – 1.24)	0.37	0.49
IVSD [mm]	**0.43 (0.16 – 0.70)**	**0.002**	**0.002**	-0.08 (-0.56 – 0.41)	0.76	0.76	0.08 (-0.13 – 0.29)	0.47	0.47
Relative wall thickness	0.01 (-0.01 – 0.02)	0.46	0.53	-0.01 (-0.03 – 0.02)	0.63	0.64	0.00 (-0.01 – 0.01)	0.58	0.64
Left ventricular mass index [g/m^2]	**4.46 (1.05 – 7.87)**	**0.010**	**0.014**	0.57 (-5.19 – 6.34)	0.85	0.85	1.74 (-0.83 – 4.30)	0.18	0.21
E/A	-0.04 (-0.11 – 0.03)	0.25	0.40	0.04 (-0.08 – 0.16)	0.50	0.58	-0.04 (-0.09 – 0.01)	0.09	0.15
E/e'	0.06 (-0.35 – 0.48)	0.76	0.81	0.11 (-0.66 – 0.88)	0.78	0.78	-0.06 (-0.38 – 0.26)	0.71	0.81
Diastolic Dysfunction ***	1.22 (0.65 – 2.18)	0.52	0.66	0.97 (0.21 – 3.28)	0.97	0.97	0.99 (0.58 – 1.64)	0.96	0.96
Left atrial volume index [ml/m^2]	0.04 (-0.78 – 0.86)	0.93	0.93	-0.62 (-1.96 – 0.73)	0.37	0.42	**-0.66 (-1.32 – -0.00)**	**0.049**	0.08
Left atrial ejection fraction [%]	4.75 (-0.83 – 10.34)	0.10	0.24	7.59 (-11.89 – 27.08)	0.44	0.71	1.63 (-3.28 – 6.53)	0.51	0.68
Left atrial strain [%]	-2.52 (-6.76 – 1.72)	0.24	0.33	0.67 (-6.69 – 8.03)	0.86	0.86	-2.83 (-6.06 – 0.40)	0.09	0.20

ABI mean	-0.02 (-0.05 – 0.00)	0.05	0.07	0.03 (-0.02 – 0.08)	0.18	0.24	-0.01 (-0.03 – 0.01)	0.19	0.25
Carotid intima-media thickness [mm]	-0.01 (-0.03 – 0.01)	0.26	0.35	-0.01 (-0.05 – 0.02)	0.47	0.54	0.01 (-0.01 – 0.02)	0.26	0.30
Carotid plaques/stenosis ***	1.23 (0.81 – 1.84)	0.32	0.36	1.70 (0.76 – 3.65)	0.18	0.24	0.96 (0.68 – 1.34)	0.80	0.80
Myocardial infarction ***	**3.27 (0.94 – 10.07)**	**0.046**	0.12	3.69 (0.17 – 30.81)	0.28	0.53	1.19 (0.26 – 4.05)	0.80	0.99
Stroke ***	0.17 (0.01 – 0.83)	0.09	0.14	0.00	0.99	0.99	**2.20 (1.00 – 4.62)**	**0.042**	0.08

