

## Supplementary Materials

### History of gestational diabetes mellitus or hypertensive disorders of pregnancy and risk of chronic kidney disease

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**Supplementary Table 1. ICD-10 codes and OPCS-4 codes used to ascertain major diseases**

<b>Major diseases</b>	<b>ICD-10 codes</b>
Gestational diabetes mellitus	O244
Hypertensive disorders of pregnancy	O11, O13, O14, O140, O141, O142, O149, O15, O150, O151, O152, O159
Chronic kidney disease	
ICD-10 code	N18, N18.1, N18.2, N18.3, N18.4, N18.5, N18.9
OPCS-4 codes	L74.1-74.6, L74.8-74.9, M01.2-01.9, M02.3, M08.4, M17.2, M17.4, M17.8-17.9, X40.2, X40.5-40.6, X41.1-41.2
Hypertension	I10, I11, I11.0, I11.9, I12, I12.0, I12.9, I13, I13.0, I13.1, I13.2, I13.9, I15, I15.0, I15.1, I15.2, I15.8, I15.9
Hyperlipidemia	E78.0, E78.1, E78.2, E78.4, E78.5
Diabetes	E10, E10.1, E10.2, E10.3, E10.4, E10.5, E10.6, E10.7, E10.8, E10.9, E11, E11.0, E11.1, E11.2, E11.3, E11.4, E11.5, E11.6, E11.7, E11.8, E11.9, E12, E12.1, E12.8, E12.9, E13, E13.1, E13.2, E13.3, E13.5, E13.6, E13.7, E13.8, E13.9, E14, E14.1, E14.2, E14.3, E14.4, E14.5, E14.6, E14.7, E14.8, E14.9
Cardiovascular Disease	I20-I25, I60-I64

CKD: Chronic kidney disease; HDP: hypertensive disorders of pregnancy; GDM: gestational diabetes mellitus; ICD-10: International Statistical Classification of Diseases, Tenth Revision codes; OPCS-4: Office of Population Censuses and Surveys Classification of Interventions and Procedures.

**Supplementary Table 2. Baseline characteristics of women with and without history of GDM/HDP in the UK Biobank in the cross-sectional analysis**

	<b>Overall (172,133)</b>	<b>Non-GDM/HDP (168,629)</b>	<b>GDM/HDP (3,504)</b>	<b><i>P</i> value<sup>a</sup></b>
<b>Age, mean (SD), years</b>	56.96 (7.84)	57.05 (7.79)	52.58 (8.59)	< 0.001
<b>BMI, mean (SD), kg/m<sup>2</sup></b>	27.11 (5.05)	27.08 (5.03)	28.36 (5.77)	< 0.001
<b>Ethnicity (White, %)</b>	165,083 (95.9)	161,827 (96.0)	3,256 (92.9)	< 0.001
<b>Education (High level, %)</b>	76,238 (44.3)	74,525 (44.2)	1,713 (48.9)	< 0.001
<b>Townsend deprivation index, mean (SD)</b>	-1.54 (2.94)	-1.55 (2.94)	-1.39 (3.02)	0.023
<b>Smoking status, <i>n</i> (%)</b>				< 0.001
<b>Never</b>	104,446 (60.7)	102,107 (60.6)	2,339 (66.8)	
<b>Previous</b>	55,980 (32.5)	54,991 (32.6)	989 (28.2)	
<b>Current</b>	11,707 (6.8)	11,531 (6.8)	176 (5.0)	
<b>Alcohol consumption, <i>n</i> (%)</b>				< 0.001
<b>Special occasions only or never</b>	41,465 (24.1)	40,520 (24.0)	945 (27.0)	
<b>Less than 14 units per week</b>	103,535 (60.1)	101,392 (60.1)	2,143 (61.2)	
<b>Daily or almost daily</b>	27,133 (15.8)	26,717 (15.8)	416 (11.9)	
<b>Clinical laboratory markers, mean (SD)</b>				
<b>eGFR, ml/min/1.73 m<sup>2</sup></b>	88.85 (12.89)	88.79 (12.85)	91.98 (14.18)	< 0.001
<b>UACR, mg/g</b>	10.80 (16.75)	10.77 (16.58)	12.22 (23.42)	< 0.001

