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RESEARCH ARTICLE

Postpartum haemorrhage and risk of cardiovascular disease in later life: A population-based record linkage cohort study

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Abstract

Objective: To investigate the association between postpartum haemorrhage (PPH) and subsequent cardiovascular disease.

Design: Population-based retrospective cohort study, using record linkage between Aberdeen Maternity and Neonatal Databank (AMND) and Scottish healthcare data sets.

Setting: Grampian region, Scotland.

Population: A cohort of 70 904 women who gave birth after 24 weeks of gestation in the period 1986–2016.

Methods: We used extended Cox regression models to investigate the association between having had one or more occurrences of PPH in any (first or subsequent) births (exposure) and subsequent cardiovascular disease, adjusted for sociodemographic, medical, and pregnancy and birth-related factors.

Main Outcome Measures: Cardiovascular disease identified from the prescription of selected cardiovascular medications, hospital discharge records or death from cardiovascular disease.

Results: In our cohort of 70 904 women (with 124 795 birth records), 25 177 women (36%) had at least one PPH. Compared with not having a PPH, having at least one PPH was associated with an increased risk of developing cardiovascular disease, as defined above, in the first year after birth (adjusted hazard ratio, aHR 1.96; 95% confidence interval, 95% CI 1.51–2.53; $p < 0.001$). The association was attenuated over time, but strong evidence of increased risk remained at 2–5 years (aHR 1.19, 95% CI 1.11–1.30, $P < 0.001$) and at 6–15 years after giving birth (aHR 1.17, 95% CI 1.05–1.30, $p = 0.005$).

Conclusions: Compared with women who have never had a PPH, women who have had at least one episode of PPH are twice as likely to develop cardiovascular disease in the first year after birth, and some increased risk persists for up to 15 years.

KEYWORDS
cardiac, cardiovascular disease, health outcomes, hypertension, mortality, postpartum haemorrhage, pregnancy, Scotland

1 | INTRODUCTION

The incidence of PPH has increased in many high-income countries (HICs) over recent decades.[1–5] Globally, PPH accounts for one-quarter of all maternal deaths, representing around 70 000 maternal deaths each year.[6–8] Maternal death from PPH is rare in HICs, but the increasing incidence of PPH means that it remains a significant issue for maternal morbidity.[1,4,5,9]

The association between PPH and acute physical complications, such as hypovolaemic shock, sepsis and disseminated intravascular coagulation, is well established.[10,11] Relatively few studies have investigated the longer-term outcomes,[12–18] particularly beyond 5 years after PPH. A recent systematic review concluded that women may experience long-lasting negative impacts from PPH, including cardiovascular disease (CVD).[19] Two studies included in this review explored the potential association between PPH and the longer-term risk of CVD.[20,21] Both found an association between PPH requiring blood transfusion and hospitalisation for CVD, but did not find a similar association for PPH without transfusion.[20,21] A comparable English cohort study using linked primary care databases explored the longer-term risk of hypertension and CVD, and found no difference in CVD risks over a median follow-up of 4 years.[22] No published studies to date have taken account of the potential for associations to vary over time.

A potential association between PPH and subsequent CVD remains unclear, but is biologically plausible. Extreme blood loss after birth may result in major haemodynamic instability leading to haemorrhagic shock or end-organ damage,[23,24] with the potential for impaired cardiac function leading to an increased risk of CVD, particularly ischaemic heart disease (IHD), in later life. Given the high health burden related to CVD, affecting approximately 7.6 million in the UK,[25] the impact of PPH on CVD is worthy of further research. We carried out a population-based record-linked cohort study to investigate the association between primary PPH and the development of CVD in a Scottish population. The objectives were to estimate the incidence and relative risk of CVD among women who had at least one PPH, compared with women who never had a PPH, and to investigate whether any association between PPH and CVD is modified by mode of birth or hypertensive disorders of pregnancy (HDPs).

2 | METHODS

This study is reported according to the Reporting of Studies Conducted Using Observational Routinely Collected Data (RECORD) guideline (Appendix S1).[26]

2.1 | Study design and data sources

This study was a population-based retrospective cohort study using data from health record linkage.

