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Pre-eclampsia and cardiovascular risk: a long-term nationwide cohort study on over 120 000 Finnish women

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ABSTRACT

Objectives To investigate the impact of pre-eclampsia on the future cardiovascular risk in Finnish women

Design A registry-based nationwide controlled cohort study.

Setting Women hospitalised for pre-eclampsia in 1969–1993 and control women with a history of normotensive pregnancies followed from the pre-eclampsia diagnosis until 2019 for cardiovascular outcomes.

Participants 31 688 women with and 91 726 control women without a history of pre-eclampsia.

Primary outcome measures Incidences of and deaths from ischaemic heart disease (IHD), myocardial infarction (MI) and stroke.

Results In total, 25 813 (81.5%) women had pre-eclampsia without severe features, 4867 (15.4%) had pre-eclampsia with severe features and 1006 (3.2%) women developed eclampsia. Women with a history of pre-eclampsia showed elevated risks for IHD (HR 1.52, 95% CI 1.44 to 1.59), MI (HR 1.66, 95% CI 1.52 to 1.81) and stroke (HR 1.40, 95% CI 1.32 to 1.48). The risks for death from IHD (HR 1.50, 95% CI 1.28 to 1.75), MI (1.63, 95% CI 1.30 to 2.05) and stroke (1.44, 95% CI 1.03 to 2.01) were also elevated. Pre-eclampsia with severe features or eclampsia was accompanied with 15% higher IHD risk, 19% higher MI risk and 26% higher stroke risk than pre-eclampsia without severe features. The highest risk elevations of 30% for IHD, 32% for MI and 30% for stroke were observed in women with recurrent pre-eclampsia (n=4180).

Conclusion Pre-eclampsia-related significant elevations in CVD risks of Finnish women with inherently high risk for these diseases were of the same magnitude as reported previously from other countries. Thus, women with a history of pre-eclampsia should be screened and treated early for modifiable cardiovascular risk factors.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study included a large and comprehensive nationwide population with a total of 123 414 women.
⇒ The follow-up lasted for a mean of 33 years; at its end, more than half of the women were over 60 years of age.
⇒ Mutual risk factors for pre-eclampsia and cardiovascular diseases, such as diabetes mellitus, essential hypertension and obesity, could not be reported. However, women with pre-existing ischaemic heart disease or stroke were excluded from the study population.

INTRODUCTION

Cardiovascular diseases (CVD) remain women's leading cause of death worldwide, despite growing awareness and novel treatment possibilities.[1] Furthermore, women have a worse outcome than men after a vascular event,[2 3] which may derive from the fact that cardiovascular research has focused predominantly on men. Finnish women have been characterised with a high cardiovascular risk for decades, and despite the recent decreasing trend in the risk, the mortality rate for ischaemic heart disease (IHD) in Finnish women was 36% higher than the average in the European Union in 2017.[4] The causal mechanisms behind this phenomenon are unknown, but presumably genetic, dietary and other lifestyle factors are involved.

Pre-eclampsia is a pregnancy-specific vascular disorder that affects, on average, 3.8% of pregnancies in Europe.[5] The incidence ranges from 4.6% to 13.9% of pregnancies in Finland, based on different studies.[6–8] A history of pre-eclampsia predisposes a woman to an approximately two-fold CVD risk later in life.[9 10] A question arises of whether Finnish women, being inherently at high risk for CVD, could respond to a pre-eclamptic pregnancy with larger rises in CVD incidence than do women of other origins. We therefore conducted a nationwide, long-term cohort study to assess the impact of pre-eclampsia on the future CVD risk in Finnish women.

METHODS

Participants

We collected women hospitalised for pre-eclampsia in 1969–1993 (n=31 688) from the Hospital Discharge Register of the Finnish Institute for Health and Welfare. Since the

