Investigating Risk Factors for Postpartum Haemorrhage

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Thesis submitted for the degree of Doctor of Philosophy

Trinity Term 2023

Abstract

Background: The incidence of postpartum haemorrhage (PPH), excessive bleeding after childbirth, has increased in high-income countries and the reasons for this are not well understood. One possible explanation for the increase is a rise in prevalence of key risk factors in the population. However, evidence about risk factors for PPH is contradictory and no systematic review or synthesis of the literature from high-income countries has been conducted to date. There is very little evidence about risk factors for PPH among women who are considered at low-risk of complications.

Methods: A systematic review and narrative synthesis of the evidence about risk factors for PPH in high-income countries was conducted. A case-control study was carried out to examine the incidence and risk factors for PPH among women who gave birth in UK midwifery units over a six-month period in 2019-20. Using data about births over a 31-year period in Aberdeen in Scotland, a case-control study was used to estimate the incidence, explore the risk factors for PPH and examine how these have changed over time.

Results: The systematic review identified the following risk factors as 'likely' or 'very likely' to be independently associated with PPH: race/ethnicity, hypertensive disorders, previous PPH, multiple pregnancy, placenta praevia, chorioamnionitis, assisted conception, antepartum haemorrhage, induction of labour, prolonged second stage of labour, prolonged third stage of labour, expectant management of the third stage, maternal pyrexia in labour, instrumental birth, genital tract trauma, retained placenta, and higher birthweight. Several factors that are considered well-established risk factors for PPH, including for example, maternal age, parity, BMI and caesarean birth were rated as 'unclear' in terms of their association with PPH, often because of conflicting evidence. Very little evidence was identified about risk factors for PPH among low-risk women.

In UK midwifery units, the incidence of PPH requiring transfer to obstetric care was 3.7% (95% CI 3.6-3.95). Risk factors independently associated with PPH broadly aligned with previous research conducted among low- and higher-risk women.

The Aberdeen case-control study found that the incidence of PPH increased from 5% in 1986 to 24% in 2016 in women giving birth vaginally, with similar increases in women giving birth by caesarean and in low-risk women. Risk factors for PPH broadly aligned with previous research, the risk of PPH increases with the number of risk factors present for each woman and the prevalence of almost all risk factors increased over the 31-year period.

Conclusion: This thesis provides a comprehensive synthesis of the evidence about risk factors for PPH in high-income countries. This confirms several risk factors for PPH that are widely cited in clinical guidelines, but calls into question the strength of evidence for some others often considered as 'well-established'. Women considered at low-risk of complications still experience PPH and the risk factors for PPH in this population are similar to those in the general birthing population. The incidence of PPH in the UK has increased over the past three decades, including among low-risk women. This trend appears, in part, to be explained by an increase in the prevalence of key risk factors in the population and the concurrent rise in the overall number of risk factors among woman in the birthing population.

Acknowledgements

I would like to express my deepest appreciation to my supervisors, Rachel Rowe and Jenny Kurinczuk, for providing me with constant encouragement, guidance, and swift feedback throughout my thesis journey. Your attention to detail and expertise have been invaluable in helping me to refine my ideas and improve the quality of my writing and research. I feel very lucky to have had you both as supervisors.

I am also grateful to my colleague, Su Mon Latt, for her support and assistance with the multiple and lengthy stages of my systematic review, and for being an understanding friend who could share in the highs and lows of the thesis journey. Thanks also to Thomas Morgan, Alice Roberts and Olivia Martin for your invaluable contributions to my systematic review; navigating a complicated data extraction form over many Zoom calls was no small undertaking and I am very grateful for your help. Charles Opondo, thank you for providing statistical support and advice on my systematic review – and for helping me have confidence in my research.

To my lovely colleagues at the Australian Institute of Health and Welfare, your support and flexibility through this whole journey have been a gift. Being able to continue as part of the Perinatal Data Unit team throughout nearly four years overseas has been hugely rewarding and a great privilege. I would also like to thank the Nuffield Department of Population Health for providing the funding for my studentship and making my doctoral studies possible. To Exeter College, for providing a grant to support my research, for being a place to call home and a fantastic community that has made my Oxford experience so special – truly the friendliest college.

I would also like to express my thanks to my wonderful friends, both near and far, for their unwavering encouragement and patience throughout my thesis journey. To the friends who helped me get

through multiple lockdowns and kept life entertaining when our world shrunk to just a few rooms, to those who shared lively conversations and DPhil angst, and helped Oxford feel like home, who provided distraction and aided my focus in (almost) equal measure, to those who supplied the cookies in times of trial, cooked me dinners, sent encouragement in many forms and who never doubted that I could do this, I am eternally grateful for you.

Finally, I would like to express my heartfelt gratitude to my family. To my sisters, Katie and Sarah, thank you for being great listeners, dedicated cheerleaders and a source of laughter and love. To my Mum and Dad, who have always been my biggest supporters, thank you for your love and belief in me, for being a source of strength and inspiration, for helping me feel proud of what I'm doing, and always being just a phone call away. I could not have got to Oxford or completed this thesis without you.

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List of abbreviations

ACOG	American College of Obstetricians and Gynecologists
AMND	Aberdeen Maternal and Neonatal Databank
AMU	Alongside midwifery unit
aOR	Adjusted odds ratio
APH	Antepartum Haemorrhage
ART	Assisted Reproduction Techniques
BMI	Body Mass Index
CI	Confidence Interval
CLFM	Children in Low-income Families Measure
CTL	Control
EBL	Estimated Blood Loss
CS	Caesarean Section
FIGO	International Federation of Gynecology and Obstetrics.
FMU	freestanding midwifery unit
g	Grams
HRoB	High risk of bias
hrs	Hours
ICD	International Classification of Disease
ICU	Intensive Care Unit
IV	Intravenously
kg	Kilograms
L	Litres
LRoB	Low risk of bias
mins	Minutes
mL	Millilitres
MMR	Maternal mortality rate
MROP	Manual removal of placenta
NHS	National Health Service
NICE	National Institute of Health and Clinical Excellence
NS	Mon-significant
OECD	Organisation for Economic Co-operation and Development
OR	Odds ratio
OU	Obstetric unit
PPH	Postpartum haemorrhage
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PTSD	Post Traumatic Stress Disorder
RANZCOG	Royal Australian and New Zealand College of Obstetricians and Gynaecologists
RBC	Red blood cell

RCOG	Royal College of Obstetricians and Gynaecologists
RoB	Risk of bias
ROM	Rupture of membranes
SAMM	Severe Acute Maternal Morbidity
Sig	Significant
SIMD	Scottish Indices of Multiple Deprivation
SPPH	Severe postpartum haemorrhage
SVD	Spontaneous Vaginal Delivery
UK	United Kingdom
UKMidSS	UK Midwifery Study System
UKOSS	United Kingdom Obstetric Surveillance System
uOR	Unadjusted odds ratio
USA	United States of America
VB	Vaginal birth
WHO	World Health Organisation

Chapter 1: Background

1.1 Introduction

Postpartum haemorrhage (PPH), or excessive bleeding after childbirth, is a leading cause of maternal mortality and morbidity worldwide (1). Approximately 14 million women experience a PPH each year, and, of these, 70,000 result in maternal mortality (2). The vast majority (approximately 90%) of maternal deaths caused by PPH occur in low-income countries (3, 4). While, in high-income countries, maternal death as a consequence of PPH is rare, PPH is still a leading cause of maternal death. In 2017-19 the maternal mortality ratio (MMR) for death due to haemorrhage in the United Kingdom, for example, was 0.64 per 100,000 maternities (5). In Australia in 2015-17 the MMR for obstetric haemorrhage was 0.23 per 100,000 maternities (6).

While mortality associated with PPH is low in high-income countries, the incidence of PPH has been increasing over the past three decades and the reasons for this increase are not well understood (7-9). Rising rates of obstetric intervention in labour and birth, including induction and augmentation of labour, and instrumental and caesarean birth, are considered to have contributed to the increased incidence of PPH (10, 11). The growing prevalence of potential risk factors for PPH, including multiple pregnancy, obesity, advanced maternal age at birth, and hypertension, has also been associated with the increased incidence (7, 9, 12). However, studies that have accounted for these changing practices and risk profiles still observe an increased risk of PPH (10, 13, 14). Furthermore, many of the risk factors that are associated with PPH show inconsistent associations across different studies and many women who have a PPH do not have any identified risk factors (15, 16). Taken together, this suggests there may be unidentified risk factors contributing to this trend.

1.2 Postpartum haemorrhage over time

Excessive blood loss after childbirth, and its potentially life-threatening consequences, has been documented throughout human history. The earliest known reference to PPH dates back to 1500 BCE in the Ebers Papyrus, an ancient Egyptian medical textbook, which describes treatments for postpartum blood loss using a drink made of dates and honey (17). In the 17th century, postpartum bleeding for up to a month after childbirth was considered a healthy part of the birthing process, however, retained products of birth were acknowledged to represent a grave danger to the mother, the cure for which was suggested to be bloodletting, which would draw blood away from the womb (18). In the 18th and 19th centuries, with advances in modern medicine, including anaesthesia, which enabled the expanded use of caesarean birth (19), and the more widespread use of forceps to reduce prolonged or obstructed labour (20), childbirth became significantly safer (21). While the data related to the historical occurrence of PPH are sparse and potentially inaccurate, the general trend of decreasing rates of maternal mortality associated with PPH, which is more-reliably documented, is likely to be reflective of the decline in the occurrence of PPH (22).

Maternal death caused by PPH, has declined dramatically, particularly in high-income countries, in the past 150 years, as has the overall MMR (21, 23). Significant improvements in obstetric practice, access to care and improved standards of living are likely contributory factors to this precipitous decline (21). The availability of transfused blood as well as oxytocin for management of the third stage of labour are also likely to have contributed to the reduction in mortality associated with PPH. However, as illustrated in Figure 1 below, in England and Wales both of these changes to practice occurred after an already significant drop in mortality from all causes of PPH. The professionalisation of midwifery practice, as seen in the USA in the late 19th century (24) and as reflected in the 1902 UK Midwifery Act (21) may also have contributed to improved outcomes.

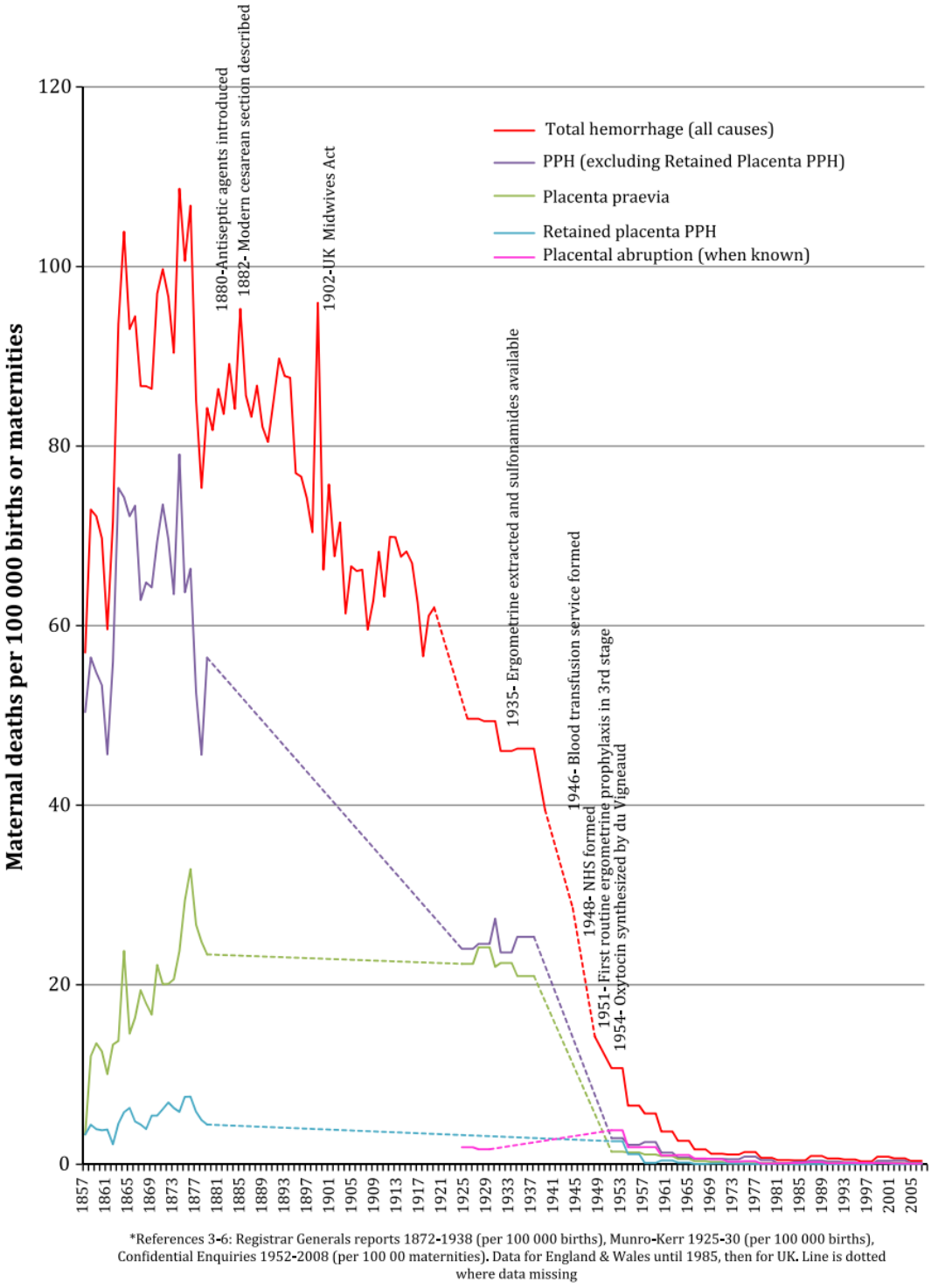


Figure 1.1 Maternal mortality rates by cause of haemorrhage in England and Wales/UK, 1847–2008 (from Kerr & Weeks 2015: p667 (21))

Maternal death from PPH is now exceptionally rare in high-income countries (25). A study of eight European countries found that maternal death caused by obstetric haemorrhage occurred in 0-1.4 per

100,000 live births (26) and a similarly low rate was observed in Australia in 2015-17 (6). Despite the increased incidence of PPH in recent decades (7, 8, 10, 12), there has not been a commensurate increase in the rate of maternal deaths caused by PPH (6, 21). While this suggests that current management is generally effective, severe maternal morbidity caused by PPH is markedly more common than maternal mortality and is a significant concern because of the short and long-term health implications for women (27, 28).

1.3 Outcomes following postpartum haemorrhage

Postpartum haemorrhage potentially has severe health implications for women, in both the short and longer term (29, 30). Immediately following the birth, anaemia can result from excessive blood loss, which can cause dizziness in the postpartum period and make it more difficult for women to recover from the birth (31). Blood transfusion may be required to replace blood volume and the potential risks associated with this include transfusion reaction, allergic reaction and infection (32). Infection has been shown to be more common among women who have had a PPH, particularly where the cause of PPH was retained products (33, 34). Women who have a severe PPH may have longer hospital stays, which can contribute to their increased risk of infection and can have negative implications for mother-baby bonding, breastfeeding and for women's wellbeing (35).

High volumes of blood loss can cause severe maternal morbidity, including hypovolemic shock, disseminated intravascular coagulation, hepatic failure, renal failure, and respiratory distress syndrome (36). Hysterectomy may be performed in cases where it is considered a necessary life-saving measure to stop the bleeding. While relatively uncommon among women who have had a PPH, occurring in around 0.45 per 1000 births in the UK (37), the consequent infertility can affect the subsequent health and wellbeing of the mother and her partner (38). In the longer term, potential health impacts associated with PPH also include psychological problems, including flashbacks and nightmares (39), and an increased risk of cardiovascular disease (40, 41).

The prevalence and potential severity of both short and long-term poor outcomes for women who have a PPH highlight the importance of understanding more about risk factors for PPH, particularly in the context of increasing incidence in high-income countries. Against this background, the aetiology of PPH and the various definitions and diagnostic criteria for PPH used internationally, are also important.

1.4 Causes of postpartum haemorrhage

There are four broad causes of PPH, often referred to by the mnemonic "the four T's" (42) representing 'tone', 'trauma', 'tissue', and 'thrombin'. These causes of PPH can occur individually or in combination.

'Tone' refers to a potential cause of PPH whereby a lack of uterine tone prevents the uterus from contracting and remaining firm after the birth. This can result in the failure of blood vessels to constrict causing significant blood loss from the placental bed and other areas of the uterus (23, 43). Uterine atony is the most common cause of PPH, accounting for 60-80% of PPH in high-income countries (16, 43).

Injury or 'trauma' to the birth canal or surrounding tissues during the birth, including perineal tears and cervical lacerations, is another potential cause of PPH. Trauma can be caused spontaneously through birth of the baby, by forceps or vacuum extraction or through lacerations during caesarean birth (44). Approximately 20% of PPH cases are caused by trauma (43).

'Tissue' retention or the incomplete expulsion of the placenta or fetal membranes after the birth can prevent the uterus from contracting and lead to significant blood loss (42). Retained placental tissue is the cause of approximately 10% of PPH (43).

Finally, blood disorders or abnormalities in the clotting system can prevent the blood from clotting properly and lead to excessive bleeding (44). Such 'thrombin' disorders can be pre-existing conditions, such as haemophilia or von Willebrand disease, or can develop during pregnancy such as HELLP syndrome (44). Such causes of PPH account for less than 1% of cases (43, 45).

Early identification of the cause of excessive blood loss is critical, as this will determine the most appropriate course of treatment and management (44).

