

Multi-fetal pregnancy, preeclampsia and long-term cardiovascular disease

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Table S1. ICD codes for exposures and outcomes

Exposure variables					
ICD 10		ICD 9		ICD 8	
Preeclampsia					
O11	Preeclampsia superimposed on chronic hypertension	642H	Pre-eclampsia or eclampsia superimposed on pre-existing hypertension		
O14	Preeclampsia			637	Pre-eclampsia, eclampsia and toxicosis not further specified
Q14.0	Mild to moderate preeclampsia	42E	Mild or unspecified preeclampsia		
O14.1	Severe preeclampsia	642F	Severe preeclampsia		
O14.2	HELLP syndrome				
O14.9	Preeclampsia, unspecified			637,99	Toxicosis not further specified
O15	Eclampsia	642G	Eclampsia	637,10	Eclampsia
Essential hypertension					
I10	Essential hypertension	401	Essential hypertonia	400	Malign essential hypertension
				401,99	Benign essential hypertension
		402	Hypertension with cardiac disease	402,99	Hypertension with cardiac disease
	Hypertensive renal disease	403	Essential hypertension with chronic kidney disease	403,99	Essential hypertension with chronic kidney disease
I12		404	Hypertension with cardiac and kidney disease	404	Hypertension with cardiac and kidney disease
I15	Secondary hypertension	405	Secondary hypertension		
O10	Pre-existing hypertension complicating pregnancy, childbirth and the puerperium	642C	Other unspecified essential hypertension complicating pregnancy, childbirth, and the puerperium		
O11	Preeclampsia superimposed on chronic hypertension	642H	Pre-eclampsia or eclampsia superimposed on pre-existing hypertension		
Diabetes mellitus, pregestational					
E10	Type 1 diabetes mellitus	250	Diabetes mellitus		
E11	Type 2 diabetes mellitus	648A	Diabetes mellitus		
E12	Malnutrition-related diabetes mellitus				

- E13 Other specified diabetes mellitus
- E14 Unspecified diabetes mellitus
- O24.1 Type 2 diabetes mellitus, pregestational
- O24.2 Malnutrition-related diabetes mellitus, pregestational
- O24.3 Unspecified diabetes mellitus, pregestational

Diabetes mellitus, gestational

- O24.4 Diabetes mellitus, gestational 648W Abnormal glucose tolerance during pregnancy

Outcome variables

ICD 10		ICD 9		ICD 8	
Ischemic heart disease					
I20	Angina pectoris	413	Angina pectoris	413	Angina pectoris
I21	Acute myocardial infarction	410	Acute myocardial infarction	410	Acute myocardial infarction
I22	Subsequent myocardial infarction	411	Other acute and subacute forms of ischemic heart disease	411	Other acute and subacute forms of ischaemic heart disease
I23	Certain current complications following acute myocardial infarction	412	Old myocardial infarction	412,91	Old myocardial infarction, with no information of hypertension
I24	Other acute ischaemic heart diseases	414W	Other chronic ischemic heart disease, specified	414,00	Asymptomatic ischaemic heart disease, with hypertension
I25	Chronic ischaemic heart disease	414X	Chronic ischemic heart disease, unspecified	414,99	Asymptomatic ischaemic heart disease, with no information of hypertension
		414A	Coronary arteriosclerosis of native coronary artery		

Heart failure

- I11.0 Hypertensive heart disease with (congestive) heart failure
- I13.0 Hypertensive heart and renal disease with (congestive) heart failure

I13.2	Hypertensive heart and renal disease with both (congestive) heart failure and renal failure				
I50	Heart failure	428	Congestive heart failure, unspecified	428.99	Heart failure, unspecified
Cerebrovascular disease					
I60.0-7	Subarachnoid haemorrhage	430	Subarachnoid haemorrhage	430	Subarachnoid haemorrhage
I61	Intracerebral haemorrhage	431	Intracerebral haemorrhage	431	Intracerebral haemorrhage
I62	Other nontraumatic intracranial haemorrhage	432	Other and unspecified intracranial haemorrhage	433	Cerebral thrombosis
I63	Cerebral infarction	434	Occlusion of cerebral arteries	434	Cerebral embolism
I64	Stroke, not specified as haemorrhage or infarction	436	Acute cerebrovascular disease, incompletely defined	436	Acute, cerebrovascular disease, not further defined
I65	Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction	433	Occlusion and stenosis of precerebral arteries	432	Occlusion of precerebral arteries
I66	Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction	437B	Other generalised ischaemic cerebrovascular disease	437	Generalised ischaemic cerebrovascular disease
I67.2	Cerebral arteriosclerosis	437A	Cerebral arterioerosclerosis		
I69	Sequelae of cerebrovascular disease	438	Later effects by cerebrovascular disease	438	Cerebrovascular disease, not further defined
G45	Transient cerebral ischaemic attacks and related syndromes	435	Transient cerebral ischemia	435	Transient cerebral ischaemia

Table S2. Maternal and pregnancy characteristics according to singleton pregnancy without and with preeclampsia or multi-fetal pregnancy without and with preeclampsia in first deliveries in the restricted population of 186 775 births **1995-2010**