register did not include personal identification numbers prior to 1969, we were not able to trace pre-eclampsia patients from an earlier period. For pre-eclampsia diagnoses, we employed the codes from International Classification of Diseases, Eighth Revision (ICD-8) 637.03; 637.04; 637.09; 637.10 and 637.99; and ICD Ninth Revision (ICD-9) codes 6423A, 6425A, 6424A and 6426A. Pre-eclampsia diagnoses were further categorised as pre-eclampsia without severe features (637.03; 637.09; 637.99; 6423A and 6424A referring to the clinical presentation of mild pre-eclampsia), pre-eclampsia with severe features (637.04 and 6425A referring to the clinical presentation of severe pre-eclampsia) and eclampsia (637.10 and 6426A). If a woman had been admitted to the hospital repeatedly with different pre-eclampsia diagnoses, we classified her according to the most severe one that she had been diagnosed with, when defining the type of her pre-eclampsia. We traced three controls for each pre-eclamptic woman who had had normotensive pregnancies during 1969–1993. These control women (n=91 726), matched by age (±6 months), place of residence at the index day and the total number of pregnancies, were collected from the national population register. Thus, the final study population consisted of 123 414 women.

Follow-up and outcomes

The follow-up for the pre-eclamptic and the matched control women started from the date of the pre-eclampsia diagnosis. The follow-up for each woman continued until primary outcome, death from any cause, emigration or the end of follow-up (31 December 2019), whichever came first.

The primary outcomes were any event of IHD, its most acute form myocardial infarction (MI), stroke and deaths from these diseases. These outcomes were selected for being the most common primary and the most reliably detectable manifestations of CVD. The diagnoses were collected according to ICD-8 codes 410–414 for IHD, 410 for MI and 430–432, 434 and 436 for stroke; ICD-9 codes 410–414 for IHD, 410 and 412 for MI and 430–436 for stroke; and ICD 10th Revision (ICD-10) codes I20–25 for IHD, I21–23 for MI and I60-64 for stroke. The non-fatal outcome diagnoses were received from the Hospital Discharge Register (1969–1993) and the Care Register for Health Care (1994–2019) of Finnish Institute for Health and Welfare. The fatal outcomes were collected from the Causes of Death Register of Statistics Finland in 1971–2019. These national registries are accurate and reproducible.[11 12] Several subgroup analyses within the pre-eclamptic population were performed to investigate the impact of different maternal and obstetrical features on future IHD, MI and stroke risks. Altogether 4 174 132 woman-years accumulated in the follow-up for IHD, 4 255 279 in the follow-up for MI and 4 189 619 in the follow-up for stroke.

Statistical methods

The incidences of IHD, MI, stroke and deaths from these events were recorded in the pre-eclamptic and control groups, and the relative HRs with 95% CIs were calculated with Cox proportional regression. Within the pre-eclamptic cohort, the incidences of IHD, MI and stroke were compared between pre-eclamptic subgroups using Cox proportional regression. Crude HRs were considered representative due to the detailed matching of the groups according to the available background data. Thus, adjusted HRs were not calculated. All statistical analyses were conducted using R software.

Patient and public involvement

The involvement of patients or the public was not achievable in this retrospective register-based study.

RESULTS

The cohorts were comparable in terms of relevant background data (table 1). More than half of the women were younger than 30 years on the index day, and 65% of the pre-eclamptic women were nulliparous. The majority of the study subjects lived in Southern or Western Finland, which corresponds to the distribution of the national population. The mean follow-up time was 33.4 years in the pre-eclampsia group and 33.6 years in the control group, and the mean age was 62.0 years in the pre-eclamptic group and 62.2 years in the control group at the end of the follow-up. Progression to eclampsia was reported in 1006 women, 8 of whom died due to it.

The most frequent outcomes were IHD and stroke, whereas IHD death was the most common fatal outcome (table 2). The risks for all primary outcomes were significantly higher in the pre-eclamptic group than in the control group. The greatest difference between the groups was shown in the risk of MI (HR 1.66, 95% CI 1.52 to 1.81), followed by MI death (HR 1.63, 95% CI 1.30 to 2.05) and any IHD (HR 1.52, 95% CI 1.44 to 1.59). Both IHD and stroke occurred in 1.0% of the pre-eclamptic women (n=313) and in 0.6% of the control women (n=522) (p<0.001).