1.5 Definition and measurement of postpartum haemorrhage

The definition of PPH varies widely between countries (46). The WHO defines PPH as "blood loss of 500mL or more from the genital tract following childbirth" (23). This definition has been adopted as standard practice in many countries, including the UK (44), France (47), Australia and New Zealand (48). However, other definitions are also commonly used, including the ICD-10 classification, which differentiates between modes of birth in terms of blood loss volume, with 500mL being the threshold for vaginal birth and 750mL for caesarean birth (49). The threshold of 1000mL, regardless of mode of birth, has been adopted by the American College of Obstetricians and Gynaecologists (ACOG) and is used in US and Canadian practice (43). This definition of PPH is also used variably in the Netherlands, Italy, Australia and Norway (50-52). The higher threshold for PPH is considered to reflect the blood loss volume that would be associated with symptoms of hypovolemia (43), while the lower threshold (500mL) is argued to reflect the amount of blood loss that could lead to shock and deterioration if left untreated (53).

One of the most common methods for estimating blood loss volume after birth is visual estimation by a clinician. However, diagnoses of PPH that rely on visual estimation of amount of blood loss, irrespective of the chosen threshold, have been called into question because of the inaccurate and subjective nature of visual assessment (54). Visual estimation has been consistently demonstrated to

lead to underestimation of blood loss, particularly at very high volumes, compared with more objective measures such as calibrated sheets and weighing swabs (55, 56). However, these more objective methods can be difficult to use as standard practice in maternity care as they are more resource intensive and can be more time consuming to set up and measure. This is particularly problematic in cases of rapid blood loss when urgent recognition and diagnosis is required to initiate appropriate treatment.

A more objective method of assessment is to compare haematocrit levels between admission or late pregnancy and postpartum measurements (57). This method allows a diagnosis of PPH based on objective criteria (e.g. 10% drop in haematocrit levels between measurements). However, this method has been criticised as it may not be clinically useful in an emergency and does not account for the speed of blood loss, which may be more relevant for a woman's ability to physiologically compensate (58).

Alternative definitions of PPH have been suggested based on the presentation of symptoms of haemodynamic instability (59). However, women who are otherwise healthy are likely to be able to physiologically compensate for significant amounts of blood loss prior to the presentation of symptoms (58). Diagnoses based on the assessment of decompensation, therefore, are problematic as they may lead to delayed treatment and contribute to further blood loss and deterioration (60).

1.5.1 Definitions of severe postpartum haemorrhage

Definitions of severe PPH (SPPH) are similarly disparate. Those that are based on blood loss volume, regardless of how this is measured, range from 1000mL to 2500 mL (8, 44). The RCOG differentiates between three classifications of PPH; 500-1000mL as mild, 1000-2000ml as moderate, and ≥2500mL as severe (44), while other bodies and organisations simply differentiate between PPH and SPPH.

Other definitions of SPPH include blood loss requiring transfusion, or requiring a transfusion of four or more units of blood products (61); blood loss requiring hysterectomy, return to theatre or admission to high dependency unit (62); or requiring uterine arterial embolization (63). However, diagnosis based on a treatment, either required or received, presents potential bias in terms of a clinician's subjective assessment, resource availability at the time of the birth, and policies regarding indications for such treatments (64).

It has also been suggested that the speed of blood loss, for example blood loss > 150ml/minute within 20 minutes, should be used to diagnose SPPH because this impacts urgency of treatment and potential ability to physiologically compensate and recover from haemorrhage (36). However, speed of blood loss can be difficult to objectively measure in a clinical setting and there has been limited research into PHH or SSPH diagnosis based on the speed of blood loss (65).

It is clear that timely recognition and diagnosis of PPH and SPPH is critical to initiating treatment and management. However, what is less clear from existing research is whether the definition or criteria used to assess PPH have a bearing on women's outcomes. An integrative review synthesising studies about estimation of blood loss highlighted a lack of research about the criteria used to initiate treatment in a clinical setting, which may be more relevant for outcomes than the selected definition of PPH (65). Given that a woman's individual ability to physiologically compensate for blood loss depends on a complex array of environmental, obstetric and medical factors (58), it is unlikely that any single definition of PPH or SPPH could accurately capture significant blood loss for every individual. Clinician's ability to recognise women who may be at higher risk of PPH and to appropriately respond to emerging risk in the birth episode is likely to be more relevant to maternal outcomes than the definition of PPH.

Notwithstanding challenges for clinical management, the differences in the definitions used for PPH and practices for measurement of blood loss also contribute to challenges in comparing and synthesising research about PPH incidence and risk factors across settings.

1.6 Incidence in high income countries

Estimates of the incidence of PPH vary widely between countries and healthcare settings (4, 8, 46, 66). Variations in the definitions of PPH make international comparisons of incidence difficult, but regardless of the definition employed, studies in high-income countries have shown an increasing incidence of PPH in the past three decades (8, 10, 12, 67). In Switzerland, the incidence of PPH increased from 2.5% in 1993 to 4.5% in 2014 (10). In the Netherlands, incidence rose from 4.1% in 2000 to 6.4% in 2013 (14). The incidence of PPH increased from 1.5% to 4.1% between 1999 and 2009 in Ireland (9). And in Victoria, Australia, the incidence of PPH increased by 50% over the 11-year period 2003-2013, from 9.0% to 13.5% (7).

One potential explanation for the increased incidence of PPH relates to the increase in proportions of instrumental and caesarean birth, which are both associated with higher volumes of blood loss (7, 13, 68). However, while this might account for some of the increased incidence in the birthing population overall, it cannot explain the increase in PPH seen across all modes of birth (Figures 1.2 and 1.3 below).

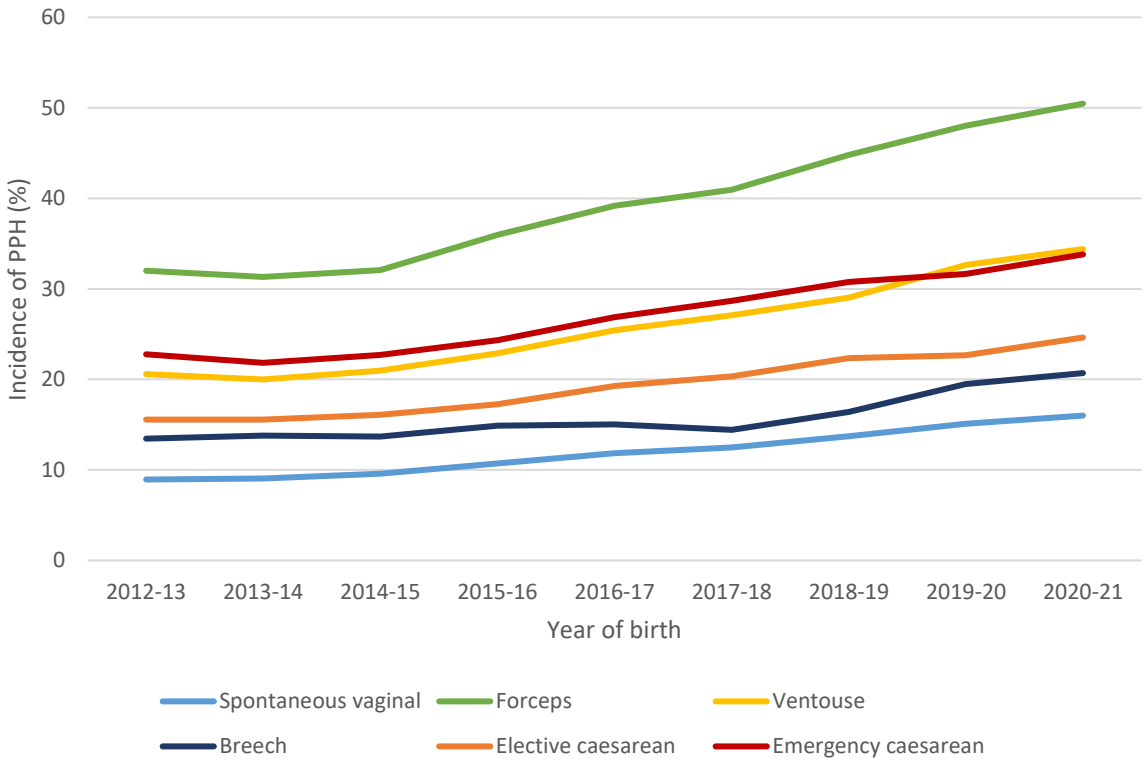


Figure 1.2 Incidence of PPH in England 2012-2021, by mode of birth (data from NHS Digital 2013-2021 (69-77))

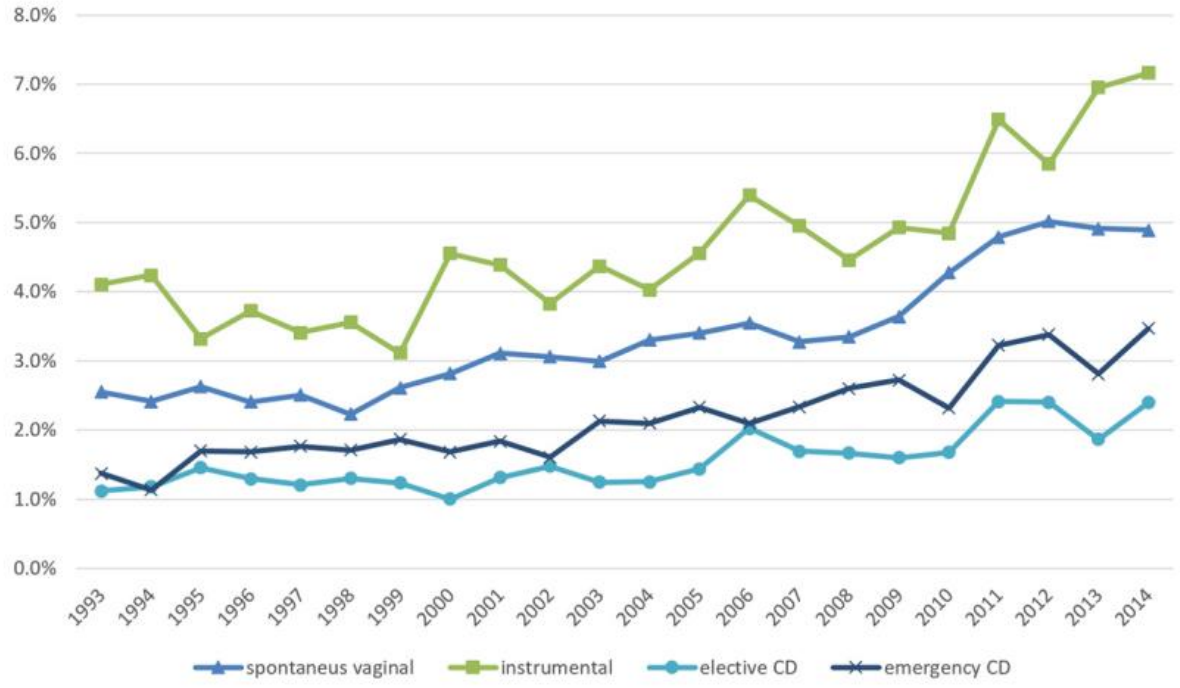


Figure 1.3 Incidence of PPH by mode of birth in Switzerland 1993-2014 (from Kaelin Agten 2017; p4 (10))

Both the UK (Figure 1.2) and Switzerland (Figure 1.3) use the WHO definition of PPH (blood loss ≥500mL) and while the incidence of PPH differs between these two settings, there is a clear upward trend across all modes of birth in both countries. Kaelin Agten and colleagues statistically controlled for maternal sociodemographic and medical practice changes over time and reported that these did not explain the increase in incidence of PPH over the 22-year period (10). Similarly, an Australian population-based study of births in the years 2003-2013 reported that while the prevalence of some risk factors increased over the study period, this did not fully explain the increase in incidence of PPH over the 11-year period (7).

It could be argued that increased awareness of PPH and improvements in clinical practices regarding the estimation and recording of blood loss may have improved case ascertainment and explain the observed increased incidence in PPH over the past three decades. While it is difficult to completely account for either of these factors, studies that have examined the trend by cause of PPH, have noted that the rise in incidence is most marked for atonic PPH (9, 33). If the increase were explainable by improved awareness and measurement, a similar increase in incidence across all causes of PPH would be expected. Given that this is not the case, greater awareness of PPH and improved measurement of blood loss is not likely to fully account for the trend. The observation of increased incidence of PPH in settings where blood loss measurement practices have remained stable also casts doubt on the plausibility of this potential explanation.

It seems likely that the increased incidence of PPH across high-income countries cannot be wholly accounted for by changes in measurement practices or by increased prevalence of known risk factors in the population. Investigation of this, however, is made more complicated by the fact that there is inconsistent evidence about what the risk factors for PPH are.

1.7 Risk factors for postpartum haemorrhage

Over the past three decades, there has been extensive research conducted to investigate the risk factors associated with PPH (35, 46, 68, 78). However, this research presents conflicting findings in terms of which risk factors are significantly associated with PPH. For example, advanced maternal age is often cited as a risk factor for PPH (46) and there is some observational research that suggests higher maternal age is associated with an increased risk of PPH (46, 78, 79). However, several studies report no association between advanced maternal age and PPH, after adjustment for confounding factors including pre-existing comorbidities (51, 80-82). A systematic review of maternal antenatal characteristics reported that, based on six studies from high- and low-income countries, there was no significant relationship between maternal age ≥35 and PPH (83). Similarly, for example, higher BMI is often reported as a risk factor for PPH, and while the same systematic review of six studies concluded that BMI ≥25 was associated with an increased risk of PPH, several other studies have reported no association between obesity or higher BMI and PPH, compared with women of a healthy weight.

When the research conducted for this thesis was started, in 2019, there was no published systematic review or synthesis of the risk factors for PPH in high-income countries. Previous research to describe the literature included an overview of existing research from both high and low-income countries, although this was not a systematic review and the authors did not attempt to synthesise the evidence in a structured way (46). A systematic review about risk factors for atonic PPH in both was published in 2021, however, the review included studies from both high- and low-income countries (78).

The guidelines and recommendations provided by national and international professional bodies about the management of PPH reflect the uncertainty in the literature regarding potential risk factors. A recent review of national and international organisations' guidelines for the management of PPH reported strong agreement across all guidelines in terms of highlighting third stage management as key to reducing the occurrence and severity of PPH (84). Active management of the third stage of

labour is recommended by all guidelines and supported by a Cochrane review and meta-analysis highlighting benefits in terms of reducing blood loss volume and reduced risk of postpartum blood transfusion, compared with expectant management of the third stage (84, 85). However, there is little agreement between clinical guidelines about the factors that could be identified prior to the third stage of labour to assess whether a woman might be at increased risk of having a PPH.

The Royal Australian and New Zealand College of Obstetrics and Gynaecology's Clinical Guidance for the Management of PPH states that most women who have a PPH do not have identifiable risk factors and recommends that women with known risk factors receive "appropriate management in the antenatal and intrapartum periods" (48),p5. However, the guideline does not specify what the 'known risk factors' for PPH might be. The French College of Gynaecologists and Obstetricians' guidelines are similarly ambiguous in terms of specifying risk factors for PPH, also indicating that risk factors are 'not predictive' but that previous PPH and risk factors related to labour and delivery (not specified) should be attended to closely (47).

In the UK, the national guidelines for managing PPH are developed by the Royal College of Obstetricians and Gynaecologists (RCOG) and presented as 'Green-top' guidelines. These guidelines recommend, "Clinicians must be aware of risk factors for PPH and should take these into account when counselling women about place of delivery" (44) p52. However, the guidelines do not refer to specific risk factors that should be considered when planning the place of birth. They do present a summary of risk factors of PPH (Figure 1.4), however, most these would not be known at the time that place of birth is being planned.

Risk factor	The four Ts	OR (95% CI)
Multiple pregnancy	Tone	3.30 (1.00–10.60)[16] 4.70 (2.40–9.10)[24]
Previous PPH	Tone	3.60 (1.20–10.20)[16]
Pre-eclampsia	Thrombin	5.00 (3.00–8.50)[16] 2.20 (1.30–3.70)[31]
Fetal macrosomia	Tone	2.11 (1.62–2.76)[20] 2.40 (1.90–2.90)[24]
Failure to progress in second stage	Tone	3.40 (2.40–4.70)[23] 1.90 (1.20–2.90)[31]
Prolonged third stage of labour	Tone	7.60 (4.20–13.50)[16] 2.61 (1.83–3.72)[20]
Retained placenta	Tissue	7.83 (3.78–16.22)[20] 3.50 (2.10–5.80)[23] 6.00 (3.50–10.40)[24]
Placenta accreta	Tissue	3.30 (1.70–6.40)[23]
Episiotomy	Trauma	4.70 (2.60–8.40)[16] 2.18 (1.68–2.76)[20] 1.70 (1.20–2.50)[24]
Perineal laceration	Trauma	1.40 (1.04–1.87)[20] 2.40 (2.00–2.80)[23] 1.70 (1.10–2.50)[24]
General anaesthesia	Tone	2.90 (1.90–4.50)[31]

Figure 1.4 Risk factors and the associated level of risk for PPH (from Mavirdes at al. 2016 (44))

A Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis consensus statement on prevention and treatment for PPH presents a similar list of risk factors, adding chorioamnionitis and mode of birth (pre-labour and intrapartum caesarean and instrumental birth) to the list of known risk factors. In contrast to the RCOG guideline, the consensus statement does not mention 'failure to progress in second stage' or placenta accreta as potential risk factors.

Finally, the American College of Obstetricians and Gynaecologists (ACOG) guidelines also acknowledge that PPH can be unpredictable but provide a longer list of potential risk factors and an example of a risk assessment tool, which is recommended for use at admission (Table 1.1)(43).