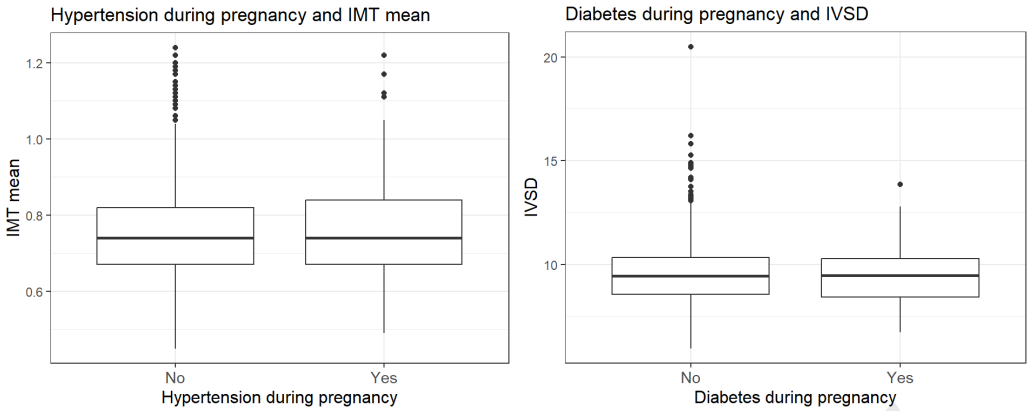
*** logistic regression models

Supplement table 5

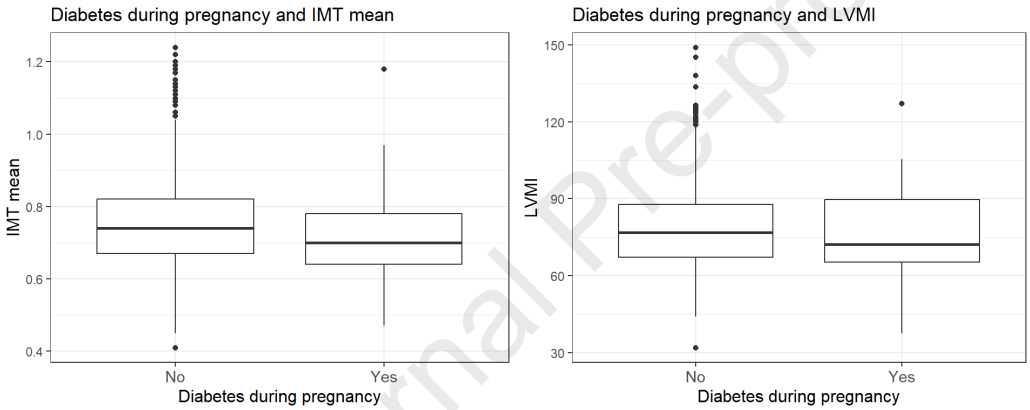
Mulitvariable regression models†						
	High birth weight			**Low fetal birth weight**		
Parameters	Odds ratio(95% CI)	p-value	p adjust	Odds ratio (95% CI)	p-value	p adjust
Body mass index [kg/m2]	**1.22 (0.55 – 1.89)**	**<0.001**	**<0.001**	-0.47 (-1.24 – 0.29)	0.22	0.22
Diabetes	0.77 (0.39 – 1.42)	0.43	0.43	1.40 (0.70 – 2.61)	0.31	0.33
Current smoking	0.99 (0.68 – 1.42)	0.97	0.97	1.08 (0.71 – 1.60)	0.72	0.72
Hypertension ***	**0.66 (0.48 – 0.91)**	**0.010**	**0.014**	1.08 (0.75 – 1.56)	0.69	0.69
Dyslipidaemia ***	1.01 (0.67 – 1.49)	0.96	0.96	1.11 (0.71 – 1.70)	0.64	0.64
sBP [mmHg]	**-2.78 (-5.34 – -0.22)**	**0.034**	**0.047**	2.32 (-0.58 – 5.21)	0.12	0.16
dBP [mmHg]	**-1.88 (-3.23 – -0.53)**	**0.006**	**0.009**	-0.57 (-2.11 – 0.96)	0.46	0.65
HbA1c [%]	-0.04 (-0.09 – 0.02)	0.23	0.26	-0.05 (-0.12 – 0.01)	0.11	0.12
Total cholesterol [mg/dl]	-0.76 (-6.37 – 4.85)	0.79	0.79	-2.35 (-8.74 – 4.04)	0.47	0.47
LDL-C [mg/dl]	-0.75 (-5.94 – 4.45)	0.78	0.94	-4.35 (-10.30 – 1.59)	0.15	0.20
Troponin I [pg/ml]	-0.22 (-0.67 – 0.22)	0.33	0.44	0.06 (-0.45 – 0.56)	0.83	0.94
NTproBNP [pg/ml]	17.60 (-14.69 – 49.89)	0.29	0.33	0.68 (-35.57 – 36.94)	0.97	0.97
Heart rate [bpm]	**-1.74 (-3.48 – -0.00)**	**0.050**	0.07	-1.52 (-3.48 – 0.44)	0.13	0.17
RR interval [ms]	18.79 (-2.78 – 40.35)	0.09	0.12	23.82 (-0.55 – 48.19)	0.06	0.09
PQ interval [ms]	2.14 (-2.14 – 6.42)	0.33	0.44	4.73 (-0.06 – 9.52)	0.05	0.14
P duration [ms]	**3.17 (0.35 – 5.98)**	**0.027**	0.055	2.80 (-0.37 – 5.96)	0.08	0.16
QRS [ms]	-0.03 (-1.79 – 1.73)	0.97	0.97	0.79 (-1.19 – 2.77)	0.43	0.58
QTc (Bazett) [ms]	1.01 (-2.15 – 4.16)	0.53	0.67	1.22 (-2.34 – 4.77)	0.50	0.67
Left ventricular ejection fraction [%]	-0.22 (-1.11 – 0.66)	0.62	0.64	0.65 (-0.34 – 1.64)	0.20	0.32
IVSD [mm]	-0.00 (-0.22 – 0.22)	0.99	0.99	0.13 (-0.12 – 0.38)	0.30	0.30
Relative wall thickness	-0.00 (-0.01 – 0.01)	0.51	0.58	0.01 (-0.01 – 0.02)	0.24	0.34
Left ventricular mass index [g/m^2]	0.28 (-2.38 – 2.94)	0.83	0.83	2.37 (-0.63 – 5.38)	0.12	0.16