Either pre-eclampsia with severe features or eclampsia was accompanied with 15% higher risk of IHD, 19% higher risk of MI and 26% higher risk of stroke than exposure to pre-eclampsia without severe features (table 3). Recurrence of pre-eclampsia predicted the highest risk elevations. Differences in risks between pre-eclamptic singleton and twin pregnancies did not reach statistical significance. Women of the lowest age quartile at the pre-eclampsia diagnosis, that is under 24 years, were observed to have 34% greater stroke risk than women aged 24 years or older. Women who lived in Northern or Eastern Finland were at 31%, 29% and 12% higher risks for IHD, MI and stroke, respectively, compared with women from Southern or Western Finland.

DISCUSSION

Our nationwide results show that a prior pre-eclamptic pregnancy is associated with risk rises of approximately

Table 1 Background and follow-up data for the pre-eclampsia group and the control group without history of pre-eclampsia

		Pre-eclampsia group		Control group	
		n	%	n	%
		31 688	**100**	**91 726**	**100**
Age at index day (years)	14–20	1490	4.6	42 382	4.6
	20–24	7660	24.2	22 020	24.0
	25–29	10 888	34.4	31 689	34.6
	30–34	7020	22.2	20 399	22.2
	35–39	3564	11.2	10 250	11.2
	40–50	1094	3.5	3130	3.4
	Mean (SD)	28.6 (5.70)	NA	28.6 (5.67)	NA
	Median (IQR)	27.9 (24.4–32.3)	NA	28.0 (24.5–32.3)	NA
County	Southern	13 342	42.1	39 037	42.6
	Western	8998	28.4	25 837	28.2
	Eastern	4893	15.4	14 140	15.4
	Northern	4455	14.1	12 712	13.9
Age at the end of follow-up (years)	<50	2129	6.7	5814	6.3
	50–59	11 074	34.9	31 496	34.3
	60–69	12 728	40.2	37 059	40.4
	70–79	5189	16.4	15 501	16.9
	≥ 80	568	1.8	1856	2.0
	Mean (SD)	62.0 (8.71)	NA	62.2 (8.92)	NA
	Median (IQR)	61.8 (56.3–68.0)	NA	62.1 (56.5–68.2)	NA
Duration of follow-up (years)	Mean (SD)	33.4 (7.69)	NA	33.6 (7.84)	NA
	Median (IQR)	32.7 (27.8–38.9)	NA	32.8 (28.9–39.0)	NA
Type of pre-eclampsia	Without severe features	25 814	81.5	NA	NA
	With severe features	4867	15.4	NA	NA
	Eclampsia	1007	3.2	NA	NA

IQR, interquartile range (25th and 75th percentile); NA, not available.

Table 2 Incidence and mortality of ischaemic heart disease (IHD), myocardial infarction (MI) and stroke among pre-eclamptic women and control group, followed in 1969–2019

	Pre-eclampsia group (n=31 688)		Control group (n=91 726)		HR (95% CI)*
	n	Rate per 100 000 woman years	n	Rate per 100 000 woman years	
IHD	2331	217	4526	146	1.52 (1.44 to 1.59)
IHD death	239	22	464	14	1.50 (1.28 to 1.75)
MI	777	52	1375	49	1.66 (1.52 to 1.81)
MI death	116	19	206	10	1.63 (1.30 to 2.05)
Stroke	1693	156	3518	114	1.40 (1.32 to 1.48)
Stroke death	51	4	103	3	1.44 (1.03 to 2.01)

*Control group as reference population.

Table 3 Impact of different maternal features on the risk of ischaemic heart disease (IHD), stroke and myocardial infarction (MI) in women with a history of pre-eclampsia, followed in 1969–2019

		n	IHD HR (95% CI)	MI HR (95% CI)	Stroke HR (95% CI)
Type of pre-eclampsia	Without severe features	25 814 (81.5%)	1.00	1.00	1.00
	With severe features or eclampsia	5874 (18.5%)	1.15 (1.04 to 1.27)	1.19 (1.01 to 1.40)	1.26 (1.12 to 1.41)
Eclampsia	No	30 681 (96.8%)	1.00	1.00	1.00
	Yes	1007 (3.2%)	0.85 (0.68 to 1.07)	0.80 (0.54 to 1.19)	1.15 (0.91 to 1.45)
Recurrence of pre-eclampsia	No	27 506 (86.8%)	1.00	1.00	1.00
	Yes	4180 (13.2%)	1.30 (1.16 to 1.45)	1.32 (1.09 to 1.60)	1.30 (1.14 to 1.47)
Number of fetuses in the index pregnancy	Singleton	30 862 (78.4%)	1.00	1.00	1.00
	Twins	826 (21.6%)	0.83 (0.62 to 1.09)	0.77 (0.49 to 1.22)	0.73 (0.51 to 1.03)
Age at index day (years)	<24	7053 (22.3%)	1.06 (0.94 to 1.20)	1.08 (0.87 to 1.36)	1.34 (1.17 to 1.52)
	≥24	24 635 (77.7%)	1.00	1.00	1.00
County	Southern or western	22 340 (70.5%)	1.00	1.00	1.00
	Northern or eastern	9348 (29.5%)	1.31 (1.20 to 1.42)	1.29 (1.11 to 1.49)	1.12 (1.01 to 1.24)