Low risk	Medium Risk	High Risk
Singleton pregnancy	Prior caesarean or uterine scarring	Previa, accrete, percreta
Less than four previous deliveries	More than four previous deliveries	Haematocrit < 30
Unscarred uterus	Multiple gestation	Bleeding at admission
Absence of PPH history	Large uterine fibroids	Known coagulation defect
	Chorioamnionitis	History of PPH
	Magnesium sulphate use	Abnormal vital signs
	Prolonged use of oxytocin	

Table 1.1 Example of a Risk Assessment Tool (adapted from Shields et al. 2017 (43))

The ACOG guidelines acknowledge the limitations of risk assessment tools, noting that many have demonstrated low specificity, below 60% and limited discrimination among low-risk women (43). While a risk assessment tool may be useful for identifying women at high risk, the clinical value of existing tools appears to be limited. Two recent systematic reviews of prediction models for PPH both concluded that, of 14 (86) and 16 (87) studies presenting prognostic models of PPH, none were appropriate for implementation in clinical practice. This assessment was a product of the models' high risk of bias, lack of internal or external validation, and problematic selection of predictors, including from univariable analyses (86, 87).

It is evident that assessment of women's risk of PPH is challenging, and this is reflected in the conflicting evidence from observational studies, the ambiguity of clinical guidelines, and the performance of prognostic models. This appears to be particularly evident for women who might be considered to be at low risk of complications (43). A substantial factor contributing to this difficulty stems from the uncertainty surrounding the identification of risk factors for PPH, how they may be interrelated and whether the factors differ for women who would otherwise be considered 'low-risk'.

1.8 Postpartum haemorrhage in 'low-risk' women

The definition of 'low-risk' varies by context but generally it refers to women who are giving birth to a singleton baby with vertex presentation at term and with no underlying medical or obstetric factors that might place them at a higher risk of complications during labour and birth (43, 44, 88). While

strictly speaking it is not the woman herself who is 'low-risk', but her social and clinical characteristics that mean that she has a lower risk of experiencing complications, the phrase 'low-risk woman' is widely used and is used throughout this thesis in the interest of brevity. The proportion of women considered to be low-risk also varies based on definition and context, but is likely to be substantial in high-income countries. In the UK, a population-based study of women giving birth in 2011 found that 45% of women met the above definition of low-risk (89). A Dutch study of nulliparous women in 1990-1995 reported that 41% of pregnancies were considered low-risk, although their criteria also included 'uneventful first and second stage of delivery' (81). A study of over 10 million births in 2011-2013 in the USA identified that 38% of women met the criteria for low-risk prior to the onset of labour (90). A similar proportion (42%) of women were identified as low-risk in a New Zealand Study of 40,000 births in 2006-2007 (91). Despite the fact that low-risk women constitute a large proportion of the birthing population, the existing literature on risk factors for PPH primarily focuses on the general population of women giving birth. However, prior research has indicated that low-risk women still experience PPH (15, 33, 81, 91, 92).

Women who are considered low-risk of complications may be eligible to plan birth in midwifery led unit or at home and an understanding of their potential risk of complications, including PPH, is an important factor informing that decision. In many high-income countries, women are supported to make an informed choice about their planned place of birth and a midwifery unit (MU) may be a preferred option for many low-risk women (93). In the UK, where support for women's choices around place of birth has been a central focus of maternity care policy (94), around 13% of births occur in MUs (95). MUs in the UK can either be located on the same site as an obstetric unit (OU), referred to as an alongside midwifery unit (AMU), or on a separate site, referred to as a freestanding midwifery unit (FMU). Care in MUs is provided by midwives and transfer to an OU is required if medical, anaesthetic or obstetric services are needed. Transfer may take only a few minutes in the case of AMUs, where the OU is located another floor or area within the site, or may involve considerable travel time in the

case of some FMUs, where transfer takes place by ambulance. Because of the potential delay in access to medical treatments for women who give birth in MU, recognition of women who might be at increased risk of PPH is critical.

An accurate understanding of a woman's potential level of risk is not just important for women who wish to consider planning birth in a midwifery unit or at home. For women who wish to plan birth in an obstetric setting, understanding their potential level of risk is relevant for counselling on decisions such as the management of third stage of labour. It also is important for clinicians' preparedness for PPH, which may include ensuring availability of blood products. For these reasons, an understanding of the risk factors for PPH among low-risk women, including whether these are different to those observed in the general birthing population, is an important area requiring research.

1.9 Aims and objectives of thesis

The overarching aim of this research was to investigate the risk factors for PPH, to inform changes to clinical practice and policy and ultimately improve outcomes for women. To achieve this aim, the following four research objectives were developed:

1. To synthesise the evidence about risk factors for PPH in high-income countries and describe the current gaps in the knowledge base
2. To identify maternal, perinatal and intrapartum factors that may increase the risk of a woman experiencing (a) PPH and (b) SPPH
3. To identify maternal, perinatal and intrapartum factors risk factors that may increase the risk of PPH in healthy women with straightforward pregnancies
4. To examine whether the incidence of PPH has changed over time and explore whether this is associated with changes in the prevalence of key risk factors.

Three studies were conducted to address these aims and are presented in the following three chapters of this thesis.

1. Chapter 2: A systematic review and narrative synthesis of risk factors associated with postpartum haemorrhage in high-income countries (Objective 1)
2. Chapter 3: A national case-control study of the incidence and risk factors for postpartum haemorrhage occurring in midwifery units in the UK (Objectives 3 and 4)
3. Chapter 4: A case-control study investigating the incidence, temporal trends and risk factors for postpartum haemorrhage in a Scottish population (Objectives 2, 3, & 4)

The methods, results, and strengths and limitations of each of these three studies are presented in their corresponding chapters in this thesis. Because of the inter-related nature of the findings of the three studies, and to avoid undue repetition, the findings are discussed together, in the context of other related literature, in the final overarching discussion chapter (Chapter 5), which also considers implications for policy and practice and for future research.

Chapter 2: Risk factors for postpartum haemorrhage in high income countries

2.1 Introduction

There is a large body of published research about risk factors for PPH, but estimates of association between putative risk factors and PPH vary widely (23, 33, 46, 78). When the research conducted for this thesis began there was no published systematic review of studies investigating risk factors for PPH in high-income countries. One systematic review published since has focused on risk factors for atonic PPH, including research conducted in high- and low-income countries (78). A comprehensive systematic review would provide valuable information for identifying which women might be at higher risk of PPH and thus provide greater opportunities for prevention. Furthermore, this also provided an opportunity to synthesise the evidence about risk factors for PPH among low-risk women.

2.2 Aims and objectives

The aim of this study was to conduct a systematic review and synthesis of studies examining factors associated with an increased risk of PPH among women giving birth in high-income countries. The key objectives were to:

1. Identify all studies investigating risk factors for PPH in high income countries, examine the strength of these associations and summarise gaps in the knowledge base;
2. Consolidate and describe the evidence for risk factors associated with PPH and SPPH in high-income countries;
3. Consolidate and describe the evidence for risk factors associated with PPH and SPPH among women who may be considered at lower risk of complications during labour and birth.

2.3 Methods

2.3.1 Protocol

The protocol for this systematic review was registered in the PROSPERO international prospective register of systematic reviews (CRD42020165783) and was reported according to Preferred Reporting

Items for Systematic Reviews and Meta-Analyses (PRISMA) (96) and Systematic Review without Meta-analyses (SWiM) (97) guidelines.

2.3.2 Inclusion criteria

Population

Studies of women giving birth in high-income countries, as defined by Organisation for Economic Co-operation and Development (OECD) membership at the time of the study (98), were included.

Exposure

Studies reporting the statistical relationship between at least one risk factor and the diagnosis of PPH were included. Risk factors were defined as any attribute, characteristic or exposure that may increase the likelihood of experiencing a PPH. This included, but was not limited to, maternal socio-demographic and clinical characteristics; pregnancy and obstetric history factors; and labour and birth care. Studies examining the potential protective effect of such factors were also included.

Comparison

Studies were eligible for inclusion if they included a sample of women who experienced primary PPH, and a sample of comparator women, derived from the same population, who did not experience PPH.

Outcome

The outcome of interest was diagnosis of primary PPH, including SPPH. Given the range of definitions for PPH and SPPH used globally, the review did not exclude studies based on the definition of PPH or SPPH, and also included those where the stated outcome of interest was postpartum blood transfusion, where this was considered by the study authors as a marker or indicator of primary PPH.

2.3.3 Exclusion criteria

The review excluded studies that:

- Investigated secondary PPH only or included secondary PPH and primary PPH together
- Did not include a comparison (control) population of women who did not experience PPH
- Had a qualitative, clinical trial or case study design
- Defined the population by a procedure to manage PPH, such as postpartum hysterectomy
- Were not peer reviewed
- Were published in languages other than English

2.3.4 Search strategy

The search strategy was designed in consultation with an information librarian. A combination of medical subject headings (MeSH) and free-text terms relating to PPH and risk factors were used to identify relevant studies. The search terms for Medline, Embase and Web of Science are provided in Appendix A.1. One researcher (ME) conducted searches of Embase, Medline and Web of Science for studies published up to and including February 2020. Searches were conducted on February 4 2020 (Medline and Embase) and 5 Feb 2020 (Web of Science).

2.3.5 Screening and selection

Articles identified through the search strategy were imported into the reference management software EndNote (99) and duplicates were removed. Remaining articles were uploaded to the systematic review management software package Covidence (100) where titles and abstracts were screened by one reviewer (ME) and evaluated against the eligibility criteria. The full text of all articles included based on the initial screening were reviewed independently by two reviewers for further inclusion or exclusion. Any disagreement about the eligibility of a study for inclusion was resolved by discussion and a consensus reached, involving a third reviewer where necessary.

2.3.6 Data extraction

Data were extracted by two reviewers, independently. Two data extraction forms were created to facilitate the accurate extraction of study characteristics and results. Information about the following characteristics of the study and population were extracted and entered into Covidence software (see Appendix A.3 for the data extraction form):

- Authors
- Year of publication
- Country
- Year/s of study
- Aims and objectives
- Definition of PPH
- Study design
- Inclusion and exclusion criteria
- Sample size
- Rates/incidence of PPH

Information about data analysis and study results was extracted using a bespoke data extraction form, designed by ME, in Microsoft Excel. The data extraction form (Appendix A.4) was developed in consultation with two reviewers, piloted for usability and accuracy, and facilitated extraction of the following information:

- Statistical methods
- Variables adjusted for in the multivariable analysis
- Risk factors investigated
- Statistics (odd ratios (OR), relative risk (RR), means, medians)
- Confidence intervals
- p values

Extracted data were compared between reviewers using a combination of visual assessment and Microsoft Excel conditional formatting to identify discrepancies between the two reviewers' forms. Where differences were identified, the original paper was consulted and a discussion between the reviewers resolved any remaining inconsistencies.

2.3.7 Definition of postpartum haemorrhage and severe postpartum haemorrhage

All definitions of PPH and SPPH that fitted the inclusion criteria were considered as eligible for inclusion in the review. However, in order to synthesise the literature consistently, for the purposes of comparing and describing outcomes, PPH and SPPH were defined in the following standardised way.

PPH: All studies where the stated outcome was primary PPH, typically blood loss of 500mL of more, were defined as examining PPH. Studies that used a threshold higher than 500mL but less than 1500mL were classified as examining PPH, regardless of the terminology employed in the paper. This included those, for example, that considered blood loss of >1000mL as an outcome and described this as SPPH.

SPPH: All studies that stated they were examining SPPH and defined this as blood loss ≥1500mL were defined as examining SPPH. Studies for which the reported cut-off for SPPH was blood loss of <1500mL blood loss, or where other diagnostic criteria were applied, were classified as examining PPH.

2.3.8 Risk of bias

Risk of bias in individual studies was assessed qualitatively using the Risk of Bias in Non-randomized Studies (ROBANS) tool, which was considered appropriate given the observational nature of the included studies and the acceptable validity and reliability of the tool (101).

Studies were evaluated based on the level of bias in six pre-determined domains:

1. Participant selection
2. Confounding variables
3. Exposure (risk factor) measurement
4. Outcome (PPH) assessment
5. Incomplete data, and
6. Selective reporting

The guideline for assessing risk of bias against these domains was adapted for the specific research question (Appendix A.2). Two reviewers independently assessed the risk of bias in each domain as

'low', 'high', or 'unclear'. Differences in ratings were resolved through discussion between the two reviewers.

For the purposes of the narrative synthesis, studies that were considered to have a high risk of bias in terms of confounding (i.e. those that did not adjust at all for confounding factors) were referred to as 'high risk of bias' (HRoB) while those that were considered to have a low risk of bias on this domain were referred to as 'low risk of bias' (LRoB).

2.3.9 Data synthesis and analysis

Included studies and their characteristics were summarised in structured tables and described in terms of year of publication, country and years of data, study population, definition of PPH/SPPH, number of women and the incidence of PPH/SPPH.

A meta-analysis of risk factors was planned in the study protocol, however, after data extraction was complete, it became clear that studies were too heterogeneous to warrant a meta-analysis. Heterogeneity was assessed in terms of: clinical heterogeneity (different definitions of PPH/SPPH; different inclusion/exclusion criteria of populations; different definitions/categorisation of risk factors); and methodological heterogeneity (statistical tests and risk factors adjusted for in analyses). This heterogeneity meant that combining results from studies with different methods that adjusted for different confounding factors would produce misleading summary statistics (due to the 'non-collapsibility' of ORs) (102). For this reason, and consistent with best practice for a systematic review based on observational studies with a high degree of heterogeneity (97), it was not considered appropriate to carry out a meta-analysis and a narrative synthesis of risk factors for PPH was conducted.

Risk factors were categorised into the following groups:

1. Maternal characteristics
2. Pre-existing medical factors
3. Obstetric history

4. Current pregnancy factors
5. Intrapartum factors
6. Birth-related factors
7. Baby characteristics

The classification of risk factors into these categories was performed by ME and was reviewed by two supervisors to ensure clinical accuracy and clarity for interpretation. The risk factors investigated, reported statistics (e.g. OR, adjusted OR (aOR), unadjusted OR (uOR), proportions), confidence intervals and levels of statistical significance for all risk factors investigated were summarised in structured tables according to the categories above. The 'most-adjusted' statistics reported for each risk factor were included in the tables and the narrative synthesis. That is, if a study had reported percentages, uOR and aOR for a given risk factor, the aOR was reported in the tables; where aOR were not available, uOR were reported; and where uOR were not reported, numbers or percentages were reported. Where uOR were not reported, manual calculations of uOR were not conducted but numbers or proportions and statistical significance (or non-significance) were reported. Unless otherwise stated, CI are all 95% level of significance. The definition of PPH/SPPH used in each study and mode of birth were included in the tables to provide context for interpretation.

The number of studies that investigated each risk factor was tallied. Risk factors that were investigated by five or more studies were included in the narrative synthesis. Within each category, risk factors were ordered in tables from the most commonly analysed to the least. For example, within the 'Maternal characteristics' category, 'Age' had 45 studies that examine that risk factor, followed by 'Race/ethnicity' with 14, therefore 'Age' was presented in the results first, followed by 'Race/ethnicity'. The results for risk factors that were investigated by four or fewer studies were also summarised in tables (Appendix A.5), but were not included in the narrative synthesis.

The terminology used by individual studies to describe risk factors or categories was retained to ensure fidelity to the original results and avoid creating the misleading impression of similarity across studies. This was the case even when terms were considered synonymous, for example, for presentation of the baby, the terms 'cephalic' and 'vertex' were both included in the results tables as they were both used by different studies. For the purpose of the narrative synthesis, findings for risk factors and categories that could reasonably be described together were combined in the text.

2.3.9.1 Determining the strength of evidence for a risk factor

A structured approach was used to determine the strength of evidence for any given risk factor. The unit of analysis for this was the number of 'analyses' examining each risk factor, rather than the number of studies. Most studies conducted and reported on one analysis, for example, one primary outcome in one study population. However, several studies reported more than one analysis. This included, for example, examining risk factors for PPH and SPPH separately, or examining risk factors for one outcome, but in more than one population (e.g. different countries) or sub-population (e.g. different modes of birth). Counting analyses, rather than studies, provided a more accurate representation of the findings of each study as it allowed studies that found a significant association for a given risk factor in one population but not in the other to be counted as such in the narrative synthesis. The only exception to this approach was for studies reporting two different measures of the same outcome (for example, PPH of 500mL or more and PPH of 1000mL or more), which were counted as one analysis for the purposes of determining strength of evidence. If a study found a significant association for either (or both) definitions of PPH employed, this was counted as one significant result for the purposes of tallying the number of risk factors.

The number of LRoB analyses that were statistically significant ($p<0.05$) at the adjusted level was tallied for each risk factor. This was divided by the number of LRoB analyses (unadjusted and adjusted) that were conducted for that risk factor and multiplied by 100 to provide a proportion of significant adjusted results. For example, if an LRoB study reported only unadjusted ORs or proportions for a

particular risk factor, this was counted in the total number of analyses (denominator) but not the total number of significant adjusted ORs (numerator). This approach was designed to reflect the proportion of studies that found an independent risk factors for PPH, which can only be ascertained through adjusted analyses, rather than reflect the number of univariable associations, which may be a product of confounding. Studies that did not report any adjusted results were considered HRoB in terms of confounding, as none of the results presented had been adjusted for confounding factors. These studies were not included in the calculations to determine the strength of the evidence of the risk factor, however, they were included in the tables and were summarised in the narrative synthesis, where applicable.