E/A	-0.00 (-0.05 – 0.05)	0.98	0.98	-0.03 (-0.09 – 0.03)	0.33	0.43
E/e'	**-0.40 (-0.72 – -0.07)**	**0.017**	**0.028**	**0.69 (0.31 – 1.07)**	**<0.001**	**<0.001**
Diastolic Dysfunction ***	0.82 (0.45 – 1.42)	0.49	0.66	**2.19 (1.30 – 3.60)**	**0.002**	**0.005**
Left atrial volume index [ml/m^2]	0.52 (-0.12 – 1.17)	0.11	0.18	0.50 (-0.21 – 1.21)	0.17	0.27
Left atrial ejection fraction [%]	3.59 (-2.01 – 9.19)	0.21	0.38	0.11 (-4.79 – 5.00)	0.97	0.97
Left atrial strain [%]	-1.08 (-4.42 – 2.26)	0.53	0.70	-1.98 (-5.61 – 1.65)	0.28	0.38
ABI mean	0.92 (0.64 – 1.32)	0.67	0.81	-0.02 (-0.04 – 0.01)	0.14	0.19
Carotid intima-media thickness [mm]	**0.03 (0.01 – 0.04)**	**0.001**	**0.001**	**-0.02 (-0.04 – -0.00)**	**0.046**	0.07
Carotid plaques/stenosis ***	0.00 (-0.02 – 0.02)	0.67	0.67	0.98 (0.66 – 1.45)	0.93	0.93
Myocardial infarction ***	0.67 (0.10 – 2.57)	0.61	0.97	2.99 (0.79 – 9.29)	0.07	0.20
Stroke ***	0.46 (0.11 – 1.31)	0.21	0.33	0.20 (0.01 – 0.94)	0.11	0.18

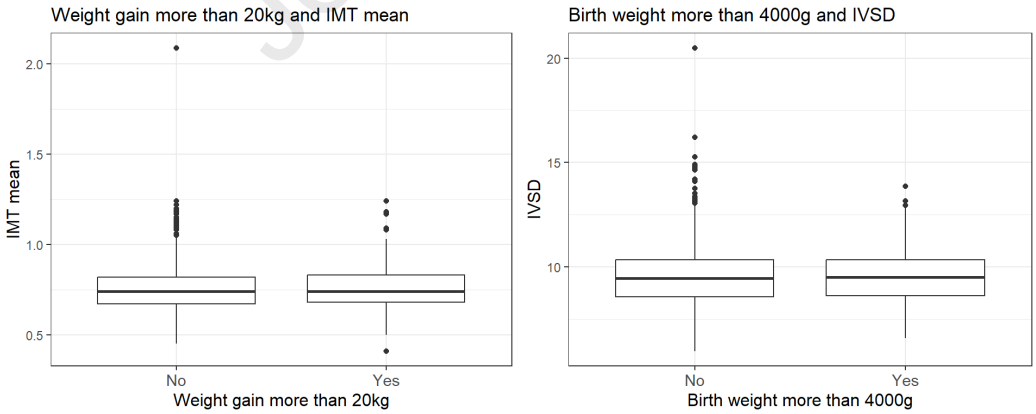
Table 4& 5: Demographic characteristics and electrocardiographic, echocardiographic and vascular parameters in women with adverse pregnancy outcomes gestational hypertension, gestational diabetes, excessive gestational weight gain, high (>4kg) and low (<2.5kg) fetal birth weight vs. those without (APO) – multivariable regression models; *** logistic regression models†: adjusted for age, type II diabetes mellitus, hypertension, dyslipidaemia, smoking; p adjust: adjusted p values according to Benjamini-Hochberg | **Bold font: p <0.05**; *Smoking:* current smoking upon inclusion*; sBP*: systolic blood pressure; *dBPT:* diastolic blood pressure; Body mass index (weight/$height^2$); $HbA1_c$: Glycated hemoglobin $A1_c$: LDL-C: Low-density lipoprotein cholesterol; NTproBNP: N-terminal prohormone of brain natriuretic peptide; IVSD [mm]: Interventricular septal thickness at end diastole; Relative Wall Thickness (2x posterior wall thicknes/ left ventricular diastolic diameter); LVMI [g/m^2]: left-ventricular mass index (Left ventricular mass/Body Surface Area); LAVI [mL/m^2]: Left atrial volume index (Left atrial volume/Body Surface Area); ABI: Ankle-brachial index; CIMT[mm]: Caroti intima-media thickness