50% for CVD in the Finnish female population with an inherently high cardiovascular risk. However, the observed risk elevations are of the same magnitude as those reported from other Nordic countries, the UK and the USA (table 4). Thus, Finnish women do not respond to a prior pre-eclampsia with an exceptionally high CVD risk. Our results are in line with results from Northern Finland Birth Cohort 1966 that reported pre-eclamptic women (n=242) to have 36% higher risk for IHD than women with a prior normotensive pregnancy (n=8 297); however, the risk of stroke did not differ between the groups.[13]

The underlying mechanisms of increased CVD risk in women with prior pre-eclampsia are unknown. The causes may operate already prior to gestation, since, for example, hypertension, hyperlipidaemia, insulin resistance, obesity, chronic kidney disease and autoimmune diseases are associated with increased risks of both pre-eclampsia and CVD.[14–18] Hyperinsulinaemia may be a particularly important determinant, at least in Finnish pre-eclamptic women, as it is often present both during[17] and 17 years after pre-eclamptic pregnancy.[19] Primary causes potentially generate endothelial dysfunction, which is a key factor in both pre-eclampsia and CVD.[20]

Table 4 Representative cohort studies from Nordic countries, the UK and the USA on the association of pre-eclampsia and risk of IHD or stroke

Study	N of women with/without history of pre-eclampsia	Origin of the study	Duration of follow-up time (years)	RR (95% CI) for IHD	RR (95% CI) for stroke
Wikström *et al*[22]	20 469*/383 081	Sweden	Mean 15	1.7 (1.5 to 2.0)	NR
Lykke *et al*[21]	25 184/643 935	Denmark	Median 14.6	1.82 (1.65 to 2.00)	1.53 (1.38 to 1.69)
Bhattacharya *et al*[33]	2026/23 935	Scotland	NR	1.18 (0.99 to 1.41)	1.16 (0.93 to 1.45)
Männistö *et al*[13]	242/8297	Northern Finland	Mean 39.4	1.36 (1.01 to 1.83)	1.19 (0.68 to 2.09)
Haug *et al*[34]	1391/21 766	Norway	Median 18	1.78 (1.26 to 2.52)†	1.46 (1.08 to 1.97) for women of 40–70 years of age
Leon *et al*[35]	25 554/1 277 811	UK	Median 9.25	1.67 (1.54 to 1.81)	1.9 (1.53 to 2.35)
Garovic *et al*[36]	298/596	Minnesota, USA	Median 36.2 for pre-eclamptic women and 35.8 for referents	1.85 (1.23 to 2.78)	1.40 (0.89 to 2.22)
The present study	31 728/92 168	Finland	Mean 34	1.52 (1.44 to 1.59)	1.40 (1.32 to 1.48)

*Including also women with gestational hypertension.
†Myocardial infarction only.
IHD, ischaemic heart disease; NR, not reported; RR, relative risk.

Alternatively, pre-eclampsia might evoke permanent endothelial impairment, which manifests decades later as different forms of CVD.