<b>Urate, mg/dL</b>	4.56 (1.11)	4.56 (1.10)	4.58 (1.15)	0.165
<b>Creatinine, mg/dL</b>	0.73 (0.13)	0.73 (0.13)	0.73 (0.16)	0.557
<b>Triglycerides, mg/dL</b>	138.90 (76.16)	138.88 (76.04)	139.89 (81.71)	0.435
<b>LDL-C, mg/dL</b>	140.92 (33.69)	141.06 (33.67)	134.36 (33.68)	< 0.001
<b>HDL-C, mg/dL</b>	61.42 (14.41)	61.47 (14.41)	58.93 (14.41)	< 0.001
<b>Fasting glucose, mg/dL</b>	91.23 (18.69)	91.09 (18.21)	97.70 (34.08)	< 0.001
<b>CRP, mg/dL</b>	0.27 (0.43)	0.27 (0.43)	0.29 (0.42)	0.013
<b>Medication use, <i>n</i> (%)</b>				
<b>Antihypertensive drug</b>	31,442 (18.3)	30,579 (18.1)	863 (24.6)	< 0.001
<b>Statin</b>	22,824 (13.3)	22,225 (13.2)	599 (17.1)	< 0.001
<b>Diabetes, <i>n</i> (%)</b>	6,599 (3.8)	5,616 (3.3)	983 (28.1)	< 0.001
<b>Hypertension, <i>n</i> (%)</b>	40,570 (23.6)	39,348 (23.3)	1,222 (34.9)	< 0.001
<b>Hyperlipidemia, <i>n</i> (%)</b>	20,777 (12.1)	20,286 (12.0)	491 (14.0)	< 0.001
<b>CVD, <i>n</i> (%)</b>	5,071 (2.9)	4,948 (2.9)	123 (3.5)	0.052

<sup>a</sup>*P* values were obtained from analysis of variance for continuous variables and chi-squared test for categorical variables. BMI: Body mass index; CRP: C-reactive protein; CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; GDM: gestational diabetes mellitus; HDL-C: high-density lipoprotein cholesterol; HDP: hypertensive disorders of pregnancy; LDL-C: low-density lipoprotein cholesterol; SD: standard deviation; UACR: urine albumin-to-creatinine ratio.

**Supplementary Table 3. Associations between GDM/HDP and renal function markers in the cross-sectional analysis**

	<b>Model 1</b>	<b>Model 2</b>	<b>Model 3</b>
	<b><math>\beta</math> (95%CI)<sup>a</sup></b>	<b><math>\beta</math> (95%CI)<sup>b</sup></b>	<b><math>\beta</math> (95%CI)<sup>c</sup></b>
<b>GDM/HDP</b>			
eGFR <sub>cys</sub>	-0.07 (-0.10--0.04)	0.00 (-0.02-0.03)	-0.00 (-0.02-0.02)
eGFR <sub>cr</sub>	-0.01 (-0.04-0.02)	0.02 (-0.01-0.05)	0.02 (-0.01-0.05)
UACR	0.11 (0.08-0.14)	0.12 (0.08-0.15)	0.08 (0.05-0.11)
Urate	0.14 (0.11-0.17)	0.03 (-0.00-0.06)	-0.01 (-0.04-0.02)
Creatinine	0.03 (-0.00-0.06)	0.00 (-0.03-0.03)	-0.01 (-0.04-0.02)
<b>GDM</b>			
eGFR <sub>cys</sub>	-0.08 (-0.13--0.04)	0.03 (-0.01-0.08)	0.00 (-0.04-0.04)
eGFR <sub>cr</sub>	0.05 (-0.01-0.10)	0.08 (0.03-0.14)	0.08 (0.03-0.13)
UACR	0.20 (0.14-0.26)	0.20 (0.14-0.26)	0.12 (0.06-0.18)
Urate	0.12 (0.06-0.17)	-0.04 (-0.09-0.01)	-0.09 (-0.14--0.04)
Creatinine	-0.02 (-0.08-0.03)	-0.06 (-0.11--0.01)	-0.06 (-0.11--0.01)
<b>HDP</b>			
eGFR <sub>cys</sub>	-0.06 (-0.09--0.03)	-0.01 (-0.04-0.02)	0.00 (-0.03-0.03)
eGFR <sub>cr</sub>	-0.03 (-0.07-0.00)	-0.01 (-0.04-0.03)	0.00 (-0.03-0.04)
UACR	0.08 (0.04-0.12)	0.09 (0.05-0.13)	0.07 (0.03-0.11)
Urate	0.15 (0.11-0.19)	0.05 (0.02-0.09)	0.02 (-0.02-0.05)
Creatinine	0.05 (0.01-0.08)	0.02 (-0.01-0.06)	0.01 (-0.02-0.05)

<sup>a</sup>Adjusted for age, ethnicity, education, and Townsend deprivation index; <sup>b</sup>Additionally adjusted for BMI, smoking status, and alcohol consumption; <sup>c</sup>Further adjusted for triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, blood glucose, C-reactive protein, and medication use. CI: Confidence interval; eGFR<sub>cr</sub>: estimated glomerular filtration rate using creatinine; eGFR<sub>cys</sub>: estimated glomerular filtration rate using cystatin C; GDM: gestational diabetes mellitus; HDP: hypertensive disorders of pregnancy; UACR: urine albumin-to-creatinine ratio.