The Aberdeen Maternity and Neonatal Databank (AMND) was used for data on PPH, maternal sociodemographic characteristics and birth-related information.[27] The AMND includes sociodemographic, pregnancy, labour-related, birth and neonatal data for all pregnancy events occurring in the Grampian Region of Scotland from 1949 to the present day, with a coverage ranging from 99% of all births in Aberdeen to 97% of all births across the region.[27]

Data from AMND were linked to outcomes from the following routine Scottish data sources (Table S1):

1. The Scottish General Acute Inpatient and Day Case – Morbidity Record (SMR01),[28] which contains episode-level demographic and clinical data about all hospital inpatient and day case discharges from acute care in the National Health Service (NHS) Scotland.
2. Prescribing Information System (PIS),[29] which provides data about all medicines prescribed and dispensed in the community in Scotland.
3. National Records of Scotland (NRS) – deaths data,[30] which contains statutory data about all deaths occurring in Scotland compiled from death registrations.
4. TrakCare (the patient management system used by NHS Scotland), which was used with the Community Health Index (CHI) number to identify women who were lost to follow-up (i.e. moved out of the Grampian region to other parts of Scotland) during the study period.

Data linkage was processed at the Grampian Data Safe Haven (DaSH) in Scotland by DaSH staff. Deterministic record linkage was carried out using the CHI number, which uniquely identifies a patient within the NHS in Scotland, to generate the linked data set.[31]

2.2 | Study population

The study population included all women who gave birth after 24 completed weeks of gestation in Aberdeen Maternity Hospital, from 1 January 1986 to 31 December 2016. Both singletons and multiple births were included and only permanent registered patients with NHS Scotland were included, to minimise the loss to follow-up of visitors.

To reduce the risk of exposure misclassification, we excluded women whose first birth was not recorded in the AMND, those with conflicting parity information (where the recorded parity was the same for two birth records for the same woman) and those who may have had at least of one of their births outside of the Grampian region (where the recorded parity for two birth records for the same women was not consecutive, despite the first birth being recorded in the AMND). To ensure the temporality of outcome measurement, we excluded birth records for women who had a CVD outcome event (as defined under the outcomes below) before the first birth or before their first PPH, and also birth records occurring after the CVD outcome event.

2.3 | Exposures

The primary exposure of interest was primary PPH, defined as blood loss of ≥500 mL within 24 h of childbirth.[32] We

chose this definition to be inclusive, to account for potential underestimation of blood loss and because the physiological impact of blood loss is likely to be the same, irrespective of the mode of birth.[5,33–35] For births in which the blood loss volume was <500 mL, but a PPH management (Bakri ballooning, arterial embolisation and emergency peripartum hysterectomy) was also recorded, a PPH was considered to have occurred. Blood transfusion was not used as part of our definition because no data were available about the indication for transfusion and timing. Women who had a PPH in any birth recorded in the AMND during the study period were the 'exposed' group, compared with women who did not have a PPH in any birth, who represented the 'unexposed' group.

We considered severe primary PPH as a secondary exposure, defined as blood loss of ≥1500 mL from the genital tract or births with Bakri ballooning and/or arterial embolisation and/or emergency peripartum hysterectomy, regardless of the blood loss volume.

2.4 | Outcome

The primary outcome for this study was a composite CVD outcome identified up to 32 years after childbirth. This was defined as the time to first occurrence of one of the following events after the first birth:

- At least three prescriptions within any 365-day period of selected medications commonly used to treat CVD. This definition was used to identify regular medication for CVD and to exclude the prescription of such medication for other indications, including, for example, a one-off prescription of a diuretic.
- Any CVD-related hospitalisation for selected CVDs, recorded as the main condition of diagnosis or in any other diagnostic fields.
- Death in which the main or secondary cause was CVD.

Table S2 shows how these outcome events were operationalised within each of the data sources.

2.5 | Follow-up

Follow-up for each woman began on the date of her first birth recorded in the AMND during the study period, irrespective of whether she had a PPH in her first birth. Follow-up for all women ended on whichever occurred first of the following:

- 31 December 2018 (the end date of the period covered by the data linkage)
- date the woman experienced the outcome event
- date the woman became lost to follow-up (e.g. date of migration outside the Grampian region)
- date of death (recorded in NRS deaths).

Figure S1 illustrates the total follow-up duration for a woman with several birth records.