The risk factors that were included in the narrative synthesis were described in terms of the likelihood of the variable being a risk factor for PPH/SPPH based on the criteria set out in Box 1, ranging from 'Not a risk factor' to 'Very likely' a risk factor. This rubric was adapted from Ende et al. (78) with changes made to their 'Definite' category, which was defined by Ende et al. as "Majority (more than 50%) low and moderate risk of bias positive" (78). For the purposes of this review, the 'Definite' category was divided into two categories: 'Likely' and 'Very likely'. This change was made in part because 50% of LRoB studies was considered too low a proportion to categorise a risk factor as 'definite'. This change also enabled a distinction between risk factors for which the overwhelming majority of results were in one direction, with a small minority in the opposing direction (now classified as likely), from risk factors with either a large proportion of studies having conflicting results or only a minority of studies with a significant association (unclear). The Ende (78) assessment classified both of these types of risk factor results as 'unclear'.

Very likely

More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.

Likely

Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.

OR

More than 80% of LRoB analyses found a significant association in the same direction, but at least one study found a significant effect in the opposite direction. At least 5 LRoB studies examined the risk factor.

Unclear

Less than 50% of LRoB analyses found a significant association.

Between 50% and 80% of LRoB analysis found a significant association, but in conflicting directions.

Not a risk factor

No LRoB analyses found a significant association.

Box 2.1 Defining the likelihood of a risk factor having a true association with PPH

2.3.9.2 Magnitude of effect

For the purposes of describing study findings consistently, the criteria set out in Table 2.1 were used to describe the magnitude of effect for each risk factor associated with PPH. In principle, the magnitude of any given effect estimate (e.g. OR) should be assessed in the context of the prevalence of the outcome in the unexposed group (103). However, when comparing magnitude of effect across different studies it was not possible to take the prevalence into account. Therefore, a rubric was created to facilitate uniform description and support interpretation of the magnitude of the effect, based on the approach described by Chen et al. (103) which maps ORs to Cohen's *d*. The cut-offs selected were based on the prevalence of the outcome in the unexposed group being 5%. While the actual prevalence of either PPH or SPPH in the unexposed (control) groups, would have varied widely,

this was considered a reasonable cut-off, given that the median incidence of PPH across the studies was 5%.

Table 2.1 Definition of magnitude of effect for risk factors

Small effect	OR between 1 and 1.52
Moderate effect	OR between 1.53 and 2.74
Large effect	OR between 2.75 and 4.72
Very large effect	OR >4.72

2.4 Results

A total of 26,607 articles were identified through the search of databases (Figure 2.1). After removal of duplicates (n=10,329), 16,368 were screened for potential inclusion through title and abstract review. Stage one of screening eliminated 16,155 articles and therefore 213 were further screened through full text review. A total of 53 studies met all criteria and were therefore included in the review.

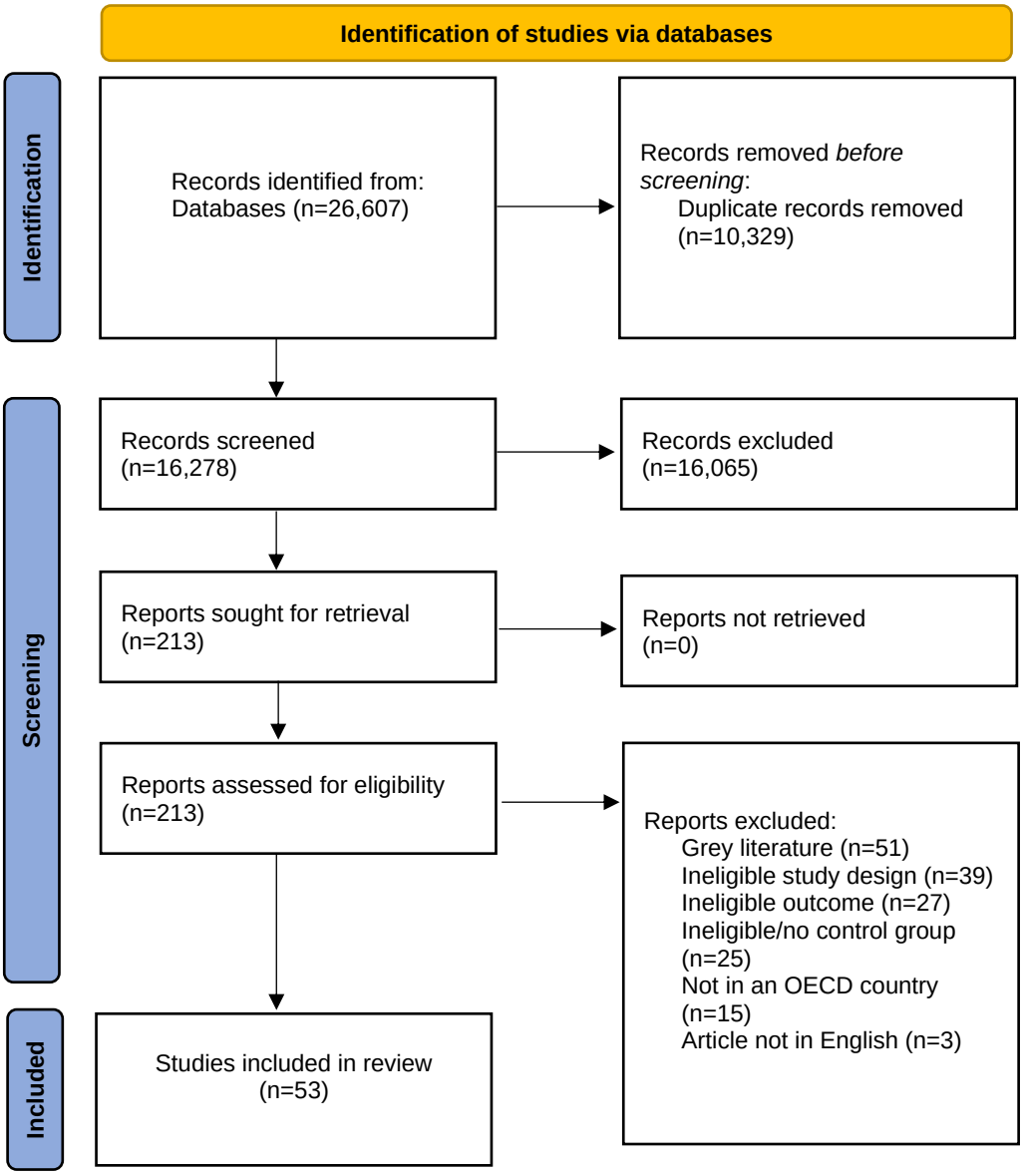


Figure 2.2 PRISMA flow chart of studies

2.4.1 Study characteristics

The 53 studies in this review reported data collected in 14 different countries (Table 2.2). This comprised seven reporting data from Australia, six from Canada, six from Japan, five from the USA, four from each of France, Norway, the Netherlands and the UK, three from each of Israel, Italy, South Korea and Sweden, one from Germany and one from Switzerland. Data were from the years 1952-2016, with most data coming from births that occurred after the year 2000. Most studies were conducted in obstetric units and most data sources were hospital records. Study size varied widely, ranging from 209 to 55,140,088 women. The most common definition of PPH was blood loss ≥500mL

and the most common definition of SPPH was blood loss ≥1500mL. The incidence of PPH ranged from 0.43% to 33.7%, while the incidence of SPPH ranged from 0.1% to 14.4%.

While many studies limited the population to singleton and/or vaginal births, most examined risk factors among the general population of women giving birth. A small number included only high or low-risk women. Three studies restricted analyses to women who could be considered at higher risk of PPH due to a diagnosis of 'gestational hypertension or mild pre-eclampsia' (51) placenta praevia (104) or incomplete placenta praevia (63). Five studies examined a low-risk population, including only women described as having: no "known clinical complication" (50), being "low-risk women who gave birth after 37 weeks' to a live baby with cephalic presentation " (105) "good mental and physical health and Class II-III physical status" (106), and no "pre-existing risk factors for postpartum haemorrhage" (15). One study investigated women giving birth in midwifery units (107), which are generally only available to women at lower risk of complications, but, the admission criteria for birth in midwifery units in Japan were not described. The protocol for this systematic review included an aim to consolidate the evidence for risk factors among low-risk women, however, as there were only five studies that focused specifically on low risk women and the definitions of low risk were difficult to compare, a separate synthesis of these findings was not considered appropriate.

Table 2.2 Summary of included studies

Author, year	*Country & years of data*	*Study population*	*Definition of PPH/SPPH*	*Number of women*	*Incidence of PPH/ SPPH*
Allen, 1989 (108)	Australia 1982-1986	All births in Tasmania during the study period, excluding those with retained placenta.	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	**PPH:** 7.2%
Bais, 2004 (81)	The Netherlands 1999-1995	All nulliparous women who gave birth vaginally after 20 weeks of gestation.	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	**PPH 1:** 19% **PPH 2:** 4.2%
Biguzzi, 2014 (109)	Italy 2007-2009	All women who gave birth vaginally to a singleton after 37 weeks' gestation at the obstetric unit of a hospital in Milan, Italy, in the study period.	**PPH:** CBL ≥500mL	3,219	**PPH:** 26.9%
Biguzzi, 2011 (110)	Italy 2007-2009	All women who gave birth vaginally to a singleton after 37 weeks' gestation at the obstetric unit of a hospital in Milan, Italy, in the study period.	**PPH:** CBL ≥500mL	**Total:** 6,011 **PPH:** 1,435 **CTL:** 4,576	**PPH:** 24%
Bonnet, 2013 (111)	Canada and France 2004-2006	Canada: All hospital births in the study period.in Canada, excluding Quebec, Newfoundland, Prince Edward Island, Nova Scotia, New Brunswick, and British Columbia France: All births in maternity units in three regions of France, comprising 20% of nationwide births.	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	**France** **PPH:** 4.5% **Canada** **PPH:** 4.8%
Briley, 2013 (56)	UK 2008-2009	All women giving birth in two maternity services in London between 1 August 2008 and 31 July 2009.	**PPH:** EBL ≥500mL	9,937	**PPH:** 33.7%
Butwick, 2017 (112)	USA 2002-2012	Women who gave birth by caesarean at a tertiary care obstetric centre, between January 2002 and December 2012.	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	**SPPH:** 3.6%

Author, year	*Country & years of data*	*Study population*	*Definition of PPH/SPPH*	*Number of women*	*Incidence of PPH/ SPPH*
Buzaglo, 2014 (113)	Israel 1988-2012	All first singleton births that took place at the Soroka University Medical Center between the years 1988 and 2012.	**PPH:** EBL ≥500mL	56,394	**PPH:** 0.79%
Choe, 2016 (82)	South Korea 2002-2013	All women with a diagnostic (ICD) code for birth in Korea during the study period aged 14-44 years.	**PPH:** ICD-10 code O72.0-O72.3 or transfusion	65,479	**PPH:** 2.4%
Combs, 1991a (57)	USA 1978-1988	Women who gave birth by caesarean between 1978-1988 with a gestational age of 20 weeks or more and no antenatal bleeding.	**PPH:** Haematocrit decrease of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	**PPH:** 6.4%
Combs, 1991b (61)	USA 1978-1988	Women who gave birth vaginally between 1978-1988 with a gestational age of 20 weeks or more and no antenatal bleeding.	**PPH:** Haematocrit decrease of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	**PPH:** 3.9%
Davey, 2019 (114)	Australia 2009-2013	All women who gave birth in Victoria, Australia, from 1 January 2009 to 31 Dec 2013.	**SPPH:** EBL ≥1500mL	364,701	**SPPH:** 1.4%

Author, year	*Country & years of data*	*Study population*	*Definition of PPH/SPPH*	*Number of women*	*Incidence of PPH/ SPPH*
Dionne, 2015 (115)	France 2004-2006	Nulliparous women having a vaginal birth with vertex presentation at a French maternity unit belonging to one of six perinatal networks.	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	**PPH 1:** 3,852 **PPH 2:** 1,048 **CTL:** 762	**PPH 1:** 2.63% **PPH 2:** 0.71%
Endo-Kawamura, 2016 (116)	Japan 2011-2013	Women who had antenatal care on or after gestational week 32 at a university hospital and gave birth vaginally to singleton infants on or after 35 weeks' gestation at the same hospital during the 3-year study period.	**PPH:** EBL ≥700mL	**Total:** 1,032 **PPH:** 104 **CTL:** 928	**PPH:** 10%
Eto, 2016 (107)	Japan 2001-2006	Women giving birth in midwifery centres in Japan.	**PPH 1:** EBL ≥500g **PPH 2:** EBL ≥800g **PPH 3:** EBL >1000g	**CTL:** 2,524 **PPH 1:** 524 **PPH 2:** 147 **PPH 3:** 158	**PPH 1:** 12.9% **PPH 2:** 3.6% **PPH 3:** 3.9%
Farina, 2017 (50)	Italy 2014-2016	Women who had a normal singleton pregnancy at term, without any known clinical complication, seen for care at the University of Bologna hospital who gave a blood measurement of Placental Protein 13.	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390	**PPH:** 3.45%*
Firmin, 2019 (117)	France (Western French Guiana) 2014-2015	Women giving birth at the Centre Hospitalier de l'Ouest Guyanais hospital in Western French Guiana after 20 weeks' gestation and with a baby weighing at least 500g.	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	**PPH:** 6.17%

Author, year	*Country & years of data*	*Study population*	*Definition of PPH/SPPH*	*Number of women*	*Incidence of PPH/ SPPH*
Flood, 2019 (7)	Australia 2003-2013	All women who gave birth in Victoria, Australia, between January 2003 and December 2013.	**PPH:** EBL ≥500mL **SPPH:** EBL ≥1500mL	**Total:** 364,574 **PPH:** 79,437 **SPPH:** 5120	**PPH:** 21.79% **SPPH:** 1.4% *
Ford, 2007 (13)	Australia 1994-2002	Women having at least a first and second consecutive pregnancy resulting in a singleton birth at > 400g or 20 weeks' gestation in the study period.	**PPH:** ICD 9 and 10 codes	752,374	NA
Fukami, 2019 (118)	Japan 2013-2016	All women giving birth vaginally to a singleton, live born baby after 22 weeks of gestation in one of the tertiary perinatal facilities in Japan.	**PPH:** CBL ≥1000mL ** ** Calibrated blood loss using drapes	**N:** 1,068 **PPH:** 93 **SPPH:** 22	**PPH:** 8.7% **SPPH:** 2.1%
Gilbert, 1987 (119)	UK 1984-1985	Women having a singleton vaginal birth, not complicated by a retained placenta, at a single maternity unit between August 1984 and January 1985.	**PPH:** CBL ≥500mL	**N:** 437 **PPH:** 86 **CTL:** 351	**PPH:** 19.7%*
Henry, 2005 (62)	Australia 2003-2003	Women giving birth vaginally from February to June 2003 at a tertiary teaching hospital in Western Australia.	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**N:** 1,066 **CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	**PPH**: 12% **SPPH**: 4.7%
Hiersch, 2016 (120)	Israel 2012-2014	All women giving birth after 34 weeks' gestation to a singleton live born baby by vacuum assisted vaginal delivery in a university-affiliated tertiary hospital.	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	**N:** 1,154 **PPH:** 295 **CTL:** 859	**PPH:** 25.6%
Kaelin Agten, 2017 (10)	Switzerland 1993-2014	All women who gave birth after 24 weeks' gestation between January 1993 and December 2014.	**PPH:** EBL ≥500mL	**N:** 739,444 **PPH:** 22,940 **SPPH:** 761	**PPH:** 3.1% **SPPH:** 0.1%

Author, year	*Country & years of data*	*Study population*	*Definition of PPH/SPPH*	*Number of women*	*Incidence of PPH/ SPPH*
Kaufner, 2016 (106)	Germany 2012-2013	Women who gave birth vaginally or by planned caesarean who were of good mental health and Class II-III physical status according to the American Society of Anesthesiologists' classification.	**PPH:** EBL ≥500mL	**N:** 209 **PPH:** 28 **CTL:** 181	**PPH:** 13.4%*
Khireddine, 2012 (105)	France 2004-2006	Low-risk women who gave birth after 37 weeks' gestation to a live baby with cephalic presentation in 106 French maternity units between December 2004 and November 2006.	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH:** 4,450 **SPPH:** 1,125	**PPH:** 4.5%
Koopmans, 2014 (51)	The Netherlands 2005-2008	Women with gestational hypertension or mild pre-eclampsia who gave birth to a singleton with cephalic presentation between 35 and 41 weeks' gestation.	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH**: 118 **CTL:** 1,014	**PPH:** 10.4%
Kramer, 2011 (12)	Canada 1978-2007	Singleton births that occurred at Montreal's Royal Victoria Hospital between January 1, 1978, and January 31, 2007.	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	**N:** 103,726 **PPH:** 2,346 **SPPH:** 39	**PPH:** 2.3% **SPPH:** 0.19%
Lee, 2017 (63)	South Korea 2006-2016	Women with incomplete placenta previa who gave birth between 24 and 41 weeks' gestation; excluding those with complete placenta previa, those with anterior placenta previa, and those with multiple births and diagnosed diseases.	**SPPH:** intraoperative blood loss ≥2000mL, postpartum transfusion of four or more pints of packed RBC, caesarean hysterectomy or uterine arterial embolization triggered by postpartum bleeding.	**N:** 210 **SPPH:** 23 **CTL:** 187	**SPPH:** 11%