It would be conceivable that the future vascular risks of pre-eclampsia are relative to the severity of pre-eclampsia. Our cohort included 1007 women with eclampsia, the most serious manifestation of pre-eclampsia. The CVD risk of this group did not distinguish from the women with a less severe disease. However, when eclamptic and pre-eclamptic women with severe features were considered as one group, the risks for IHD and stroke were higher than those of women with a history of milder forms of pre-eclampsia. Thus, the severity of pre-eclampsia is a significant determinant for future CVD risk, and this finding is in line with previous Scandinavian studies.[21 22]

The risk of recurrence is approximately 15% in the subsequent pregnancy after one pre-eclamptic pregnancy.[23] The recurrence of pre-eclampsia was associated in our study with a 1.3-fold risk for IHD, MI or stroke, in comparison with women who had had only one pre-eclamptic pregnancy. The finding is in line with a former meta-analysis.[24] Recurrent pre-eclampsia may indicate higher inherent vascular risk, which later manifests as CVD. However, recurrent pre-eclampsia may cause repeated endothelial damage in a formerly healthy vasculature, which could initiate a pathological process leading to atherosclerosis.

Multiple pregnancy is a known risk factor for pre-eclampsia.[14] However, a Swedish cohort study showed that a pre-eclamptic twin pregnancy was not accompanied with an elevated CVD risk.[25] Perhaps pre-eclampsia in a twin pregnancy derives primarily from the mother's failure to adapt to increased physiological and vascular demands rather than from an underlying tendency to vascular dysfunction. However, our study did not have sufficient statistical power to confirm the former study's results, and we detected no difference in CVD risk between pre-eclamptic twin and singleton pregnancies.

Women under 24 years at pre-eclampsia had a 34% greater stroke risk than women above this age. On the contrary, the risk of IHD showed no dependence on the maternal age. Women who were diagnosed with pre-eclampsia at a young age may possibly have a robust inherent tendency to develop hypertension, which is associated with an increased stroke risk particularly in women.[26] We might also speculate that young mothers found pre-eclampsia such a major stress factor that they postponed further pregnancies by using combined estrogen–progestin contraception, which is an established risk factor for stroke.[27] However, we have no data on the use of contraceptives of the cohort; hence, we cannot substantiate this speculation any further.

A Finnish study has reported that the occurrence of pre-eclampsia shows geographical variation, being most common in Northern and most infrequent in Southern Finland.[8] CVD risk similarly varies between different parts of the country, and IHD mortality rate has been higher in Eastern than in Western Finland for decades.[28] Therefore, it was vital for us to study a nationwide cohort. The populations in Northern and Eastern Finland responded to a prior pre-eclamptic pregnancy with larger elevations in CVD incidences than the populations of other counties, which is in line with high CVD risk in the same regions. However, these high-risk populations were relatively small in number, and the CVD risk of the total Finnish pre-eclamptic population did not exceed the general international level.

We acknowledge a number of limitations in our study. First, in an observational study design, no causal connection can be verified between history of pre-eclampsia and CVD, and a possible impact of confounders cannot be excluded. For instance, we could not record risk factors common for pre-eclampsia and CVD, such as family history, obesity, smoking, dyslipidaemia, diabetes mellitus and essential hypertension. Second, it is notable that the diagnostic criteria for pre-eclampsia were revised several times by international and national organisations during 1969–1993,[29] and the pre-eclamptic women were collected based on criteria and terminology that were valid at the time of the pre-eclampsia diagnosis. Therefore, we converted the terms of the pre-eclamptic subgroups to correspond to the up-to-date ones.[30] Third, it might be seen as a weakness that instead of collecting all CVD diagnoses as endpoints, we focused solely on events of any IHD, MI and stroke. This was a considered decision, based on the fact that these are the most prominent manifestations of CVD,[31] which practically always lead to hospitalisation.

Our study also has several strengths. First, it is among the largest ones to assess the association of pre-eclampsia and future cardiovascular risk in a matched control setting. Second, our cohort, collected from all hospitals of the country during a period of 25 years, guarantees a comprehensive national representation. Third, we focused on such pre-eclampsia types that presented uniquely during pregnancy, excluding women with pre-existing CVD. Fourth, we can rely on the accuracy of the outcome diagnoses, because they were derived from hospitals and were accurately documented into the national databases, whose reliability has been scrutinised.[11 12] Finally, due to the mean follow-up time of over 33 years, 58% of the women were over 60 years of age at the end of the follow-up, which allowed a potential CVD emerge.