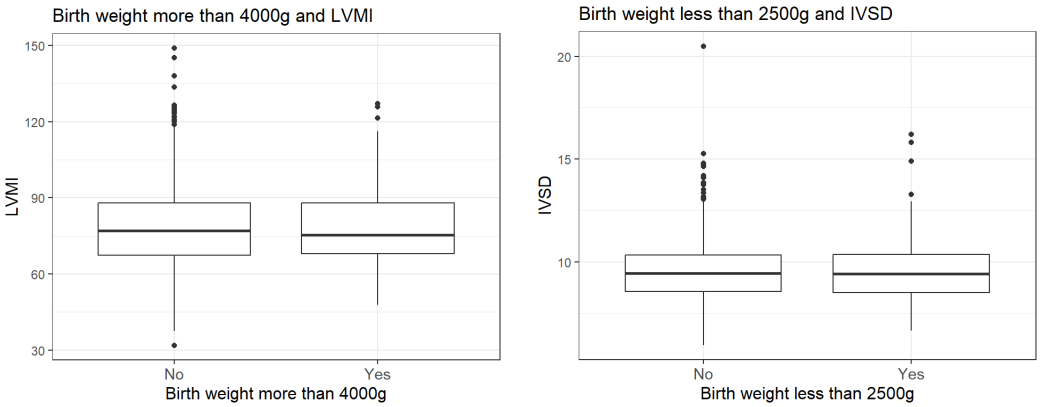
Supp.-Figure 1: Box plots. Left: women with gestational hypertension and carotid intima-media thickness (mm); right: women with gestational diabetes and indicators of left-ventricular remodeling: interventricular septum end-diastole (IVSD; mm)



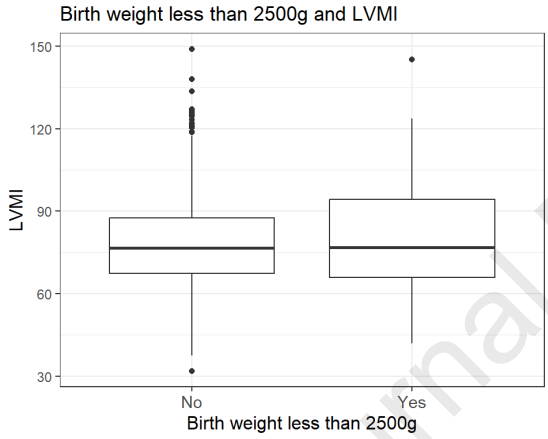
Supp.-Figure 2: Box plots; women with gestational diabetes and carotid intima-media thickness (mm; left) and indicators of left-ventricular remodeling: left ventricular mass index (LVMI; g/m^2; right)



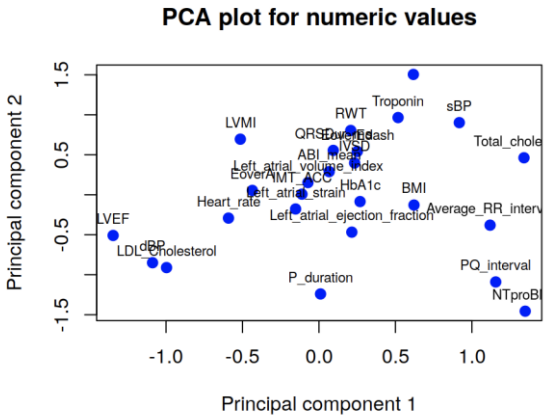
Supp.-Figure 3: Box plots. Left: women with excessive gestational weight gain (>20kg) and carotid intima-media thickness (mm); right: women that reported high fetal birth (>4kg) and indicators of left-ventricular remodeling: interventricular septum end-diastole (IVSD; mm)