2.6 | Statistical analysis

We summarised the maternal sociodemographic and clinical characteristics of the women, stratified by PPH status, using frequencies and percentages. We used univariable Cox proportional hazards regression to assess the association between PPH and CVD-free survival.[36,37] Multivariable Cox proportional hazards regression models, estimating adjusted hazard ratios (aHRs), were fitted by sequentially adjusting for potential confounding factors, informed by a causal diagram (Figure S2).[38] All models were adjusted for year of birth to account for temporal changes (the 'base model'). We then adjusted for maternal sociodemographic factors, maternal medical history, including self-reported history of CVD, and pregnancy-related factors in a hierarchical fashion: model 1 was additionally adjusted for sociodemographic factors; model 2 was additionally adjusted for maternal medical factors; and model 3 was additionally adjusted for pregnancy-related factors. Variables considered as potential confounding factors based on biological plausibility were included in models if they were associated with PPH (exposure), increased the risk of CVD in the unexposed group, and if they were not plausibly on the causal pathway between PPH and CVD.[39] For these variables, information from each birth of an individual woman was used to adjust for confounding in the multivariable model. Table S3 summarises the key variables used in the data analysis.

Log–log plots were used to assess whether the HR for the association between PPH/severe PPH and CVD was constant across the follow-up time. We used the global proportional hazards test to check the proportional hazards assumption for exposure variables and each confounding factor individually. Extended multivariable Cox regression analyses were conducted to address the violation of the proportional hazard assumptions, estimating aHRs for different periods of follow-up time after birth. Potential effect modification of the association between PPH/severe PPH and CVD was investigated for HDPs and mode of birth.

Two sensitivity analyses were carried out using model 3 to explore the association between PPH and CVD: (i) after removing women who had a self-reported history of CVD prior to their first birth; and (ii) after restricting the outcome measure to CVD-related hospitalisation.

A 'missing' category was created for all covariates with missing values (Table S4). As the proportion of missing data was lower than 5% and the missing values were unlikely to be associated with the CVD outcome, a complete case analysis was performed.[40] All analyses were conducted at the level of the woman to take all births into account and to maximise the generalisability of the study. Data were analysed using Stata 16 (StataCorp LLC, College Station, TX, USA).[41]

TABLE 1 Association between postpartum haemorrhage (PPH)/severe PPH and composite and cardiovascular disease (CVD) outcome, with sequential adjustment for potential confounding factors.

	Univariable model			Multivariable models							
				Base model[a]		Model 1[b]		Model 2[c]		Model 3[d]	
	(*n* = 70 904, PPH; *n* = 50 526, severe PPH)			(*n* = 70 904, PPH; *n* = 50 526, severe PPH)		(*n* = 63 875, PPH; *n* = 45 107, severe PPH)		(*n* = 63 402, PPH; *n* = 44 743 severe PPH)		(*n* = 63 376, PPH; *n* = 44 726 severe PPH)	
Exposure	CVD events (*n*)	HR (95% CI)	*p*-value	aHR (95% CI)	*p*-value	aHR (95% CI)	*p*-value	aHR (95% CI)	*p*-value	aHR (95% CI)	*p*-value
No PPH	6111	Reference		Reference		Reference		Reference		Reference	
Any PPH	3070	1.06 (1.02–1.11)	0.005	1.29 (1.23–1.35)	<0.0001	1.27 (1.21–1.33)	<0.0001	1.26 (1.20–1.32)	<0.0001	1.12 (1.06–1.18)	<0.0001
Any severe PPH	669	1.14 (1.05–1.23)	0.002	1.30 (1.18–1.44)	<0.0001	1.29 (1.19–1.41)	<0.0001	1.28 (1.17–1.39)	<0.0001	1.16 (1.06–1.27)	0.001

[a]Base model, adjusted for year of birth only.
[b]Model 1 adjusted for year of birth and sociodemographic factors (age at birth, body mass index, ethnicity and Scottish index of multiple deprivation).
[c]Model 2 adjusted for variables in model 1 and additionally adjusted for past medical history (anaemia and coagulation disorders, diabetes, psychiatric and mental disorders, self-reported history of cardiovascular disease) and smoking status.
[d]Model 3 adjusted for variables in model 2 and additionally adjusted for pregnancy-related factors: mode of birth, obstetric complications (hypertensive disorders of pregnancy, prelabour rupture of membranes or preterm prelabour rupture of membranes, gestational diabetes and antenatal anaemia), gestational age at birth and baby's birthweight.