To conclude, pre-eclampsia was associated with a CVD risk increase of approximately 50%. The risk rises were of the same level as those reported earlier from other countries. As many as 34% of all Finnish female deaths were caused by CVD in 2019.[32] If we apply this proportion to our pre-eclamptic population, we can approximate pre-eclampsia to cause 17 additional CVD deaths among 100 women exposed to pre-eclampsia, when they are followed until death. Thus, these women should be identified as high CVD risk persons who are in particular need of active surveillance and early treatment of modifiable CVD risk factors.

Contributors All authors (MV, JJ, MG, OY, TM, HS-P) contributed to the study design, data collection and manuscript revision. JJ performed the statistical data analysis. HS-P acts as guarantor of this study. The authors declare that they have no competing interests.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The study was approved by the research committee of the Helsinki University Hospital (HUS/222/2021) and by the Finnish Social and Health Data Permit Authority Findata (THL/3683/14.02.00/2020). This is a retrospective observational study in which we used pseudonymised social and health sector register data, therefore no further ethical approval was required. This is a retrospective observational study, in which we used pseudonymised social and health sector register data. These data are available for scientific purposes without patient consent, if the appropriate permit is obtained first. For this study, we obtained the permit from Finnish Social and Health Data Permit Authority Findata (THL/3683/14.02.00/2020).