Author, year	*Country & years of data*	*Study population*	*Definition of PPH/SPPH*	*Number of women*	*Incidence of PPH/ SPPH*
Lee, 2018 (104)	South Korea 2006-2016	Pregnant women with placenta previa who gave birth between24 and 41 gestational weeks.	**SPPH:** intraoperative blood loss ≥2000mL, postpartum transfusion of four or more pints of packed RBC, caesarean hysterectomy or uterine arterial embolization triggered by postpartum bleeding.	**N:** 506 **SPPH:** 73 **CTL:** 433	**SPPH:** 14.4%
Lisonkova, 2016 (121)	Canada 2011-2013	Women who gave birth between January 2011 and December 2013 in eight tertiary hospitals in Canada.	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	NA
Looft, 2017 (122)	Sweden 2008-2014	All primiparous women with singleton term births with cephalic presentation in one region from 2008 through October 2014.	**PPH:** EBL ≥500mL	**N:** 57,267 **SPPH:** 16,554	**PPH:** 28.9%
Magan, 2005a (123)	Australia 1998-2002	Women who gave birth by caesarean between 1998 and 2002 at King Edward Memorial Tertiary hospital in Australia.	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	**N:** 4,837 **PPH:** 125	**Elective CS PPH:** 4.84% **Non-elective CS PPH:** 6.75% **Elective CS SPPH:** 1.90% **Non-elective CS SPPH:** 3.04%
Magan, 2005b (52)	Australia 1998-2002	Women who gave birth vaginally between 1998 and 2002 at King Edward Memorial Tertiary hospital in Australia.	**PPH:** CBL≥1000mL and/or transfusion	**N:** 13,868 **PPH:** 714	**PPH**: 5.15%

Author, year	*Country & years of data*	*Study population*	*Definition of PPH/SPPH*	*Number of women*	*Incidence of PPH/ SPPH*
Malabarey, 2011 (15)	Canada 2001-2007	All women giving birth between 24 and 42 weeks' gestation who did not have pre-existing risk factors for postpartum haemorrhage.	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**N:** 15,198 **PPH:** 239 **CTL:** 14,959	**PPH:** 1.6%
Mehrabadi, 2013 (124)	Canada 2003 – 2011	All hospital births in Canada (excluding Quebec) that resulted in a live birth or stillbirth.	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	**N:** 2,193,425 **PPH:** 122,676 **SPPH:** 9,575	**PPH:** 5.6% **SPPH:** 0.48%
Merriam, 2018 (125)	USA 1998 – 2011	Women from 16 to 49 years of age hospitalised for a birth between 1998 and 2011.	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	**N:** 55,140,088 **PPH:** 1,512,212 **SPPH:** 361,081	**PPH 1:** 2.7% **PPH 2:** 0.7%
Miller, 2017 (126)	USA 2014-2015	Women who had a vaginal birth after 24 weeks' gestation.	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	**PPH:** 2.9%
Noguchi, 2017 (127)	Japan 2010- 2015	Women giving birth to a singleton after 22 weeks' gestation at the birth centre.	**SPPH:** EBL ≥1500g	**N:** 4,829 **PPH:** 127 **CTL:** 4,702	**SPPH:** 2.7%
Nyflot, 2016 (128)	Norway 2008-2011	All women admitted for labour after 23 weeks' gestation at two obstetric departments in Oslo.	**SPPH:** EBL ≥1500mL or the need for a blood transfusion	SPPH: 1,064 CTL: 2,059	**SPPH:** 2.5%
Nyflot, 2017a (45)	Norway 2008-2011	All women admitted for labour after 23 weeks' gestation at two obstetric departments in Oslo.	**SPPH:** EBL ≥1500mL or the need for a blood transfusion for excessive bleeding at the time of delivery.	SPPH: 1,064 CTL: 2,059	**SPPH:** 2.5%

Author, year	*Country & years of data*	*Study population*	*Definition of PPH/SPPH*	*Number of women*	*Incidence of PPH/ SPPH*
Nyflot, 2017b (129)	Norway 2008-2011	All women admitted for labour after 23 weeks' gestation at two obstetric departments in Oslo, excluding women with planned caesarean births.	**SPPH:** EBL ≥1500mL or the need for a blood transfusion for excessive bleeding at the time of delivery.	SPPH: 859 CTL: 1,755	N.A.
Oberg, 2014a (130)	Sweden 1997-2009	All births to primiparous women in the Medical Birth Register between 1997 and 2009.	**PPH:** ICD codes, typically EBL ≥1000mL **SPPH:** ICD code O72.3 (hemorrhage leading to coagulopathy) and/or transfusion	583,332	PPH: 6.4%
Oberg, 2014b (131)	Sweden 1997- 2009	The first two live births to individuals in Sweden 1997-2009.	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	4.6%
Rossen, 2010 (132)	Norway 1998-2007	All women with a pregnancy length between 23 and 43 weeks, who had a baby with a birth weight >300 g at Stavanger University Hospital from January 1998 to December 2007.	**PPH:** EBL ≥1000mL	41,365	**PPH:** 2.9%
Salkeld, 2008 (133)	Canada 1999-2005	Women who gave birth at 16 to 45 years and had provincially funded drug coverage.	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	NA
Sharp, 2014 (134)	UK 1952-2012	Women who gave birth to a baby >500g and who could be linked generationally through the Walk and SMR02 databases.	**PPH:** EBL ≥500mL	**N:** 25,322 **PPH:** 1,089	**PPH:** 4.3%

Author, year	*Country & years of data*	*Study population*	*Definition of PPH/SPPH*	*Number of women*	*Incidence of PPH/ SPPH*
Sheinenr, 2009 (135)	Israel 1988-2002	Consecutive singleton births at a university hospital between 1988 and 2002.	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**N:** 154,311 **PPH (all):** 666 **PPH 1:** 137 **PPH 2:** 330 **PPH 3:** 199 **CTL:** 153,645	**PPH:** 0.43%
Stones, 1993 (136)	UK 1988-1988	All births in the North West Thames region.	**PPH:** EBL ≥1000mL	**N:** 37,497 **PPH:** 498	**PPH:** 1.33%
Suzuki, 2007 (137)	Japan 2002-2006	All twin vaginal births at Japanese Red Cross Katsushika Maternity Hospital.	**PPH:** EBL ≥1000mL	**N:** 171 **PPH:** 41	**PPH:** 24%
Suzuki, 2012 (138)	Japan 2003-2011	All singleton and twin caesarean deliveries after 22 weeks' gestation.	**PPH:** PPH requiring transfusion	**N (singletons):** 4,093 **N (twins):** 508 **PPH (singletons):** 59 **PPH (twins):** 21	**PPH (singletons):** 0.6% **SPPH (twins):** 3.8%
van Stralen, 2016 (14)	The Netherlands 2000-2013	All women registered in the Dutch Perinatal Registry, who gave birth at or after 22 weeks' gestation in the study period.	**PPH:** EBL ≥1000mL	**N:** 2,406,784 **PPH:** 127,236	**PPH:** 5.3%
von Schmidt auf Altenstadt, 2013 (139)	The Netherlands 2000-2008	Women giving birth after 19 completed weeks' gestation from January 2000 until January 2008.	**PPH:** EBL ≥1000mL	**N:** 1,457,576 **PPH:** 62,864 **CTL:** 1,394,712	**PPH:** 4.3%

* Incidence calculated manually from reported data

2.4.2 Risk of bias

The risk of bias assessment classified eight studies (15%) as low risk of bias on all six domains, 22 (42%) as low risk for five of the six domains, 17 (32%) as low risk for four of the domains, and six (11%) as low risk on less than four domains (Table 2.3). There were 12 studies (23%) that were considered to be at a high risk of bias for the confounding domain because they did not present adjusted measures of effect. The most common domain for studies to be classified as 'unclear' was 'Missing or incomplete data'. This was primarily due to articles not reporting how missing data were managed.

Table 2.3 Risk of bias assessment using an adapted version of the Risk of Bias Assessment Tool for Non-randomized Studies (ROBANS)

Author, Year	***Participant selection***	***Blinding and outcome (PPH) measurement***	***Confounding variables***	***Exposure (risk factor) measurement***	***Incomplete data***	***Selective reporting (within study)***
Allen, 1988	low	low	high	low	unclear	unclear
Bais, 2004	low	low	low	low	unclear	low
Biguzzi, 2011	low	low	low	low	unclear	low
Biguzzi, 2014	low	low	low	low	unclear	low
Bonnet, 2013	unclear	unclear	low	low	low	low
Briley, 2013	low	unclear	low	low	unclear	low
Butwick, 2017	low	low	low	low	unclear	low
Buzaglo, 2014	low	low	low	low	unclear	low
Choe, 2016	low	low	low	low	unclear	low
Coombs, 1991a	low	low	low	low	unclear	unclear
Coombs, 1991b	low	low	low	low	unclear	unclear
Davey, 2019	low	low	low	low	low	low
Dionne, 2015	low	unclear	low	low	unclear	low
Endo-Kawamura, 2016	low	low	low	low	unclear	low
Eto, 2017	low	low	high	low	unclear	low
Farina, 2017	low	low	high	unclear	unclear	low
Firmin, 2019	low	low	low	low	unclear	low
Flood, 2019	low	high	high	low	low	low
Ford, 2007	low	low	low	low	low	low
Fukami, 2019	low	low	low	low	unclear	low
Gilbert, 1987	unclear	low	high	unclear	unclear	low
Henry, 2005	low	low	low	low	unclear	low

Author, Year	Participant selection	Blinding and outcome (PPH) measurement	Confounding variables	Exposure (risk factor) measurement	Incomplete data	Selective reporting (within study)
Hiersch, 2016	low	low	low	low	unclear	low
Kaelin Agten, 2017	low	low	low	low	unclear	low
Kaufner, 2017	unclear	low	low	low	low	low
Khireddine, 2012	low	low	low	low	low	low
Koopmans, 2010	low	low	low	low	low	low
Kramer, 2011	low	low	low	low	low	low
Lee, 2017	low	unclear	low	unclear	low	low
Lee, 2018	low	low	low	low	unclear	unclear
Lisonkova, 2016	low	low	low	low	unclear	low
Looft, 2017	low	low	low	low	low	low
Magan, 2005a	low	low	low	low	unclear	unclear
Magann, 2005b	low	low	low	low	unclear	unclear
Malabarey, 2011	low	low	high	low	unclear	low
Mehrabadi, 2013	low	low	low	low	unclear	low
Merriam, 2018	low	low	low	low	unclear	low
Miller, 2017	low	low	low	low	low	low
Noguchi, 2017	low	unclear	high	low	unclear	low
Nyflot, 2016	low	low	low	low	unclear	low
Nyflot, 2017a	low	low	low	low	unclear	low
Nyflot, 2017b	low	low	low	low	unclear	low
Oberg, 2014a	low	low	high	low	unclear	low
Oberg, 2014b	low	low	high	low	low	low
Rossen, 2010	low	low	low	low	unclear	low
Salkeld, 2008	low	unclear	high	unclear	unclear	low
Sharp, 2014	low	unclear	low	low	unclear	low
Sheiner, 2009	low	unclear	low	low	unclear	low
Stones, 1993	low	unclear	high	low	low	low
Suzuki, 2007	low	low	low	unclear	unclear	low
Suzuki, 2012	low	low	low	unclear	unclear	low
vanStralen, 2016	low	unclear	high	low	unclear	low
Von Schmidt auf Altenstadt, 2013	low	low	low	low	low	low

2.4.3 Risk factors

In total, 186 risk factors were investigated as potential risk factors for PPH or SPPH by the 53 included studies, with 47 risk factors being investigated by at least five studies and therefore eligible for inclusion in the narrative synthesis reported here. The most commonly investigated risk factor was maternal age, investigated by 45 studies. Table 2.4 presents the summary of the rating of risk factors included in the narrative synthesis based on the rating described in Box 2. The most common rating was 'Unclear', given to 22 (47%) of the 47 risk factors. This was either because less than 50% of studies reported significant results, because significant results were in conflicting directions, or both. Nine risk factors were rated as 'Very likely', seven as 'Likely', and five as 'Not a risk factor'. The detailed results and narrative synthesis of all risk factors investigated by five or more studies are presented below. Risk factors investigated by four or fewer studies are presented in tables in Appendix A.5.

Table 2.4 Summary of risk factors included in the narrative synthesis and their association with PPH

Risk factor	*No. studies*	*Rating*	*Rating reason*
Maternal socio-demographic characteristics			
Age	45	Unclear	Less than 50% of LRoB analyses found a significant association.
Race/ethnicity	17	Likely	Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Smoking status	13	Unclear	Less than 50% of LRoB analyses found a significant association.
Socio-economic	6	Unclear	Between 50% and 80% of LRoB analysis found a significant association but in conflicting directions.
Civil status	5	Not	No LRoB analyses found a significant association.
Healthcare/insurance status	5	Unclear	Less than 50% of LRoB analyses found a significant association.
Maternal country of birth/origin	5	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Maternal education	5	Not	No LRoB analyses found a significant association.

Risk factor	No. studies	Rating	Rating reason
		Medical factors	
Hypertension – Pre-eclampsia	15	Likely	Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Hypertension – Combined hypertensive disorders	12	Likely	Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Hypertension – Chronic hypertension	8	Likely	Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Hypertension – Gestational hypertension	6	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Weight	20	Unclear	Less than 50% of LRoB analyses found a significant association. Significant results were in conflicting directions.
Diabetes	17	Unclear	Less than 50% of LRoB analyses found a significant association. Significant results were in conflicting directions.
Anaemia	10	Unclear	Less than 50% of LRoB analyses found a significant association.
		Obstetric history	
Previous caesarean	19	Unclear	Less than 50% of LRoB analyses found a significant association. Significant results were in conflicting directions.
Previous PPH	8	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.
Previous uterine surgery	7	Unclear	Less than 50% of LRoB analyses found a significant association.
		Pregnancy factors	
Parity	36	Unclear	Between 50% and 80% of LRoB analyses found a significant association but in conflicting directions.
Gestational age	30	Unclear	Less than 50% of LRoB analyses found a significant association.
Multiple pregnancy	25	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Risk factor	*No. studies*	*Rating*	*Rating reason*
Placenta praevia	17	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.
Uterine fibroids	12	Unclear	Less than 50% of LRoB analyses found a significant association.
Chorioamnionitis	12	Likely	Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Placental abruption	12	Unclear	Less than 50% of LRoB analyses found a significant association.
Polyhydramnios	9	Unclear	Less than 50% of LRoB analyses found a significant association.
Assisted conception	8	Likely	Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Antepartum haemorrhage	8	Likely	Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Gravidity	5	Not	No LRoB analyses found a significant association.
		Labour factors	
Labour onset and induction	40	Likely	Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction
Analgesia/anaesthesia	29	Unclear	Less than 50% of LRoB analyses found a significant association.
Augmentation	20	Unclear	Less than 50% of LRoB analyses found a significant association.
Duration of second stage	20	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Overall duration of labour	15	Unclear	Less than 50% of LRoB analyses found a significant association.
Pre-labour rupture of membranes	12	Unclear	Less than 50% of LRoB analyses found a significant association.
Duration of first stage	11	Unclear	Less than 50% of LRoB analyses found a significant association.
Duration of third stage	8	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.

Risk factor	*No. studies*	*Rating*	*Rating reason*
Maternal pyrexia in labour	7	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Third stage management	5	Likely	Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction
Birth factors			
Mode of birth – instrumental	29	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Mode of birth – caesarean)	18	Unclear	Less than 50% of LRoB analyses found a significant association. Significant results were in conflicting directions.
Genital tract trauma	31	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Episiotomy	16	Unclear	Between 50% and 80% of LRoB analysis found a significant association but in conflicting directions.
Presentation	10	Unclear	Less than 50% of LRoB analyses found a significant association.
Retained placenta	10	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Baby characteristics			
Birthweight	37	Very likely	More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.
Sex	5	Not	No LRoB analyses found a significant association.

2.4.4 Maternal socio-demographic characteristics

2.4.4.1 Maternal age

Forty-five studies evaluated the association between maternal age and PPH or SPPH and, of these, 36 were considered as LRoB. Data about maternal age were conflicting, but overall most LRoB studies found no association with PPH after adjustment for other factors. Maternal age was significantly associated with PPH in 26% of LRoB analyses, and with SPPH in 20% of LRoB analyses. Of the studies that found a significant association, two studies found that lower maternal age was associated with a higher risk of PPH, and four studies found that higher maternal age was associated with an increased risk of PPH. One study (82) found that both higher and lower maternal age were associated with an increased risk of PPH, compared with a maternal age of 25-29 years. Generally, regardless of how maternal age was categorised, the magnitude of effect for maternal age as a risk factor was low, ranging from aOR=1.1 (95% CI 1.0-1.2) for maternal age ≥40 years compared with maternal age 20-34 (10), to aOR=1.88 (95% CI 1.43-2.47) for maternal age 40-44 years compared with 25-29 years (82).

Of the nine HRoB studies, four examined age as a continuous variable, mostly reporting no significant difference in the mean age between cases and controls. Four of the five HRoB studies that examined maternal age as a categorical variable found a significant association, with increased maternal age being associated with increased risk of PPH in all four.

Rating: Unclear - less than 50% of LRoB analyses found a significant association.