**Supplementary Table 4. Prospective associations between GDM/HDP and incident CKD in major subgroups in the UK Biobank**

Subgroups	CKD/Person-years	GDM/HDP <sup>a</sup>	<i>P</i> for interaction <sup>b</sup>	FDR-adjusted <i>P</i> for interaction <sup>c</sup>	GDM <sup>a</sup>	<i>P</i> for interaction <sup>b</sup>	FDR-adjusted <i>P</i> for interaction <sup>c</sup>	HDP <sup>a</sup>	<i>P</i> for interaction <sup>b</sup>	FDR-adjusted <i>P</i> for interaction <sup>c</sup>
Age groups			0.088	0.126		0.304	0.386		0.251	0.586
≤ 60	1,790/1,416,572	1.49 (1.15-1.93)			1.83 (1.27-2.65)			1.30 (0.93-1.83)		
> 60	3,812/851,172	1.18 (0.92-1.52)			1.65 (1.09-2.50)			1.03 (0.76-1.40)		
BMI groups			0.675	0.740		0.444	0.444		0.724	0.875
Underweight/Normal	4,370/1,367,352	1.46 (0.95-2.26)			2.57 (1.27-5.21)			1.23 (0.73-2.09)		
Overweight/Obesity	1,232/900,393	1.30 (1.07-1.59)			1.71 (1.27-2.31)			1.12 (0.87-1.44)		
Baseline eGFR			0.013	0.091		0.174	0.366		0.038	0.266
> 90	4,585/1,000,933	1.21 (0.97-1.49)			1.73 (1.23-2.43)			1.02 (0.78-1.33)		

≤ 90	1,017/1,266,811	1.69 (1.22-2.34)			1.79 (1.12-2.86)			1.70 (1.11-2.59)	
Diabetes			0.740	0.740		0.199	0.366		0.750 0.875
No	4,922/2,194,375	1.20 (0.94-1.52)			2.25 (0.93-5.40)			1.15 (0.90-1.47)	
Yes	680/73,370	1.05 (0.79-1.39)			1.08 (0.79-1.47)			1.06 (0.61-1.84)	
Hypertension			0.090	0.126		0.209	0.366		0.350 0.613
No	2,992/1,775,892	1.05 (0.77-1.42)			1.35 (0.84-2.18)			0.97 (0.66-1.40)	
Yes	2,610/491,853	1.50 (1.20-1.88)			2.17 (1.55-3.03)			1.22 (0.92-1.63)	
Hyperlipidemia			0.080	0.126		0.008	0.056		0.996 0.996
No	4,132/2,017,945	1.19 (0.95-1.5)			1.30 (0.87-1.95)			1.15 (0.88-1.50)	
Yes	1,470/249,800	1.60 (1.2-2.14)			2.50 (1.71-3.64)			1.15 (0.75-1.75)	
CVD			0.076	0.126		0.331	0.386		0.218 0.586
No	5,132/2,211,218	1.27 (1.05-1.54)			1.76 (1.31-2.37)			1.10 (0.86-1.40)	

Yes	470/56,527	1.94 (1.19-3.16)	2.30 (1.12-4.72)	1.69 (0.87-3.28)
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<sup>a</sup>Models were adjusted for age, ethnicity, education, Townsend deprivation index, BMI, smoking status and alcohol consumption, eGFR, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, blood glucose, C-reactive protein, and use of medication; <sup>b</sup>*P* values for interaction were derived from likelihood ratio tests comparing nested models with and without cross-product terms between the stratifying variable and GDM/HDP status; <sup>c</sup>FDR-adjusted *P* for interaction was calculated using the Benjamini-Hochberg procedure to control for multiple comparisons. BMI: Body mass index; CI: confidence interval; CKD: chronic kidney disease; CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; FDR: false discovery rate; GDM: gestational diabetes mellitus; HDP: hypertensive disorders of pregnancy; HR: hazard ratio.

**Supplementary Table 5. Prospective associations between GDM/HDP with incident CKD: main analysis and sensitivity analysis additionally adjusted for parity**

	CKD/person-years	Main analysis <sup>a</sup> HR (95%CI)	Main analysis plus parity HR (95%CI)
<b>GDM/HDP</b>			
<b>No</b>	5,477/2,222,161	1.00 (Reference)	1.00 (Reference)
<b>Yes</b>	125/45,583	1.33 (1.12-1.59)	1.33 (1.12-1.59)
<b>GDM</b>			
<b>No</b>	5,549/2,254,208	1.00 (Reference)	1.00 (Reference)
<b>Yes</b>	53/13,536	1.82 (1.39-2.40)	1.82 (1.39-2.40)
<b>HDP</b>			
<b>No</b>	5,526/2,234,795	1.00 (Reference)	1.00 (Reference)
<b>Yes</b>	76/32,949	1.14 (0.91-1.43)	1.14 (0.91-1.43)

<sup>a</sup>Adjusted for age, ethnicity, education, Townsend deprivation index, BMI, smoking status and alcohol consumption, eGFR, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, blood glucose, C-reactive protein, and use of medication; <sup>b</sup>Additionally adjusted for parity. BMI: Body mass index; CI: confidence interval; CKD: chronic kidney disease; GDM: gestational diabetes mellitus; HDP: hypertensive disorders of pregnancy; HR: hazard ratio.