Maternal and pregnancy characteristics of first births	Singleton pregnancy				Multi-fetal pregnancy			
	Without preeclampsia		With preeclampsia		Without preeclampsia*		With preeclampsia**	
	1995-2010	N	N	N	N	N	N	
N Total = 186 775	173 247	9 031	3 764	733				
BMI kg/m² %								
<18.5	2 785	1.9	93	1.2	47	1.5	7	1.2
18.5-24.9	101 461	68.9	4 007	52.2	2 044	65.0	356	60.1
25-29.9	32 332	22.0	2 293	29.9	803	25.5	165	27.9
≥30	10 713	7.3	1 289	16.8	251	8.0	64	10.8
Missing	25 956		1 349		619		141	
Diabetes %								
No	171 128	98.8	8 712	96.5	3 713	98.7	723	98.6
Preexisting	874	0.5	184	2.0	16	0.4	2	0.3
Gestational	1 245	0.7	135	1.5	35	0.9	8	1.1
Kidney disease %	603	0.4	39	0.4	20	0.5	1	0.1
SLE %	126	0.1	11	0.1	4	0.1	1	0.1
Assisted reproduction %								
No	162 047	93.5	8 382	92.8	2 317	61.6	465	63.4
Ovary stimulation	2 890	1.7	191	2.1	186	4.9	25	3.4
IVF	8 310	4.8	458	5.1	1 261	33.5	243	33.2

* Multiple pregnancy without preeclampsia including triplex or more n=84

** Multiple pregnancy with preeclampsia including triplex or more n=17

Table S3. Singleton and multi-fetal pregnancies with and without preeclampsia according to later compound cardiovascular disease, and ischemic heart disease, heart failure and cerebrovascular disease separately, among 892 425 first deliveries **1973-2010**

Maternal and pregnancy characteristics of first birth 1973-2010	Total	Compound cardiovascular disease*		Ischemic heart disease		Heart failure		Cerebrovascular disease	
		N	%	N	%	N	%	N	%
Total	892 425	18 415	2.1	7 659	0.9	1 993	0.2	9 032	1.0
Singleton	880 971	18 246	2.1	7 589	0.9	1 975	0.2	8 947	1.0
Singleton without preeclampsia	847 567	17 217	2.0	7 120	0.8	1 862	0.2	8 486	1.0
Singleton with preeclampsia	33 404	1 029	3.1	469	1.4	113	0.3	461	1.4
Multi-fetal	11 454	169	1.5	70	0.6	18	0.2	85	0.7
Multi-fetal without preeclampsia	9 935	145	1.5	63	0.6	17	0.2	69	0.7
Multi-fetal with preeclampsia	1 519	24	1.6	7	0.5	1	0.1	16	1.1

* The number of compound cardiovascular disease is lower than the sum of the numbers of ischemic heart disease, heart failure and cerebrovascular disease, since some events occurred at the same time.

Table S4. Maternal and pregnancy characteristics according to later compound cardiovascular disease in the restricted population of 186 775 first deliveries **1995-2010**

Maternal and pregnancy characteristics of first births 1995-2010	Total	Compound cardiovascular disease		P-value
		N	%	
Total	186 775	987	0.5	
Maternal age at birth, years				<.0001
<30	62 804	303	0.5	
30-34	77 141	391	0.5	
35-39	39 034	22	0.6	
≥40	7 796	71	0.9	
BMI, kg/m²				<.0001
<18.5	2 932	13	0.4	
18.5-24.9	107 868	446	0.4	
25-29.9	35 593	221	0.6	
≥30	12 317	134	1.1	
Missing (n)	28 065	173		
Diabetes				<.0001
No	184 276	932	0.5	
Pregestational	1 076	36	3.4	
Gestational	1 423	19	1.3	
Kidney disease				0.7899
No	186 112	983	0.5	
Yes	663	4	0.6	
SLE				0.0092
No	186 633	984	0.5	
Yes	142	3	2.1	
Assisted reproduction				0.6741
No	173 211	922	0.5	
Ovary stimulation	3 292	17	0.5	
IVF	10 272	48	0.5	

Table S5a: Hazard ratios for later compound cardiovascular disease from maternal age three months after delivery among 457 147 women with age at end of follow-up **less than 50 years** with singleton first deliveries without and with preeclampsia and multi-fetal first deliveries without and with preeclampsia **1973-2010**

1973-2010	Unadjusted Hazard Ratio	(95% CI)	Adjusted*	(95% CI)
Singleton without preeclampsia	ref		ref	
Singleton with preeclampsia	1.58	(1.46-1.71)	1.62	(1.50-1.76)
Multi-fetal without preeclampsia	0.59	(0.47-0.74)	0.80	(0.64-1.01)
Multi-fetal with preeclampsia	0.64	(0.37-1.11)	0.96	(0.55-1.65)

* Adjusted for maternal age at delivery, chronic hypertension before first birth, level of education and time-period of birth.
Number of observations read: 455 581.

Table S5b: Hazard ratios for later compound cardiovascular disease from maternal age three months after delivery among 435 278 women with age at end of follow-up **more than 50 years** with singleton first deliveries without and with preeclampsia and multi-fetal first deliveries without and with preeclampsia **1973-2010**

1973-2010	Crude Hazard Ratio	(95% CI)	Adjusted*	(95% CI)
Singleton without preeclampsia	ref		ref	
Singleton with preeclampsia	1.58	(1.42-1.76)	1.62	(1.46-1.81)
Multi-fetal without preeclampsia	1.08	(0.85-1.36)	1.16	(0.91-1.47)
Multi-fetal with preeclampsia	1.49	(0.82-2.67)	1.63	(0.90-2.95)

* Adjusted for maternal age at delivery, chronic hypertension before first birth, level of education and time-period of birth.
Number of observations read: 433 819.