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REFERENCES

1 Mehran R, Vogel B, Ortega R, *et al*. The Lancet Commission on women and cardiovascular disease: time for a shift in women's health. *Lancet* 2019;393:967–8.
2 Burgess SN, Juergens CP, Nguyen TL, *et al*. Comparison of late cardiac death and myocardial infarction rates in women vs men with ST-elevation myocardial infarction. *Am J Cardiol* 2020;128:120–6.
3 Martínez-Sánchez P, Fuentes B, Fernández-Domínguez J, *et al*. Young women have poorer outcomes than men after stroke. *Cerebrovasc Dis* 2011;31:455–63.
4 Eurostat. Causes of death - standardised death rate by NUTS 2 region of residence. Available: https://ec.europa.eu/eurostat/databrowser/view/HLTH_CD_ASDR2__custom_2313284/default/table?lang=en [Accessed 18 Mar 2022].
5 Abalos E, Cuesta C, Grosso AL, *et al*. Global and regional estimates of preeclampsia and eclampsia: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2013;170:1–7.
6 Bastola K, Koponen P, Skogberg N, *et al*. Hypertensive disorders of pregnancy among women of migrant origin in Finland: a population-based study. *Acta Obstet Gynecol Scand* 2022;101:127–34.
7 Lamminpää R, Vehviläinen-Julkunen K, Gissler M, *et al*. Preeclampsia complicated by advanced maternal age: a registry-based study on primiparous women in Finland 1997-2008. *BMC Pregnancy Childbirth* 2012;12:47.
8 Kaaja R, Kinnunen T, Luoto R. Regional differences in the prevalence of pre-eclampsia in relation to the risk factors for coronary artery disease in women in Finland. *Eur Heart J* 2005;26:44–50.
9 Brown MC, Best KE, Pearce MS, *et al*. Cardiovascular disease risk in women with pre-eclampsia: systematic review and meta-analysis. *Eur J Epidemiol* 2013;28:1–19.
10 Wu P, Haththotuwa R, Kwok CS, *et al*. Preeclampsia and future cardiovascular health: a systematic review and meta-analysis. *Circ Cardiovasc Qual Outcomes* 2017;10:e003497.
11 Pajunen P, Koukkunen H, Ketonen M, *et al*. The validity of the Finnish hospital discharge register and causes of death register data on coronary heart disease. *Eur J Cardiovasc Prev Rehabil* 2005;12:132–7.
12 Sund R. Quality of the Finnish hospital discharge register: a systematic review. *Scand J Public Health* 2012;40:505–15.
13 Männistö T, Mendola P, Vääräsmäki M, *et al*. Elevated blood pressure in pregnancy and subsequent chronic disease risk. *Circulation* 2013;127:681–90.
14 Bartsch E, Medcalf KE, Park AL, *et al*. Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and meta-analysis of large cohort studies. *BMJ* 2016;353:i1753.
15 Frostegård J. Atherosclerosis in patients with autoimmune disorders. *Arterioscler Thromb Vasc Biol* 2005;25:1776–85.
16 Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, *et al*. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *Lancet* 2013;382:339–52.
17 Kaaja R, Laivuori H, Laakso M, *et al*. Evidence of a state of increased insulin resistance in preeclampsia. *Metabolism* 1999;48:892–6.
18 Spracklen CN, Smith CJ, Saftlas AF, *et al*. Maternal hyperlipidemia and the risk of preeclampsia: a meta-analysis. *Am J Epidemiol* 2014;180:346–58.
19 Laivuori H, Tikkanen MJ, Ylikorkala O. Hyperinsulinemia 17 years after preeclamptic first pregnancy. *J Clin Endocrinol Metab* 1996;81:2908–11.
20 Weissgerber TL, Milic NM, Milin-Lazovic JS, *et al*. Impaired flow-mediated dilation before, during, and after preeclampsia: a systematic review and meta-analysis. *Hypertension* 2016;67:415–23.
21 Lykke JA, Langhoff-Roos J, Sibai BM, *et al*. Hypertensive pregnancy disorders and subsequent cardiovascular morbidity and type 2 diabetes mellitus in the mother. *Hypertension* 2009;53:944–51.
22 Wikström A-K, Haglund B, Olovsson M, *et al*. The risk of maternal ischaemic heart disease after gestational hypertensive disease. *BJOG* 2005;112:1486–91.
23 Hernández-Díaz S, Toh S, Cnattingius S. Risk of pre-eclampsia in first and subsequent pregnancies: prospective cohort study. *BMJ* 2009;338:b2255.
24 Brouwers L, van der Meiden-van Roest AJ, Savelkoul C, *et al*. Recurrence of pre-eclampsia and the risk of future hypertension and cardiovascular disease: a systematic review and meta-analysis. *BJOG* 2018;125:1642–54.
25 Bergman L, Nordlöf-Callbo P, Wikström AK, *et al*. Multi-Fetal pregnancy, preeclampsia, and long-term cardiovascular disease. *Hypertension* 2020;76:167–75.
26 Madsen TE, Howard G, Kleindorfer DO, *et al*. Sex differences in hypertension and stroke risk in the REGARDS study: a longitudinal cohort study. *Hypertension* 2019;74:749–55.
27 Gillum LA, Mamidipudi SK, Johnston SC. Ischemic stroke risk with oral contraceptives: a meta-analysis. *JAMA* 2000;284:72–8.
28 Jousilahti P, Laatikainen T, Salomaa V, *et al*. 40-Year CHD Mortality Trends and the Role of Risk Factors in Mortality Decline: The North Karelia Project Experience. *Glob Heart* 2016;11:207–12.
29 Bell MJ. A historical overview of preeclampsia-eclampsia. *J Obstet Gynecol Neonatal Nurs* 2010;39:510–8.
30 Gestational hypertension and preeclampsia: ACOG practice Bulletin, number 222. *Obstet Gynecol* 2020;135:e237–60.
31 GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the global burden of disease study 2019. *Lancet* 2020;396:1204–22.
32 Official Statistics of Finland (OSF): Causes of death [e-publication]. ISSN=1799-5078. 2019, Appendix table 1c. Deaths by underlying cause of death and by age in 2019, females. Helsinki: Statistics Finland. Available: http://www.stat.fi/til/ksyyt/2019/ksyyt_2019_2020-12-14_tau_003_en.html [Accessed 18 Mar 2022].
33 Bhattacharya S, Prescott GJ, Iversen L, *et al*. Hypertensive disorders of pregnancy and future health and mortality: a record linkage study. *Pregnancy Hypertens* 2012;2:1–7.
34 Haug EB, Horn J, Markovitz AR, *et al*. Association of conventional cardiovascular risk factors with cardiovascular disease after hypertensive disorders of pregnancy: analysis of the Nord-Trøndelag health study. *JAMA Cardiol* 2019;4:628–35.
35 Leon LJ, McCarthy FP, Direk K, *et al*. Preeclampsia and cardiovascular disease in a large UK pregnancy cohort of linked electronic health records: a caliber study. *Circulation* 2019;140:1050–60.
36 Garovic VD, White WM, Vaughan L, *et al*. Incidence and long-term outcomes of hypertensive disorders of pregnancy. *J Am Coll Cardiol* 2020;75:2323–34.