Supp.-Figure 4: Box plots. Left: women that reported high fetal birth (>4kg) and indicators of left-ventricular remodeling: left ventricular mass index (LVMI; g/m^2); right: women that reported low fetal birth (<2.5kg) and indicators of left-ventricular remodeling: interventricular septum end-diastole (IVSD; mm)



Supp.-Figure 5: Box plots. Women that reported low fetal birth (<2.5kg) and indicators of left-ventricular remodeling: interventricular septum end-diastole (IVSD; mm)



Supp.-Figure 6: A principal component analysis was done for a better understanding of the underlying variances within the data. The analysis was done on the scaled numeric data. As the first component shows none of the variables have a strong correlation to PC1 meaning that none of them can be explained by another variable. As the plot shows most of the variables are distributed over

the first two components. Only cholesterol and diastolic blood pressure (dBP) seem to have a similar direction.

Highlights

- A history of previous adverse pregnancy outcomes was a common finding in a middle-aged urban female population
- Women with APO had more pronounced CV risk profiles and disease, possibly triggered or aggravated during pregnancy
- A history of gestational hypertension was associated with left ventricular remodeling and myocardial infarction
- Weight gain>20kg and birth weight>4kg corelated with lower left-atrial strain and higher carotid intima-media thickness
- A history of APO may indicate women in a community at increased risk of adverse cardiovascular outcomes in later life

Declaration of Interest

All participating institutes and departments from the University Medical Center Hamburg-Eppendorf contribute with scaled budgets to the overall funding of the Hamburg City Health Study (HCHS). Moreover, HCHS has received funding from the Innovative medicine initiative (IMI) under Grant No. 116074 (European public-private-partnership), Fondation Leducq (Grant Number 16 CVD 03), euCanSHare (Grant Agreement No. 825903-euCanSHare H2020) and the Deutsche Forschungsgemeinschaft (DFG project Grant TH1106/5-1; AA93/2-1). The HCHS is further supported by Joachim Herz Foundation; Deutsche Gesetzliche Unfallversicherung (DGUV); Deutsches Krebsforschungszentrum (DKFZ); Deutsches Zentrum für Herz-Kreislauf-Forschung (DZHK); Deutsche Stiftung für Herzforschung; Seefried Stiftung; Bayer; Amgen, Novartis; Schiller; Siemens; Topcon, Unilever and by donations from the "Förderverein zur Förderung der HCHS e.V.", and TePe® (2014). Sponsor funding has in no way influenced the content, conclusions or management of this study.

E.U., K.B., G.A., P.S., C.V.R. and C.A.B. have not received any project related funding.

N.M. reports personal fees from Abbott Laboratories, outside the submitted work.

CM receives study-specific funding from the German Center for Cardiovascular Research (DZHK; Promotion of women scientists' programme; *FKZ 81X3710112*), the *Deutsche Stiftung für Herzforschung*, the *Dr. Rolf M. Schwiete Stiftung*, NDD, and Loewenstein *Medical* unrelated to the current work. CM has received speaker fees from AstraZeneca, Novartis, Boehringer Ingelheim/Lilly, Bayer, Pfizer, Sanofi, Aventis, Apontis, Abbott outside this work. CM has participated in a Boehringer Ingelheim heart failure advisory board.

S.B. is supported by the Innovative medicine initiative (IMI) under Grant No. 116074, the Fondation Leducq under Grant Number 16 CVD 03, Siemens, Bayer, Astra Zeneca, Deutsche Gesetzliche Unfallversicherung (DGUV) and Novartis for project related analyses.

B.C.Z. has received an unrestricted project-related funding from BASF and Unilever for implementing a food frequency questionnaire into the interviews of the Hamburg City Health Study and reports fees from Jenapharm GmbH and BESINS Heathcare for lectures outside this work.

R.B.S has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme under the grant agreement No 648131, from the European Union's Horizon 2020 research and innovation programme under the grant agreement No 847770 (AFFECT-EU) and German Center for Cardiovascular Research (DZHK e.V.) (81Z1710103 and 81Z0710114); German Ministry of Research and Education (BMBF 01ZX1408A) and ERACoSysMed3 (031L0239). Wolfgang Seefried project funding German Heart Foundation. R.B.S has received lecture fees and advisory board fees from BMS/Pfizer and Bayer outside this work.

E.U., N.M., K.B., P.S., C.V.R, G.A, C.M., C.A.B, S.B, B.C.Z. and R.B.S. report no conflicts of interest.