3 | RESULTS

The linked data set contained information about 125 022 birth records from 72 593 women who gave birth between 1986 and 2016, 124 795 of which were births after at least 24 weeks of gestation (Figure S3). After exclusions, the final cohort included data on 121 731 births to 70 904 women. Of these, 25 177 women (36%) had at least one primary PPH, including severe PPH, and 4799 women (6%) had at least one severe PPH (Table S4). Compared with women who had never had a PPH, women who had at least one PPH were more likely to be aged 30 years or older at their first birth, to be of Black, Asian or other ethnic background, and to have a higher body mass index (BMI) at their first antenatal visit. Among women who had at least one PPH, 20 416 (81%) had one PPH, 4320 women (17%) had a PPH on two occasions and 441 women (2%) had a PPH at least three times.

3.1 | Outcome events

Prescription records accounted for most (approx. 91%) of the CVD outcome events (Figure S4). CVD-related hospitalisations accounted for 9% and death related to CVD accounted for less than 1% of first CVD events. Among women who had a PPH, and those who did not, around 13% of those who had a prescription as their first CVD event had a subsequent CVD-related hospitalisation. Over half of those who had a CVD-related hospitalisation as their first CVD event were subsequently prescribed CVD medication. Small numbers of CVD-related deaths were observed in both groups.

3.2 | Univariable and multivariable cox proportional hazards models

Figure S5 shows the overall CVD event-free survival probability for women who had at least one PPH, compared with women who did not have a PPH. In univariable analysis, women who had at least one PPH were 6% more likely to develop a CVD outcome event during the follow-up period compared with women who did not have a PPH (HR 1.06, 95% CI 1.02–1.11) (Table 1). After adjusting for year of childbirth (base model), compared with women who did not have a PPH, women who had at least one PPH were 29% more likely to develop a CVD outcome event during the follow-up period (aHR 1.29, 95% CI 1.23–1.35). Further adjustment for maternal sociodemographic factors (model 1) and medical history (model 2) did not materially alter this association. Additional adjustment for pregnancy-related factors, including the presence of other obstetric complications at birth (model 3), resulted in an attenuation of the association, which remained statistically significant (aHR 1.12, 95% CI 1.06–1.18). The results were similar for women who had at least one severe PPH.

Plots of hazard function against analysis time (Figure S6) and the global proportional hazards test indicated that the association between PPH and the CVD outcome, and also the association between several confounding variables (mode of birth, gestational age at birth, HDPs and birthweight of the baby) and the CVD outcome, were not constant over time.

3.3 | Extended Cox regression models for different time periods

During the first year after birth, in the fully adjusted model (model 3), compared with women who did not have a PPH, women who had at least one PPH were almost twice as likely to have a CVD outcome event (aHR 1.96, 95% CI 1.51–2.53; Figure 1; Table 2). Beyond the first year after birth, this association remained, but attenuated over time (aHR 1.19 at 2–5 years; aHR 1.17 at 6–15 years). Beyond 15 years after birth, women who had at least one PPH were 36% less likely to experience a CVD event compared with women who did not have a PPH (aHR 0.64, 95% CI 0.55–0.75). Models for the association between severe PPH and the CVD composite outcome over time showed a similar pattern to the results for any PPH (Table 2).

3.4 | Potential effect modification by hypertensive disorders of pregnancy and mode of birth

There was strong evidence of effect modification ($p = 0.003$) by HDPs in the fully adjusted model (Table 3), with higher aHRs for the association between PPH/severe PPH and the CVD outcome among women who had at least one birth affected by HDPs, compared with women who did not. There was only weak evidence of effect modification ($p = 0.09$) by mode of birth (Table S5).

The results of both sensitivity analyses are described in Appendix S2 (Tables S6 and S7).