**Supplementary Table 6. Major chronic conditions as potential mediators of the association between prior GDM and incident CKD**

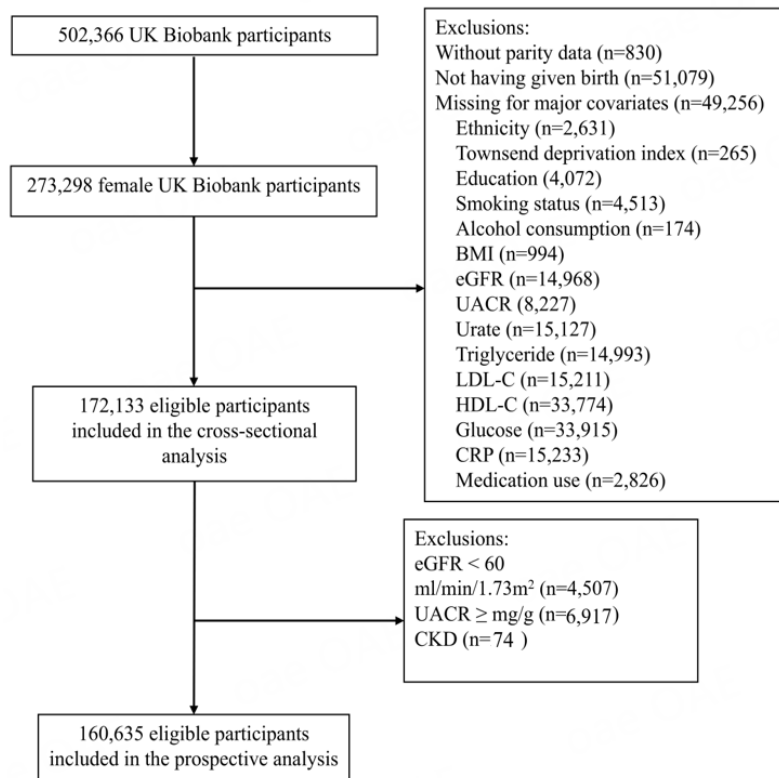
<b>Mediators</b>	<b>Indirect effect <math>\beta</math> (95%CI)</b>	<b>Direct effect <math>\beta</math> (95%CI)</b>	<b>Proportion mediated (95%CI)</b>	<b><i>P</i> value</b>
Diabetes	0.195 (-0.130, 0.478)	0.406 (0.347, 0.465)	67.6% (44.1%, 100%)	0.002
Hypertension	0.609 (0.296, 0.880)	-0.009 (-0.041, 0.020)	-1.4% (-9.2%, 3.5%)	0.630
Hyperlipidemia	0.601 (0.285, 0.879)	-0.001 (-0.031, 0.026)	-0.1% (-6.1%, 4.4%)	0.988
CVD	0.548 (0.211, 0.857)	0.053 (-0.023, 0.120)	8.7% (-3.6%, 28.0%)	0.148

CI: Confidence interval; CKD: chronic kidney disease; CVD: cardiovascular disease; GDM: gestational diabetes mellitus.

**Supplementary Table 7. Major chronic conditions as potential mediators of the association between prior HDP and incident CKD**

<b>Mediators</b>	<b>Indirect effect <math>\beta</math> (95%CI)</b>	<b>Direct effect <math>\beta</math> (95%CI)</b>	<b>Proportion mediated (95%CI)</b>	<b><i>P</i> value</b>
Diabetes	0.131 (-0.129, 0.350)	0.003 (-0.023, 0.034)	1.9% (-100%, 92.1%)	0.938
Hypertension	0.078 (-0.163, 0.304)	0.056 (0.035, 0.079)	41.7% (-100%, 100%)	0.284
Hyperlipidemia	0.129 (-0.120, 0.355)	0.004 (-0.006, 0.015)	3.1% (-44.8%, 39.9%)	0.566
CVD	0.105 (-0.154, 0.324)	0.028 (-0.013, 0.069)	21.1% (-100%, 100%)	0.404

CI: Confidence interval; CKD: chronic kidney disease; CVD: cardiovascular disease; HDP: hypertensive disorders of pregnancy.



**Supplementary Figure 1.** Flowchart of participant eligibility. BMI: Body mass index; CKD: chronic kidney disease; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; UACR: urine albumin-to-creatinine ratio.