Table 2.5 Included studies investigating maternal age as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Bais, 2004	**PPH 1:** ≥35 years: 1.21 (0.82-1.79) **PPH 2:** ≥35 years: 1.32 (0.68-2.79)	uOR uOR	NS NS	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Biguzzi, 2011	5 year increments: 1.15 (1.06-2.24)	aOR	Sig	VB	**PPH:** EBL ≥500mL	6,011	Low
Bonnet, 2013	**Canada:** <20: 1.19 (1.08-1.30) 20-24: 1.09 (1.03-1.16) 25-34: ref ≥35: 0.91 (0.84-0.97) **France:** <20: 1.83 (1.14-2.94) 20-24: 1.04 (0.89-1.22) 25-34: ref ≥35: 0.98 (0.85-1.12)	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	Low
Briley, 2013	For each 10 years: 0.93 (0.73-1.19)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low

Note, for all subsequent tables:
RoB: Risk of bias
uOR: Unadjusted odds ration
aOR: Adjusted odds ratio
NS: non-significant
EBL: Estimated blood loss
VB: Vaginal birth
CS: Caesarean section

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Butwick, 2017	**Pre-labour CS:** <34: ref 34-37: 1.16 (0.63-2.14) ≥38: (1.17 (0.64-2.14) **Intrapartum CS:** <30: ref ≥30: 0.69 (0.48-1.0)	aOR aOR	NS NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **PPH:** 269 **CTL:** 550 **Intrapartum CS** **PPH:** 278 **CTL:** 572	Low
Buzaglo, 2014	PPH mean: 24.5 CTL mean: 24.1 P=0.630	Mean dif	NS	VB	**PPH:** EBL ≥500mL	56,394	Low
Choe, 2016	15-19: 2.99 (1.78-5.01) 20-24: 1.09 (0.86-1.38) 25-29: ref 30-34: 1.11 (0.99-1.25) 35-39: 1.34 (1.15-1.57) 40-44: 1.88 (1.43-2.47)	aOR	Sig	VB, CS	**PPH:** ICD-10 code O72.0-O72.3 or transfusion	65,479	Low

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Davey, 2019	**All women:** <20: 1.13 (0.9-1.4) 20-34: ref ≥35: 1.11 (1.03-1.2)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
	Women who experienced labour: <20: 1.11 (0.9-1.3) 20-34: ref ≥35: 1.01 (0.9-1.1)	uOR	NS				
Dionne, 2015	**PPH 1:** ≤25: 1.08 (0.88-1.33) 26-35: ref ≥35: 1.29 (0.93-1.78)	aOR	NS	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048	Low
	PPH 2: ≤25: 1.08 (0.83-1.41) 26-35: ref 35+: (0.80-1.81)	aOR	NS		**PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL		
Endo-Kawamura, 2016	**Mid-pregnancy blood test:** ≥35 years: 1.75 (1.15-2.68) <35 years: ref	aOR	Sig	VB	**PPH:** EBL ≥700mL	1,032	Low
	Pre-delivery blood test: ≥35 years: 1.77 (1.16-2.71) <35 years: ref	aOR	Sig				

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Eto, 2016	**PPH:** 31.4 (4.3) **CTL:** 31.8 (4.2) p=0.029 **PPH2:** 31.1 (4.4) **CTL:** 31.8 (4.2) p=0.005 **PPH3:** 31.0 (4.2) **CTL:** 31.8 (4.2) p=0.026	Mean (SD)	NS Sig NS	VB	**PPH 1:** EBL ≥500g **PPH 2:** EBL ≥800g **PPH 3:** EBL >1000g	**CTL:** 2,524 **PPH 1:** 524 **PPH 2:** 147 **PPH 3:** 158	High
Farina, 2017	**PPH:** 32 (3.0) **CTL:** 32(4.64) p=0.906	Mean dif	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390	High
Firmin, 2019	**PPH:** <18: 7.1% 18-34: 74.7% ≥35: 18.2% **CTL:** <18: 8.5% 18-34: 75.3% 35+: 16.2% p=0.797	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Ford, 2007	**1994-1995** ≤19: 1.02 (0.91-1.13) 20-34: ref ≥35: 1.02 (0.95-1.09) **2002** ≤19: 0.87 (0.74-1.02) 20-34: ref ≥35: 1.01 (0.93-1.09)	aOR aOR	NS NS	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low
Fukami, 2019	**CTL:** ≤19: 5.2% 20-35: 66.9% 35-40: 23.4% ≥40: 4.5% **PPH:** ≤19: 3.2% 20-35: 66.7% 35-40: 22.6% ≥40: 7.5% $p < 0.05$	%	NS	VB	**PPH:** CBL ≥1000mL	1,608	Low

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Henry, 2005	**CTL:** <30: 42 30-39: 78 40-49: 5 **PPH 1:** <30: 45 30-39: 71 40-49: 9 **PPH 2:** <30: 17 30-39: 27 40-49: 6	n	NS	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low
Hiersch, 2016	**PPH:** >35 years: 16.3% P > 0.05 **CTL:** >35 years: 17.9%	%	Sig	VB (vacuum only)	**PPH:** EBL ≥500mL, hemoglbon drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	≤19: 0.9 (0.8-1.0) 20-34: ref 35-39: 1.0 (1.0-1.0) ≥40: 1.1 (1.0-1.2)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Kaufner, 2016	**CTL:** 30 (6) **PPH:** 29 (6) P=0.677	Mean (SD)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low
Khireddine, 2012	**CTL:** <25: 15.4% 25-34: 67.9% ≥35: 16.7% **PPH 1:** <25: 18.0% 25-34: 67.4% ≥35: 14.6 **PPH 2:** <25: 18.7% 25-34: 68.2% ≥35: 13.1% p=0.01	%	NS	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2:** 1,125	Low
Koopmans, 2014	Maternal age (years): 1.04 (1.0-1.1)	aOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Kramer, 2011	**PPH:** <20: 0.8 (0.5-1.2) 20-34: ref ≥35:1.0 (0.9-1.2) **SPPH:** <20: 4.7 (0.5-42.2) 20-34: ref ≥35: 2.9 (1.3-6.6)	aOR aOR	NS Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lee, 2017	Maternal age ≥35: 2.56 (0.77-8.51) <35: ref	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210	Low
Lee, 2018	≥35 years: 1.79 (1.00-3.20)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506	Low

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Lisonkova, 2016	**PPH:** <20: 4.70% 20-24: 11.49% 25-29: 26.11% 30-34: 31.85% 35-39: 19.06% ≥40: 6.79% P=0.07 **CTL:** <20: 1.84% 20-24: 9.25% 25-29: 25.20% 30-34: 36.22% 35-39: 21.52% ≥40: 5.77%	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	PPH: 393 CTL: 393	Low

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Looft, 2017	**All:** ≤24: (9461) 25-29:(18613) 30-34: (20291) ≥35: (8868) Missing: 34 **PPH:** ≤24: 2439 25-29: 5273 30-34: 6064 ≥35: 2770 Missing: 8	n	NA	VB	**PPH:** EBL ≥500mL	PPH: 57,267 All: 57,267	Low
Malabarey, 2011	**PPH:** 31.1 (4.9) **CT:** 31.1 (5.1) P=1	Mean (SD)	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Mehrabadi, 2013	<20: 1.47 (1.34-1.61) 20-24: ref 25-29: 0.87 (0.81-0.92) 30-34: 0.86 (0.81-0.92) 35-39: 0.98 (0.91-1.05) ≥40: 1.10 (0.98-1.23)	aOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Merriam, 2018	**PPH 1:** 16-17: ref 18-19: 0.98 (0.95-1.0) 20-24: 0.95 (0.93-0.97) 25-29:0.93 (0.91-0.95) 30-34: 0.92 (0.90-0.94) ≥35: 0.85 (0.92-0.97) PPH 2: 16-17: ref 18-19: 0.96 (0.92-1.00) 20-24: 0.87 (0.83-0.90) 25-29: 0.78 (0.75-0.81) 30-34: 0.80 (0.76-0.83) ≥35: (0.86-0.94)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Miller, 2017	**PPH:** 31 (27-35) **CTL:** 32 (27-35) P=0.57	Median (IQR)	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Noguchi, 2017	Maternal age (years): 1.5 (no CI) p=0.03	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500g	4829	High
Nyflot, 2016	**SPPH:** 32 years (29-36) b 32 years (29-350	Median (IQR)	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Nyflot, 2017a	14-19: 2.23 (0.96-5.17) 20-24: ref 25-29: 1.14 (0.82-1.60) 30-34: 1.24 (0.90-1.71) 35-39: 1.36 (0.98-1.91) ≥40: 1.45 (0.96-2.21)	uOR	NS	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	Age ≥35: 1.76 (0.96-1.43)	uOR	NS	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low
Oberg, 2014a	<20: ref 20-34: 1.56 (1.46-1.68) ≥35: 2.0 (1.90-2.20)	uOR	Sig	VB, CS	**PPH:** ICD codes, typically EBL ≥1000mL	583,332	High
Oberg, 2014b	<20: ref 20-34: 1.36 (1.21-1.52) ≥35: 1.57 (1.39-1.78)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Rossen, 2010	**VB** ≥35: 1.2 (1.1-1.5) **CS** ≥35: 1.7 (1.3-2.4)	aOR aOR	Sig Sig	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
Salkeld, 2008	**PPH:** 26.2 years (6.14) **CTL:** 26.0 years (5.93)	Mean (SD)	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High
Salkeld, 2008	**PPH:** 25 years (31-31) **CTL:** 25 years (21-30)	Median (IQR)	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2460 **CTL:** 23,943	High

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Sharp, 2014	≤20: 1.13 (0.77-1.65) ≥40:1.32 (0.73-2.38)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	25,322	
Sheiner, 2009	**PPH 1:** 28.4 (5.7) **PPH 2:** 28.8 (5.7) **PPH 3:** 29.2 (6.1) **CTL:** 28.4 (5.9) p=0.152	Mean (SD)	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645	High
Stones, 1993	<20: 0.81 (0.45-1.43)	uRR (99% CI)	NS	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Stones, 1993	35+: 1.42 (1.00-2.02)	uRR (99% CI)	NS	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Suzuki, 2007	Age ≥ 35: 1.03 (0.45-2.34)	uOR	NS	CS	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 130	Low
Suzuki, 2012	**Singletons:** <20: na 20-39: ref ≥40: 1.02 (0.40)	uOR	NS	CS	**PPH:** PPH requiring transfusion	**Singletons:** 17,405 **Twins:** 916	Low
	Twins: 20-39: ref ≥40: 3.38 (0.87-13)	aOR	NS				

Author, year	*Effect size & definitions*	*Measure of effect*	*Significance*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
van Stralen, 2016	<20: 0.67 (0.64-0.71) 20-24: 0.75 (0.74-0.77) 25-29: 0.91 (0.90-0.92) 30-34: ref 35-39: 1.07 (1.05-1.09) ≥40: 1.18 (1.14-1.22)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	**Total cohort:** ≤19: 0.62 (0.58-0.67) 20-24: 0.71 (0.69-0.73) 25-29: 0.86 (0.84-0.88) 30-34: ref 35-39: 1.09 (1.07-1.11) ≥40: 1.15 (1.09 – 1.21) **Non-induced, spontaneous delivery:** ≤19: 0.63 (0.57-0.68) 20-24: 0.71 (0.68-0.74) 25-29: 0.85 (0.83-0.88) 30-34: ref 35-39: 1.08 (1.05-1.12) ≥40: 1.13 (1.05-1.21)	uOR uOR	Sig Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.4.2 Race/ethnicity

Seventeen studies examined race or ethnicity as a risk factor for PPH/SPPH. Of these, 15 were considered to be LRoB. More than half (59%) of LRoB analyses found a significant association between race/ethnicity and PPH/SPPH after adjusting for other factors. Generally, White/Caucasian ethnicity was the reference group and was the most common ethnicity in the populations studied. For most studies, ethnicities other than White/Caucasian were at a higher risk of PPH, with Black and Hispanic ethnicity associated with greater odds of PPH/SPPH, compared with other racial/ethnic groups. Studies that found a significant association were conducted in Europe, UK, USA, and Australia while LRoB studies that did not find an association, after adjustment, were conducted in Europe, USA, Australia and Israel. The magnitude of the effect was generally small to moderate.

The one HRoB study that reported a significant association at the univariable level (14), reporting that being non-Caucasian was associated with lower odds of PPH compared with being Caucasian (uOR 0.91; 95% CI 0.90-0.92).

Rating: Likely - Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.

Table 2.6 Included studies investigating race/ethnicity as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Bais, 2004	**PPH 1:** Western European: 1.32 (1.00-1.73) Not Western European: ref **PPH 2:** Western European: 1.96 (1.12-3.49) Not Western European: ref	aOR uOR	Sig NS	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Biguzzi, 2011	Non-Caucasian: 1.65 (1.32-2.07) Caucasian: ref	aOR	Sig	VB	**PPH:** EBL ≥500mL	6,011	Low
Biguzzi, 2014	Caucasian: 1.44 (1.11-1.77) Non-Caucasian: ref	aOR	Sig	VB	**PPH:** EBL ≥500mL	3,219	Low
Briley, 2013	Black African: 1.94 (1.35-2.79) Not Black African: ref	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	9,937	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Butwick, 2017	**Pre-labour CS:** Non-Hispanic white: ref Hispanic: 2.43 (1.02-5.78) Non-Hispanic Black: 2.42 (0.69-8.52) Asian: 1.90 (0.91-3.94) Other: 2.35 (0.73-7.58) **Intrapartum CS:** Non-Hispanic white: ref Hispanic: 1.23 (0.60-2.51) Non-Hispanic Black: 0.58 (0.17-1.95) Asian: 1.47 (0.77-2.79) Other: 0.94 (0.31-2.87)	aOR aOR	Sig Sig	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Buzaglo, 2014	**PPH:** Jewish: 63.1% Bedouins: 36.9% **CTL:** Jewish: 60.3% Bedouins: 39.7% P=0.125	%	NS	VB	**PPH:** EBL ≥500mL	56,394	Low
Combs, 1991a	Asian: 1.50 (0.97-2.33) Non-Asian: ref	aOR	NS	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Combs, 1991a	Hispanic: 1.82 (1.10-3.03) Non-Hispanic: ref	aOR	Sig	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Asian ethnicity: 1.73 (1.20-2.49) Non-Asian: ref	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Combs, 1991b	Hispanic: 1.66 (1.02-2.69) Non-Hispanic: ref	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Henry, 2005	**CTL:** Caucasian: 82 Pan-Asian: 17 Other: 1 Unknown: 25 **PPH 1:** Caucasian: 94 Pan-Asian: 21 Other: 1 Unknown: 9 **PPH 2:** Caucasian: 40 Pan-Asian: 8 Other: 1 Unknown: 1	n	NS	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low
Koopmans, 2014	Non-Caucasian ethnicity: 1.2 (0.64-2.1)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Magan, 2005b	Asian race: 1.8 (1.4-2.2) Non-Asian race	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Merriam, 2018	**PPH 1:** White: ref Black: 1.06 (1.03-1.09) Hispanic: 1.25 (1.22-1.28) Other: 1.23 (1.20-1.27) Unknown: 1.01 (0.96-1.06) **PPH 2:** White: ref Black: 1.48 (1.44-1.53) Hispanic: 1.33 (1.29-1.37) Other: 1.31 (1.27-1.36) Unknown: 1.07 (1.02-1.14)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Miller, 2017	**PPH:** Hispanic: 58 (36.5%) Non-Hispanic White: 42 (26.4%) Asian: 48 (30.2%) Non-Hispanic Black/Other: 11 (6.9%) **CTL:** Hispanic: 109 (34.3%) Non-Hispanic White: 105 (33.0%) Asian: 77 (24.2%) Non-Hispanic Black/Other: 27 (8.5%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Nyflot, 2017a	Europe/USA/Oceana: ref Middle-East/North-Africa: 0.82 (0.58-1.15) Latin-America: 1.28 (0.65-2.51) Asia: 1.31 (1.01-2.16) Subsarahan Africa: 1.51 (1.10-2.16)	uOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Rossen, 2010	**VB** Ethnicity other than Caucasian: 1.5 (1.2-1.9) **CS** Ethnicity other than Caucasian: 1.3 (0.8-2.2)	aOR aOR	Sig NS	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
van Stralen, 2016	Non-Caucasian: 0.91 (0.90-0.92) Caucasian: ref	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	**Total cohort:** European: ref Non-European descent: 1.02 (0.99-1.4) **Non-induced spontaneous delivery:** European: ref Non-European descent: 1.04 (1.01-1.07)	aOR aOR	NS Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.4.3 Smoking status

There were 13 studies that investigated smoking as a risk factor for PPH, of which nine were classified as LRoB. Most of these studies compared smokers with non-smokers, although one study (108) explored the association based on the number of cigarettes smoked per day during pregnancy. The vast majority of studies reported no significant association between smoking and PPH or SPPH. Only one study (9% of LRoB studies) reported a significant association, with smoking associated with lower odds of PPH after adjustment for other factors. One study (122) reported lower rates of PPH among smokers, but did not report the level of significance.