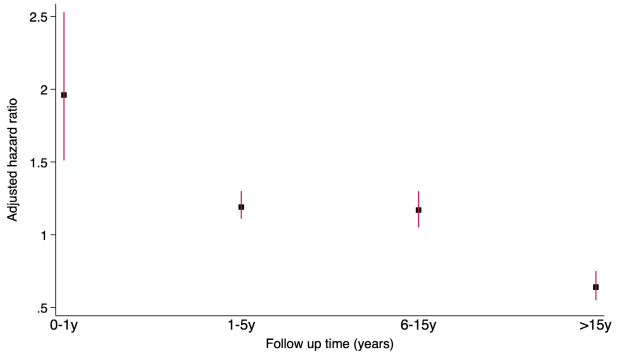

FIGURE 1 Adjusted hazard ratios for the association between postpartum haemorrhage (PPH) and cardiovascular disease (CVD) at different time intervals after birth (Table 2, any PPH, model 3, $n = 63\,376$).

4 | DISCUSSION

4.1 | Main findings

In this Scottish population-based cohort study, of the 70 904 women who gave birth between 1986 and 2016, 25 177 women had 30 417 births complicated by PPH. Women with at least one episode of PPH had an increased risk of having CVD up to 15 years following birth, after adjustment for year of birth, variation of risk over time and confounding. This association was slightly stronger in women with HDPs. Similar associations were found between severe PPH and the same CVD outcomes.

4.2 | Strengths and limitations

The main strength of this study is the large population-based cohort with long follow-up time, minimising selection bias. Stratification of cardiovascular risk by follow-up time enabled the investigation of how the risk of CVD associated with PPH changes over time.[42] Classifying the PPH exposure using all available birth records for any individual woman minimised the misclassification of exposure to PPH. Studies that have used information only from the first birth or first pregnancy typically exclude around 60% of births from the analysis.[43]

Using both prescription and hospital discharge data allowed a broader spectrum of CVD events to be captured, including individuals with CVD who did not die or require hospitalisation. The recording of estimated blood loss, and other variables in the AMND, preceded outcome assessment from SMR01, reducing recall bias. Temporality for outcome events was established by excluding women with pre-existing records of CVD-related prescriptions or hospitalisation before their first birth or first PPH.

The Grampian region has a relatively stable population and only 3.8% of women who had a birth record in the AMND migrated out of the region during the study period, minimising differential loss to follow-up.[27] Women who had births outside the Grampian region during the follow-up period were excluded to minimise potential exposure errors. With the use of routine healthcare data, although it was possible to adjust for a range of potential confounding factors, no information was available about some factors linked to pre-pregnancy risk of CVD, including blood pressure, lipid profile, genetic factors, diet and lifestyle factors.

As a 'time to (first) event' analysis was conducted, unsurprisingly 91% of the first events contributing to the composite CVD outcome were CVD-related prescriptions. Unlike CVD-related hospitalisation and death data, the prescription data did not permit the identification of a specific CVD diagnosis because similar medications could be prescribed for many diagnoses.

We chose to begin the follow-up at the woman's first birth, regardless of the timing of PPH. This meant that

TABLE 2 Association between postpartum haemorrhage (PPH) and composite cardiovascular disease (CVD) outcome for different time intervals after birth, with sequential adjustment for potential confounding factors.