Of the four HRoB studies, one reported a significant association at the univariable level, finding smokers to have 20% lower odds of PPH, compared with non-smokers (uOR 0.80; 85% CI 0.75-0.85). Given the relatively consistent finding that smoking was not significantly associated, after adjustment for other factors, but that a significant association was reported in one LRoB study, it is unclear whether smoking is a significant risk factor for PPH/SPPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.7 Included studies investigating smoking status as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Allen, 1988	Smoking and normal vaginal delivery: Non-smoker: 4.1% Smoker <10/day: 3.7% Smoker 10-20/day: 3.5% Smoker > 20/day: 3.5%	% (incidence of PPH by category)	NS	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Briley, 2013	Current smoker: 0.82 (0.53-1.28) Non-smoked: ref	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Buzaglo, 2014	Smoker: 0.9% vs 0.9%	%	NS	VB	**PPH:** EBL ≥500mL	56,394	Low
Farina, 2017	**% smokers** **PPH:** 0 **CTL:** 5.3 **p=**0.554	%	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390	High
Fukami, 2019	**CTL:** Smoker: 6.6% Non-smoker: 93.4% **PPH:** Smoker: 7.5% Non-smoker: 92.5%	%	NS	VB	**PPH:** CBL ≥1000mL	1,608	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Henry, 2005	**CTL:** Smoker: 10 Non-smoker: 84 Unknown: 31 **PPH 1:** Smoker: 12 Non-smoker: 92 Unknown: 21 **PPH 2:** Smoker: 5 Non-smoker: 39 Unknown: 6	n	NS	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low
Koopmans, 2014	Maternal smoking: 1.1 (0.62-2.0) Non-smoker: ref	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Kramer, 2011	**PPH:** Smoking in pregnancy: 1.0 (0.9-1.1) Did not smoke in pregnancy: ref **SPPH:** Smoking in pregnancy: 1.7 (0.6-5.0) Did not smoke in pregnancy: ref	aOR aOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Lisonkova, 2016	Smoking during pregnancy: 0.58 (0.35-0.95)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Looft, 2017	**All:** Smoker: 54264 Non-smoker: 2511 Missing: 492 **PPH:** Smoker: 15788 Non-smoker: 611 Missing: 155	n	NA	VB	**PPH:** EBL ≥500mL	57,267	Low
Oberg, 2014b	Smoker: 0.80 (0.75-0.85) Non-smoker: ref	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Sharp, 2014	Smoked during pregnancy: 0.79 (0.57-1.08) Did not smoke during pregnancy: ref	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	25,322	Low
Stones, 1993	Smoker: 0.89 (0.66-1.21) Non-smoker: ref	uRR (99% CI)	NS	VB, CS	**PPH:** EBL ≥1000mL	37,334	High

2.4.4.4 Socio-economic status

Six studies examined socio-economic status and PPH/SPPH, five of which were considered LRoB. There was a wide range of definitions of socio-economic status across the studies that examined this risk factor. Most studies classified this factor in relation to income or area deprivation, however one (82) categorised women based on employment, reporting lower odds of PPH among women classified as a 'worker', compared with being a 'non-worker'. Four studies found a significant association between socio-economic status and PPH, but the direction of the effect conflicted between studies. Three studies (56, 82, 125) reported that lower socioeconomic status was associated with higher odds of PPH, while one study (139) reported that higher socioeconomic status was associated with slightly higher odds of PPH (aOR=1.07; 95% CI 1.05-1.09).

One large LRoB study including over 364,000 women (114) investigated the association between SPPH and socioeconomic status and found a significant association after adjustment for other factors, with women from the least deprived socioeconomic quintile being less likely to have a SPPH compared with women in the middle quintile (aOR=0.87; 95% CI 0.7-0.9).

The one HRoB study that examined this risk factor found that high socioeconomic status was associated with an increased risk of PPH, compared with medium status (uOR 1.09; 95% CI 1.08-1.11), but this study did not adjust for confounding factors.

Most LRoB studies that examined socioeconomic status and PPH/SPPH found an association, but the direction of the effect conflicted so it is unclear whether socioeconomic status is associated with PPH/SPPH.

Rating: Unclear - Between 50% and 80% of LRoB analysis found a significant association, but in conflicting directions.

Table 2.8 Included studies investigating socioeconomic status as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Briley, 2013	Barriers - housing and services: 1.04 (0.79-1.36)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Choe, 2016	Worker: 0.87 (0.77-0.99) Non-worker: ref	aOR	Sig	VB, CS	**PPH:** ICD-10 code O72.0-O72.3 or transfusion	65,479	Low
Choe, 2016	Income groups: Lower: 1.21 (1.06-1.39) Middle: 1.15 (1.02-1.30) Upper: ref	aOR	Sig	VB, CS	**PPH:** ICD-10 code O72.0-O72.3 or transfusion	65,479	Low
Davey, 2019	**Socio-economic quintile** **All women:** 1. Most deprived: 1.03 (0.9-1.1) 2: 0.91 (0.8-1.0) 3: ref 4: 0.93 (0.8-1.0) 5. least deprived: 0.87 (0.7-0.95) Missing: 0.93 (0.8-1.0)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
	Women who experienced labour: 1. Most deprived: 1.01 (0.9-1.1) 2: 0.90 (0.8-0.99) 3: ref 4: 0.93 (0.8-1.0) 5. Least deprived: 0.83 (0.7-0.9) Missing: 0.94 (0.8-1.1)	aOR	Sig				

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Merriam, 2018	**PPH 1:** Lowest quartile: ref Second quartile: 0.99 (0.98-1.01) Third quartile: 0.99 (0.98-1.01) Highest quartile: 0.97 (0.95-0.99) Unknown: 1.05 (0.99-1.11)	aRR	Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
	PPH 2: Lowest quartile: ref Second quartile: 0.96 (0.94-0.98) Third quartile: 0.90 (0.87-0.93) Highest quartile: 0.87 (0.84-0.90) Unknown: 1.03 (0.94-1.12)	aRR	Sig				
van Stralen, 2016	High: 1.09 (1.08-1.11) Medium: ref Low: 0.93 (0.92-0.95)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	**Socioeconomic status based on neighbourhood income** **Total cohort:** High: 1.07 (1.05-1.09) Medium: ref Low: 1.00 (0.98-1.02)	aOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low
	Non-induced spontaneous delivery: High: 1.08 (1.05-1.11) Medium: ref Low: 1.01 (0.99-1.04)	aOR	Sig				

2.4.4.5 Civil/marital status

Five studies analysed civil or marital status and PPH/SPPH, of which three were considered LRoB. While there was a range of categorisations, most considered whether the women was married and/or living with a partner. None of these studies reported a significant association at the adjusted level. One study was small, including only 125 cases and 125 controls, but the largest study examining this factor included over 100,000 women, examined both PPH and SPPH and found no association after adjustment for other factors.

Two HRoB studies examined this risk factor, both reporting that living alone was associated with a lower risk of PPH, compared with living with the father, at the univariable level. Both of these studies were conducted using similar populations in Sweden. Marital/civil status is therefore not considered to be independently associated with PPH/SPPH.

Rating: Not a risk factor – No LRoB analyses found a significant association.

Table 2.9 Included studies investigating civil and marital status as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Henry, 2005	**CTL:** Married: 92 Single: 24 Unknown: 9 **PPH 1:** Married: 105 Single: 13 Unknown: 7 **PPH 2:** Married: 43 Single: 4 Unknown: 3	n	Sig	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low
Kramer, 2011	**PPH:** Married: ref Sinlge, living alone: 1.0 (0.8-1.1) Separated, divorced, wodowed: 1.2 (0.9-1.7) **SPPH:** Married: ref Sinlge, living alone: 2.1 (0.9-4.8) Separated, divorced, widowed: 1.5 (0.2-12.1)	aOR aOR	NS NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Nyflot, 2017a	Married/cohabitant: 0.70 (0.53-0.93)	uOR	NS	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Oberg, 2014a	Living with the father: ref Living alone: 0.81 (0.76-0.87) Unknown: 0.86 (0.82-0.91)	uOR	Sig	VB, CS	**PPH:** ICD codes, typically EBL ≥1000mL	583,332	High
Oberg, 2014b	Living with the father: ref Living alone: 0.89 (0.96-1.00) Unknown: 0.87 (0.76-0.96)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High

2.4.4.6 Maternal country of birth

Five studies examined country of birth as a potential risk factor for PPH/SPPH, of which three were LRoB. Two studies were conducted in Australia, two in Sweden and one in Western French Guiana (France). All studies used the study country as the reference group compared with country of birth outside of the index country. All three LRoB studies found a significant association, although only the two Australian studies found this association after adjustment for other factors. In one study (13) women born overseas, outside of Australia, had a higher odds of PPH, both in 1994-95 and in 2002 (aOR=1.21; 95% CI 1.15-1.28, and aOR=1.41; 95% CI 1.33-1.50, respectively), compared with women born in Australia.

Of the HRoB studies, conducted on similar populations in Sweden, one reported a significantly reduced risk of PPH among non-Scandinavian women, although the magnitude of the effect was small (aOR=0.95; 95% CI 0.92-0.97).

Overall, two out of three LRoB studies found a significant association, suggesting it is very likely that country of birth is a risk factor for PPH. However, this assessment should be treated with caution because only three LRoB studies investigated this risk factor and the two that reported a significant effect were both conducted in Australia.

Rating: Very likely - More than 60% of LRoB analyses reported a significant association.

Table 2.10 Included studies investigating maternal country of birth as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Davey, 2019	**All women:** Australia: ref Americas: 1.01 (0.8-1.3) North Africa and Middle East: 0.90 (0.8-1.1) North East Asia: 1.62 (1.4-1.8) North Western Europe: 0.89 (0.7-1.1) Oceania and Antarctica: 1.59 (1.4-1.8) South East Asia: 1.57 (1.4-1.8) Southern and Central Asia: 0.79 (0.7-0.9) Southern and Eastern Europe: 1.17 (1.0-1.4) Sub-Saharan Africa: 0.85 (0.7-1.1)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
	Women who experienced labour: Australia: ref Americas: 1.09 (0.8-1.4) North Africa and Middle East: 0.88 (0.7-1.1) North East Asia: 1.63 (1.4-1.9) North Western Europe: 0.91 (0.7-1.1) Oceania and Antarctica: 1.65 (1.4-1.9) South East Asia: 1.63 (1.4-1.8) Southern and Central Asia: 0.90 (0.8-1.0) Southern and Eastern Europe: 1.15 (0.9-1.4) Sub-Saharan Africa: 0.83 (0.6-1.1)	aOR	Sig				
Firmin, 2019	**France** **PPH:** 42.9% **CTL:** 48.4% p=0.197	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Ford, 2007	**1994-1995** Australia: ref Overseas: 1.21 (1.15-1.28) Not stated: 1.86 (1.38-2.51) **2002** Australia: ref Overseas: 1.41 (1.33-1.50) Not stated: 2.18 (1.03-4.60)	aOR aOR	Sig Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low
Oberg, 2014a	Scandinavian: ref Non-Scandinavian: 0.95 (0.92-0.97)	uOR	Sig	VB, CS	**PPH:** ICD codes, typically EBL ≥1000mL	583,332	High
Oberg, 2014b	Scandinavian: ref Non-Scandinavian: 0.93 (0.87-1.00)	uOR	NS	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High

2.4.4.7 Maternal education

Five studies explored the relationship between level of maternal education and PPH/SPPH, three of which were considered LRoB. Four of the studies were conducted in European countries or territories, while one was conducted in Canada.

The largest study (N=103,726) that examined education and PPH reported a small increased risk of PPH with increasing education levels, however, this study did not analyse risk factors at the multivariable level and so was considered at HRoB.

No studies reported a significant association between level of education and PPH after adjustment for other factors. Maternal education level is not therefore considered to be independently associated with PPH/SPPH.

Rating: Not a risk factor- No LRoB analyses found a significant association.

Table 2.11 Included studies investigating maternal education as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Briley, 2013	Education, skills and training: 1.03 (0.57-1.62)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Firmin, 2019	**PPH:** None: 17.1% Elementary/middle school: 47.3% High school/college: 35.6% **CTL:** None: 20.1% Elementary/middle school: 39.1% High school/college: 40.8%	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Koopmans, 2014	Higher education level: 1.3 (0.75-2.2)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Kramer, 2011	**Years of education** **PPH:** <11: 2.4% 11-12: 2.5% 13-15: 2.6% ≥16: 2.5% **SPPH:** <11: 0.31% 11-12: 0.19% 13-15: 0.20% ≥16: 0.14%	PPH/SPPH rate (%)	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Oberg, 2014b	Compulsory: ref Upper secondary (<3): 1.11 (1.03-1.20) Upper secondary (≥3): 1.21 (1.13-1.30) University: 1.25 (1.17-1.34)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High

2.4.4.8 Healthcare /insurance status

Five studies examined health insurance or healthcare coverage in relation to PPH/SPPH, and all were considered LRoB. One large US study (N >55,000,000) found that all forms of insurance were associated with lower odds of PPH compared with Medicare insurance. One study (112) found a significant association between healthcare coverage and SPPH, after adjusting for other variables, with government/other insurance being associated with a slightly increased risk of SPPH, compared with private insurance (aOR1.56 1.0-2.44). This study was relatively small (N=819) and the lower confidence bound was 1.0. It is unclear whether health insurance status is independently associated with PPH/SPPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.12 Included studies investigating healthcare/insurance status as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Butwick, 2017	**Pre-labour CS:** Private insurance: ref Government/other: 0.62 (0.35-1.07)	aOR	NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550	Low
	Intrapartum CS: Private insurance: ref Government/other: 1.56 (1.0-2.44)	aOR	Sig			**Intrapartum CS** **SPPH:** 278 **CTL:** 572	
Firmin, 2019	No healthcare coverage **PPH:** 24.3% **CTL:** 25.5% p=0.774	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Henry, 2005	**CTL:** Public: 93 Private: 25 Unknown: 7 **PPH:** Public: 93 Private: 25 Unknown: 7 **SPPH:** Public: 40 Private: 7 Unknown: 3	n	NS	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low
Merriam, 2018	**PPH 1:** Medicare: ref Medicaid: 1.04 (0.98-1.11) Private: 1.00 (0.95-1.07) Self-pay: 1.04 (0.97-1.11) Other: 1.05 (0.98-1.12) Unknown: 1.01 (0.90-1.13)	aRR	NS	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
	PPH 2: Medicare: ref Medicaid: 0.73 (0.67-0.79) Private: 0.58 (0.54-0.63) Self-pay: 0.81 (0.74-0.89) Other: 0.67 (0.61-0.74) Unknown: 0.71 (0.60-0.84)	aRR	Sig				

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Miller, 2017	**PPH:** Private: 11 (69.8%) Government-assisted/Other: 48 (30.2%) **CTL:** Private: 205 (64.5%) Government-assisted/Other: 113 (35.5%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low

2.4.5 Medical factors

2.4.5.1 Pre-eclampsia

Fifteen studies investigated pre-eclampsia/eclampsia or HELLP as potential risk factors for PPH/SPPH. Most studies examined pre-eclampsia but three also included eclampsia or HELLP in the same category. Of the 13 LRoB analyses, seven showed significantly higher odds of PPH among women with pre-eclampsia/eclampsia/HELLP, compared with those without, after adjustment for confounding variables. The magnitude of the effect ranged from 1.5-6.2.

The one HRoB study that analysed this risk factor reported a significantly higher risk of PPH for women who had pre-eclampsia, compared with no pre-eclampsia, although this was not adjusted for potential confounders (uOR=2.10; 95% CI 1.92-2.29). There were four LRoB analyses of pre-eclampsia/eclampsia and SPPH, one of which reported a significant increase in odds of SPPH. The study that reported a significant association compared 'severe preeclampsia/HELLP' to no hypertension, reporting a three-fold increase in the odds of SPPH.

Rating: Likely - More than 50% of LRoB analyses found a significant association. All significant results were in in the same direction.

Table 2.13 Included studies investigating pre--eclampsia as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Briley, 2013	Pre-eclampsia: 3.21 (0.94-10.90)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Butwick, 2017	**Pre-labour CS:** 13.7% vs 5.8% **Intrapartum CS:** Pre-eclampsia: 1.53 (0.74-3.21)	% aOR	Sig NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Combs, 1991a	Pre-eclampsia: 2.18 (1.31-3.65)	aOR	Sig	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Pre-eclampsia: 5.02 (2.98-8.47)	aOR	NS	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Firmin, 2019	Pre-eclampsia: 2.56 (1.07-4.10)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Koopmans, 2014	Pre-eclampsia: 1.6 (1.08-2.4) Gestational hypertension: ref	aOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Lisonkova, 2016	Pre-eclampsia: 6.25 (1.77-22.1)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Merriam, 2018	**PPH 1:** Pre-eclampsia/eclampsia: 2.23 (2.17-2.29) **PPH 2:** Pre-eclampsia/eclampsia: 2.80 (2.72-2.88)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Miller, 2017	**PPH:** Pre-eclampsia: 12 (7.5%) **CTL:** Pre-eclampsia: 16 (5.0%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Nyflot, 2016	**SPPH:** Severe pre-eclampsia/HELLP: 50 (4.7%) **CTL:** Severe pre-eclampsia/HELLP: 28 (1.4%)	%	np	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	Severe preeclampsia or HELLP syndrome: 3.03 (1.74-5.27)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Oberg, 2014b	Pre-eclampsia: 2.10 (1.92-2.29)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Rossen, 2010	**VB** Preeclampsia: 1.4 (1.0-1.9)	aOR	NS	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
Suzuki, 2007	Preeclampsia: 1.30 (0.38-4.38)	uOR	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 134	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
von Schmidt, 2013	**Total cohort:** Pre-eclampsia: 1.53 (1.46-1.60) **Non-induced spontaneous birth:** Pre-eclampsia: 1.91 (1.71-2.13)	aOR aOR	Sig Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.5.2 Combined hypertensive disorders

Twelve studies examined the association between combined types of hypertensive disorders and PPH/SPPH. Most studies referred to the risk factor as 'hypertension', while some explicitly combined types of hypertensive disorders. No LRoB studies examined hypertension and SPPH. Of the ten LRoB analyses of hypertension and PPH, five reported a significant increase in the risk of PPH among women with hypertension, at the multivariable level. The magnitude of effect was generally small to moderate, with aOR ranging from 1.45 to 1.92. The greatest magnitude was observed in a small study that analysed PPH among twin births separately from singletons and found a five-fold increase in the odds of PPH for women with hypertensive disorders who gave birth to twins (aOR=5.45; 95% CI 2.2-14).

Of the three HRoB studies, one found a significant increase in the odds of PPH among women with hypertension, compared with those without (uOR 1.45; 1.43-1.47), one reported no significant difference and the other did not report the level of significance.

Rating: Likely - Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.