Exposure	Time interval after birth	Base model[a] $n = 70\,904$		Model 1[b] $n = 63\,875$		Model 2[c] $n = 63\,402$		Model 3[d] $n = 63\,376$	
		aHR (95% CI)	*p*-value	aHR (95% CI)	*p*-value	aHR (95% CI)	*p*-value	aHR (95% CI)	*p*-value
Any PPH	0–1 year	2.43 (1.95–3.02)	<0.0001	2.49 (1.98–3.11)	<0.0001	2.46 (1.95–3.02)	<0.0001	1.96 (1.51–2.53)	<0.0001
	2–5 years	1.32 (1.25–1.40)	<0.0001	1.28 (1.21–1.36)	<0.0001	1.27 (1.19–1.35)	<0.0001	1.19 (1.11–1.30)	<0.0001
	6–15 years	1.39 (1.27–1.53)	<0.0001	1.35 (1.22–1.48)	<0.0001	1.35 (1.23–1.49)	<0.0001	1.17 (1.05–1.30)	0.005
	>15 years	0.88 (0.78–1.00)	0.042	0.87 (0.76–1.00)	0.058	0.87 (0.76–1.00)	0.057	0.64 (0.55–0.75)	<0.0001
Exposure	**Time interval after birth**	**Base model[a] $n = 50\,526$**		**Model 1[b] $n = 45\,107$**		**Model 2[c] $n = 44\,743$**		**Model 3[d] $n = 44\,726$**	
		aHRs (95% CI)	***p*-value**	**aHRs (95% CI)**	***p*-value**	**aHRs (95% CI)**	***p*-value**	**aHRs (95% CI)**	***p*-value**
Any severe PPH	0–1 year	2.46 (1.71–3.53)	<0.0001	2.52 (1.74–3.68)	<0.0001	2.51 (1.72–3.65)	<0.0001	1.86 (1.25–2.80)	0.002
	2–5 years	1.38 (1.24–1.53)	<0.0001	1.36 (1.22–1.51)	<0.0001	1.34 (1.20–1.49)	<0.0001	1.30 (1.16–1.46)	<0.0001
	6–15 years	1.38 (1.18–1.63)	<0.0001	1.33 (1.21–1.59)	0.001	1.34 (1.13–1.60)	0.001	1.21 (1.00–1.46)	0.047
	>15 years	0.71 (0.55–0.92)	0.009	0.71 (0.52–0.95)	0.021	0.69 (0.52–0.94	0.018	0.50 (0.37–0.69)	<0.0001

[a]Base model adjusted for year of birth only.

[b]Model 1 adjusted for year of birth and sociodemographic factors (age at birth, body mass index, ethnicity and Scottish index of multiple deprivation).

[c]Model 2 adjusted for variables in model 1 and additionally adjusted for past medical history (anaemia and coagulation disorders, diabetes, psychiatric and mental disorders and self-reported history of cardiovascular disease) and smoking status.

[d]Model 3 adjusted for variables in model 2 and additionally adjusted for pregnancy-related factors: mode of birth, obstetric complications (hypertensive disorders of pregnancy, prelabour rupture of membranes or preterm prelabour rupture of membranes, gestational diabetes and antenatal anaemia), gestational age at birth and baby's birthweight.

TABLE 3 Association between PPH and composite cardiovascular outcome in women with and without hypertensive disorders of pregnancy (HDPs) (fully adjusted model 3).

		Women without HDPs $n = 53\,451$		Women with HDPs $n = 17\,453$	
Exposure	**Time interval**	**HRs (95% CI)**	***p*-value**	**HRs (95% CI)**	***p*-value**
Any PPH	0–1 year	1.85 (1.43–2.42)	<0.0001	2.14 (1.65–2.79)	<0.0001
	2–5 year	1.12 (1.03–1.21)	0.007	1.29 (1.18–1.41)	<0.0001
	6–15 year	1.06 (0.94–1.19)	0.354	1.22 (1.08–1.38)	0.001
	15+ year	0.57 (0.48–0.67)	<0.0001	0.66 (0.55–0.78)	<0.0001
Any severe PPH	0–1 year	1.74 (1.15–2.63)	0.009	2.02 (1.34–3.05)	0.001
	2–5 year	1.20 (1.05–1.38)	0.01	1.39 (1.20–1.62)	<0.0001
	6–15 year	1.08 (0.88–1.32)	0.48	1.25 (1.01–1.54)	0.039
	15+ year	0.44 (0.32–0.61)	<0.0001	0.51 (0.37–0.71)	<0.0001

women who had more than one birth and had their first PPH in a second or subsequent birth had extra follow-up time. As 66% of women had a PPH with their first birth, the effect of this was to bias the aHRs towards the null and thus produce a conservative result. Finally, in our Scottish study population, 4% were from Black, Asian and other ethnic minority backgrounds, so generalisability to other HICs with more diverse populations may be limited.

4.3 | Interpretation (in light of other evidence)

Postpartum haemorrhage (PPH) was significantly associated with an increased risk of CVD, particularly in the first year following childbirth. Over time, the relative increase in the risk of CVD declined, and beyond 15 years the risk of CVD was lower in the PPH group. This latter finding is very unlikely to have arisen because PPH is protective for CVD. Rather, it is likely that the use of extended Cox regression models resulted in 'survival' bias associated with time to CVD outcome, because any woman having a first CVD event was censored and for the purposes of the analysis no longer 'at risk' of later CVD events.[44,45] As more PPH-exposed women had earlier events they were no longer 'at risk' of a later event, whereas a greater proportion of the non-exposed group, with fewer earlier CVD events, remained at risk of later events.

Three other population-based studies have investigated the relationship between PPH and CVD, in England, Korea and Canada.[20–22] Two found the adjusted risk of CVD was higher among women with PPH requiring blood transfusion (i.e. more severe PPH), compared with women who did not have PPH (aHR 1.60, 95% CI 1.25–2.06; aHR 1.38, 95% CI 1.13–1.68),[20,21] but none found an association between less severe PPH and hypertension or CVD.[20–22] These studies were all conducted in high-resource settings, comparable with Scotland, but they all classified a woman as having had a PPH on the basis of events in the index or first birth only. Second, records with PPH were identified using diagnostic or International Classification of Diseases Tenth Revision (ICD-10) codes which, in the absence of data about estimated blood loss, could lead to non-differential measurement errors of PPH and an underestimation of the association.[22] Finally, the use of CVD-related hospitalisation for outcome assessment in previous studies, without including CVD-related prescriptions, may have led to fewer outcomes identified and an underestimation of the true effect of PPH.

There are two possible explanations for the observed association between PPH and CVD. The first is that PPH may be an independent risk factor for subsequently developing CVD. During pregnancy the total blood volume increases to between 20% and 100% above pre-pregnancy levels, to allow for adequate fetal growth and development.[46] A postpartum blood loss of up to 500 mL may be expected to be normal and well tolerated by haemodynamic changes during birth.[47] Higher blood loss causes a lowered blood volume reducing venous return to the heart, and a consequent reduced cardiac output and overall blood supply to the organs.[48] This, in combination with hypoxaemia, can lead to ischaemic injuries of vital organs, including the heart, brain and kidneys. Although severe outcomes, including end organ failure and death, may be averted with timely treatment, PPH may nevertheless cause irreversible damage to the cardiovascular system, which may in turn lead to a higher risk of developing subsequent CVD.

Another possible explanation is that pre-existing 'occult' risk factors exist prior to pregnancy in some women and the experience of obstetric complications may 'unmask' this pre-existing susceptibility to CVD.[42,49–51] It has been established that haemodynamic changes in pregnancy and childbirth can worsen existing cardiac conditions such as coronary heart disease.[52] A growing body of research suggests that pregnancy complications may function as a 'stress test' to the cardiovascular system, exacerbating any latent cardiovascular risk by causing more vascular damage and metabolic stress on the body.[49,51,53]

More information is needed about cardiovascular risk factors before pregnancy, such as pre-pregnancy lipid profile, BMI and blood pressure, and during pregnancy and after birth, to be able to distinguish between these two possible explanations. Regardless, this creates an opportunity

for prevention or intervention, as valuable information is revealed about women's underlying cardiovascular risk.[54]

5 | CONCLUSION

Compared with women who have never had a PPH, women who have had at least one PPH (irrespective of severity) are twice as likely to develop CVD in the first year after birth and some increased risk persists for up to 15 years, after adjustment for potential confounding factors. The associated risk may be slightly higher among women with HDPs. PPH should be considered as an early indication of subsequent CVD risk, and more research should be carried out to explore the longer-term health outcomes of women's health after PPH.

AUTHOR CONTRIBUTIONS

SL, CO and RR had full access to all of the data in the study. SL and RR were responsible for the conceptualisation of the study, with input from JK. SL was responsible for statistical analysis and exporting the results from the Grampian DaSH, with supervisory support from CO. All authors were involved in the interpretation of the data. SL drafted the article and all authors were involved in the interpretation of the data and the critical revision of the article.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study cannot be made freely available because they are subject to privacy and ethical restrictions for the use of routine health administrative data. Data are available from AMND and NHS Grampian R&D via the Grampian DaSH, with the joint permission of AMND Steering Committee and NHS Grampian, Scotland (https://www.abdn.ac.uk/research/digital-research/accessing-data-1688.php).

ETHICS APPROVAL

This study was approved by the University of Aberdeen's AMND data steering committee, NHS Grampian R&D (project no. 2021OG001E; IRAS ref. 290656) on 20 January 2021.

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SUPPORTING INFORMATION

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