Table 2.14 Included studies investigating hypertensive disorders as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Allen, 1988	Hypertension: Normal vaginal delivery: 6.6% Instrumental delivery: 16.7% CS: 18.9%	% (incidence of PPH by category)	NA	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Buzaglo, 2014	Hypertensive disorders: 1.6 (1.1-2.1)	aOR	Sig	VB	**PPH:** EBL ≥500mL	56,394	Low
Hiersch, 2016	**PPH:** Hypertensive disorders: 0% **CTL:** Hypertensive disorders: 0%	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Hypertension/ pre-eclampsia/ eclampsia/ HELLP: 1.8 (1.7-1.9)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Kaufner, 2016	Hypertension/ pre-eclampsia: CTL: 2 (1%) PPH: 0% p=0.578	%	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Lisonkova, 2016	**PPH:** Hypertension during pregnancy: 19 (4.96%) **CTL:** Hypertension during pregnancy: 12 (3.13%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Mehrabadi, 2013	Hypertensive disorder: 1.92 (1.80-2.04)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Miller, 2017	PPH: Gestational or chronic hypertension: 9 (5.7%) CTL: Gestational or chronic hypertension: 19 (6.0%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Noguchi, 2017	PPH: Hypertension: 3 CTL: Hypertension: 58	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829	High
Sheiner, 2009	Hypertensive disorders: PPH: 1.6 (1.2-2.1)	aOR	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Suzuki, 2012	**Singletons:** Hypertensive disorders: 1.08 (0.49-2.4) **Twins:** Hypertensive disorders: 5.45 (2.2-14)	uOR aOR	NS Sig	CS	**PPH:** PPH requiring transfusion	**Singletons:** 17,405 **Twins:** 916	Low
van Stralen, 2016	Hypertension: 1.45 (1.43-1.47)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High

2.4.5.3 Chronic hypertension

Chronic/pre-existing hypertension was investigated as a risk factor for PPH/SPPH in eight studies, five of which were LRoB. Of the four LRoB studies analysing chronic hypertension and PPH, two observed a significantly higher risk of PPH among women with chronic hypertension. A large US-based study of over 55,000,000 births reported that chronic hypertension was associated with a small increase in the odds of PPH of at least 500mL (aOR1.04; 95% CI 1.01-1.08), but reported no significant association for PPH and/or transfusion. A large Australian study also reported a small increase in the odds of PPH in women with chronic hypertension, both in women who gave birth in 1994-95 (aOR=1.30; 95% CI 1.04-1.63) and in 2002 (aOR=1.32; 95% CI 1.02-1.73).

Of the three HRoB studies, two reported a significant increase in the risk of PPH in women with chronic hypertension, however these analyses were not adjusted for potential confounders. Two studies examined chronic hypertension and SPPH, with one (12) reporting a significant increase in the risk of SPPH among women with chronic hypertension, compared with those with no chronic hypertension (4.8; 95% CI 1.2-19.5). The study that did not find a significant association between chronic hypertension and SPPH was relatively small (N=819).

Rating: Likely - Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.

Table 2.15 Included studies investigating chronic hypertension as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*No. of patients*	*RoB*
Butwick, 2017	**Pre-labour CS:** Chronic hypertension: 1.59 (0.70-3.61)	aOR	NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550	Low
Ford, 2007	**1994-1995** Chronic/other non-pregnancy induced hypertension: 1.30 (1.04-1.63) **2002**: Chronic/other non-pregnancy-induced hypertension: 1.32 (1.02-1.73)	aOR aOR	Sig Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low
Kramer, 2011	**PPH:** Pre-pregnancy hypertension: 1.3 (0.9-1.8) **SPPH:** Pre-pregnancy hypertension: 4.8 (1.2-19.5)	aOR aOR	NS Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lisonkova, 2016	**PPH:** Chronic hypertension: 6 (1.57%) **CTL** Chronic hypertension: 0	%	NA	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*No. of patients*	*RoB*
Merriam, 2018	**PPH 1:** Chronic hypertension: 1.04 (1.01-1.08) **PPH 2:** Chronic hypertension: 1.01 (0.97-1.05)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Oberg, 2014a	Chronic hypertension: 1.29 (1.16-1.42)	uOR	Sig	VB, CS	**PPH:** ICD codes, typically EBL ≥1000mL	583,332	High
Oberg, 2014b	Chronic hypertension: 1.71 (1.38-2.12)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Stones, 1993	Essential hypertension: 1.43 (0.65-3.14)	uRR (99% CI)	NS	VB, CS	**PPH:** EBL ≥1000mL	37,334	High

2.4.5.4 Gestational hypertension

Six studies explored the association between gestational hypertension and PPH/SPPH, four of which were considered LRoB. Of the five LRoB analyses of gestational hypertension and PPH, four reported a significant increase in the odds of PPH, compared with no gestational hypertension. The magnitude of the effect differed between studies, with aORs ranging from 1.4 to 3.16. One study investigated gestational hypertension and SPPH, finding no significant association between 'gestational hypertension/pre-eclampsia' and SPPH.

Of the HRoB studies, two out of three reported no significant difference in risk among women with pregnancy induced hypertension at the univariable level.

Rating: Very likely – More than 60% of LRoB analysis reported a significant association. All significant associations were in the same direction.

Table 2.16 Included studies investigating gestational hypertension as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Briley, 2013	Gestational hypertension: 2.22 (0.87-5.63)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Ford, 2007	**1994-1995** Pregnancy induced hypertension: 1.46 (1.36-1.57) **2002** Pregnancy-induced hypertension: 1.40 (1.27-1.55)	aOR aOR	Sig Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low
Fukami, 2019	Pregnancy-induced hypertensions: 3.16 (1.65-6.06)	aOR	Sig	VB	**PPH:** CBL ≥1000mL	1,608	Low
Kramer, 2011	**PPH:** Pregnancy-induced hypertension/ pre-eclampsia: 1.4 (1.2-1.6) **SPPH:** Pregnancy-induced hypertension/ pre-eclampsia: 0.2 (0.02-1.7)	aOR aOR	Sig NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Salkeld, 2008	**PPH:** Hypertensive disorders of pregnancy: 128 (5.2%) **CTL:** Hypertensive disorders of pregnancy: 767 (3.2%)	%	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Stones, 1993	Non-proteinuric pregnancy-induced hypertension: 1.7 (1.16-2.50)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Stones, 1993	Proteinuric pregnancy-induced hypertension: 1.15 (0.32-4.19)	uRR (99% CI)	NS	VB, CS	**PPH:** EBL ≥1000mL	37,334	High

2.4.5.5 Maternal weight and body mass index (BMI)

Maternal weight and BMI was examined as a risk factor by 20 studies, with 16 of these being LRoB. BMI was analysed in a variety of ways, primarily as a categorical variable with a range of cut-offs, but also as a continuous variable. Twelve LRoB studies examined BMI/obesity and PPH, two of which reported that higher BMI (116) or obesity (123) were statistically significantly associated with a higher risk of PPH after adjustment for other factors.

Seven LRoB studies analysed BMI and SPPH, with one reporting a significantly higher in risk of SPPH among women in higher BMI categories. This relatively large study reported that BMI ≥25 was associated with a small increase in the risk of SPPH compared with a BMI of 18.5-<25, among all women and among women who experienced labour.

Two studies analysed maternal weight in kilos rather than BMI, one investigating weight gain during pregnancy and PPH, reporting no significant association, and the other examining weight in kilos at the end of pregnancy, reporting a small increase in the odds of PPH for every 5kg increment (aOR=1.04; 95% CI 1.01-1.01).

With a minority of analyses (20%) reporting a significant association between obesity/BMI and PPH/SPPH after adjustment for confounders, it is unclear whether BMI is a risk factor for PPH/SPPH.

Rating: Unclear – Less than 50% of LRoB studies reporting a significant association.

Table 2.17 Included studies investigating maternal weight/BMI as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Biguzzi, 2011	Maternal weight in 5kg increments [recorded at the end of pregnancy]: 1.04 (1.01-1.08)	aOR	Sig	VB	**PPH:** EBL ≥500mL	6,011	Low
Briley, 2013	BMI kg/m^2 per unit: 1.01 (0.99-1.04)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Davey, 2019	**All women:** <18.5: 0.86 (0.7-1.0) 18.5-<25: ref 25-<30: 1.14 (1.1-1.2) ≥30: 1.34 (1.2-1.5) Not available: 1.15 (1.0-1.3)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
	Women who experienced labour: <18.5: 0.85 (0.7-1.1) 18.5-<25: ref 25-<30: 1.12 (1.04-1.2) ≥30: 1.39 (1.3-1.5) Not available: 1.4 (1.0-1.3)	aOR	Sig				
Endo-Kawamura, 2016	**Mid-pregnancy blood test:** BMI ≥28.2 kg/m: 2.02 (1.24-3.28)	aOR	Sig	VB	**PPH:** EBL ≥700mL	1,032	Low
	Pre-delivery blood test: BMI ≥28.2 kg/m: 1.95 (1.20-3.16)	aOR	Sig				
Farina, 2017	**PPH:** 27.4 (2.80) **CTL:** 27.5 (3.47) **p=**0.917	Mean dif	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390	High

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Fukami, 2019	**CTL:** <18.4: 17.7% 18.5-24.9: 67.8% ≥25.0: 14.5% **PPH:** <18.4: 19.4% 18.5-24.9: 63.4% ≥25.0: 17.2%	%	NS	VB	**PPH:** CBL ≥1000mL	1,608	Low
Fukami, 2019	**Weight gain during pregnancy** <9.9 Kg: 56.6% 10.0-14.9 Kg: 34.6% >15.0: 8.8% **PPH:** <9.9 Kg: 38.7% 10.0-14.9 Kg: 43.0% >15.0: 18.3%	%	NS	VB	**PPH:** CBL ≥1000mL	1,608	Low
Hiersch, 2016	**PPH:** BMI: 22.4 (3.7) **CTL:** BMI: 22.7 (5.2) p=0.81	Mean (SD)	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaufner, 2016	CTL: 28 (26-32) PPH: 27 (25-32) p=0.526	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Khireddine, 2012	**CTL:** <25: 1172 (80.0%) 25-29: 220 (15.0%) ≥30: 74 (5%) Missing: 278 **PPH 1:** <25: 3127 (79.3%) 25-29: 572 (14.5%) ≥30: 241 (6.25%) Missing: 537 **PPH 2:** <25: 803 (80.9%) 25-29: 138 (13.9%) ≥30: 52 (5.2%) Missing: 132	%	Sig	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125	Low
Koopmans, 2014	Pre-pregnancy BMI: 0.96 (0.67-0.73)* *Note: the incongruent OR and CI are reported in the study. It was not possible to verify results. P = 0.08 so this was considered NS	aOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Kramer, 2011	**PPH:** < 18.5: 1.7% 18.5-<25: 2.1% 25-30: 2.8% ≥30: 3.0% **SPPH:** < 18.5: 0.00% 18.5-<25: 0.27% 25-30: 0.06% ≥30: 0.09 %	PPH/SPPH rate (%)	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lee, 2017	per unit BMI increase: 1.12 (0.93-1.34)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210	Low
Looft, 2017	**All:** <18.5: 1778 18.5-24.9: 38825 25.0-29.9: 10251 ≥30: 3616 Missing: 2797 **PPH:** <18.5: 439 18.5-24.9: 10942 25.0-29.9: 3190 ≥30: 1149 Missing: 834	n	NA	VB	**PPH:** EBL ≥500mL	57,267	Low
Magan, 2005a	Obesity: PPH: 2.28 (1.17-4.16) SPPH: 1.50 (0.50-4.49)	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Miller, 2017	<30: ref 30-34.9: 1.15 (0.69-1.90) 35-39.9: 1.01 (0.45-2.25) ≥ 40: 2.66 (0.98-7.21)	aOR	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Nyflot, 2016	BMI **SPPH:** 23.1 (21.0-26.1) **CTL:** 22.8 (20.8-25.7)	Median (IQR)	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	<18.5: 1.08 (0.74-1.59) 18.5-24.9: ref 25.0-29.9: 1.12 (0.92-1.36) 30.0-34.9: 1.16 (0.87-1.55) 35.0-39.9: 1.43 (0.85-2.40) ≥40: 1.03 (0.41-2.56)	uOR	NS	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	BMI >30: 1.29 (1.02-1.63)	uOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low
Oberg, 2014b	<20: ref 20-24: 1.13 (1.06-1.20) ≥25: 1.20 (1.13-1.29)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Stones, 1993	BMI 27+: 1.64 (1.24-2.17)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High

2.4.5.6 *Diab*etes

Diabetes was investigated as a potential risk factor for PPH/SPPH by 17 studies, of which 14 were considered LRoB. Nine studies explored diabetes of any type combined, while eight examined gestational diabetes and three pre-gestational diabetes, separately. Of the thirteen LRoB studies that analysed diabetes and PPH, two reported a significant association, although in opposing directions. One large study (N=55,140,088) (125) reported that having pre-existing diabetes was associated with a 14% lower risk of PPH of 500mL or more (aRR 0.86; 95% CI 0.82-0.90), but did not find the same association for PPH of 1000mL or more. In contrast, a study of over 65,000 births (82) reported almost double the odds of PPH among women who had diabetes (aOR=1.97; 1.49-2.60).

Four LRoB studies explored diabetes status as a risk factor for SPPH, with one (112) reporting a significant association at the adjusted level. This study only found a significant association for women who had an intrapartum CS (aOR=1.83; 95% CI 1.15-2.93), finding no significant association for women who had a pre-labour CS.

Three HRoB studies analysed diabetes as a risk factor, two of which, conducted on similar populations in Norway, reported that gestational diabetes (uOR 1.40 95% CI 1.14-1.71) (130) and diabetes (uOR 1.38 95% CI 1.26-1.52) (131) were associated with a higher risk of PPH, at the univariable level.

With only a minority (15%) of analyses finding a significant association between diabetes and PPH/SPPH, and given the inconsistent direction of this association, it is unclear whether diabetes is an independent risk factor for PPH/SPPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association and significant results were in conflicting directions.

Table 2.18 Included studies investigating diabetes as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Butwick, 2017	**Pre-labour CD:** Gestational diabetes: 1.52 (0.92-2.5) **Intrapartum CD:** Gestational diabetes: 1.83 (1.15-2.93)	aOR aOR	NS Sig	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Buzaglo, 2014	Diabetes: PPH: 4.5% CTL: 3.7%	%	NS	VB	**PPH:** EBL ≥500mL	56,394	Low
Choe, 2016	Diabetes: 1.97 (1.49-2.60)	aOR	Sig	VB, CS	**PPH:** ICD-10 code O72.0-O72.3 or transfusion	65,479	Low
Firmin, 2019	Diabetes: PPH: 6.5% CTL: 3.9% p=0.217	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Hiersch, 2016	**PPH:** Pre-gestational DM: 0.7% **CTL:** Pre-gestational DM: 1.3% p=0.53	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Hiersch, 2016	**PPH:** Gestational diabetes: 5.4% **CTL:** Gestational diabetes: 4.7% p=0.63	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaufner, 2016	Gestational diabestes: CTL: 13 (7%) PPH: 3 (11%) p=0.452	%	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low
Kramer, 2011	**PPH:** Pre-pregnancy or gestational diabetes or impaired glucose tolerance: 1.1 (0.9-1.3) **SPPH:** Pre-pregnancy or gestational diabetes or impaired glucose tolerance: 0.3 (0.1-1.4)	aOR aOR	NS NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lisonkova, 2016	**PPH:** Diabetes mellitus: 5 (1.31%) **CTL:** Diabetes mellitus: 3 (0.78%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Lisonkova, 2016	**PPH:** Gestational diabetes: 26 (7.05%) **CTL:** Gestational diabetes: 23 (6.17%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Mehrabadi, 2013	Diabetes: 0.99 (0.91-1.08)	aOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Merriam, 2018	**PPH 1:** Pre-existing diabetes: 0.86 (0.82-0.90) **PPH 2:** Pre-existing diabetes: 0.96 (0.90-1.02)	aRR aRR	Sig NS	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Miller, 2017	**PPH:** Pre-existing or gestational diabetes: 27 (17.0%) **CTL:** Pre-existing or gestational diabetes: 47 (14.8%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Noguchi, 2017	**PPH:** Diabetes: 1 **CTL:** Diabetes: 43	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829	High
Nyflot, 2016	**SPPH:** Gestational diabetes: 46 (4.3%) **CTL:** Gestational diabetes: 58 (2.8%)	%	np	VB, CS	**SPPH:** EBL ≥1500mL	SPPH: 115 CTL: 82	Low
Nyflot, 2017a	Gestational diabetes: 1.56 (1.05-2.31)	uOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1064 **CTL:** 2059	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Oberg, 2014a	Diabetes: 1.38 (1.26-1.52) No diabetes: ref	uOR	Sig	VB, CS	**PPH:** ICD codes, typically EBL ≥1000mL	583,332	High
Oberg, 2014b	Diabetes: 1.13 (0.86-1.49) No diabetes: ref	uOR	NS	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Oberg, 2014b	Gestational diabetes: 1.40 (1.14-1.71)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307 756	High
Sheiner, 2009	**PPH 1:** Gestational Diabetes: 6.6% **PPH 2:** Gestational Diabetes: 6.7% **PPH 3:** Gestational Diabetes: 6.0% SPPH: Gestational Diabetes: 6.1%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **SPPH:** 199 **CTL:** 153,645	Low

2.4.5.7 Anaemia

Ten studies explored antenatal anaemia or haemoglobin levels and risk of PPH/SPPH. A variety of different definitions or diagnoses for anaemia were used, with some studies comparing a diagnosis of anaemia with no diagnosis, and others reporting on levels of haemoglobin or haematocrit, either as categorical or continuous variables. Of the eight LRoB analyses of anaemia or haemoglobin levels and PPH, two reported statistically significant associations after adjustment for other factors. Both were conducted on similar populations in Italy and both analysed haemoglobin as a continuous variable, finding that for every 1 g/dL increment of haemoglobin present one month before delivery, the odds of PPH decreased significantly (aOR=0.84; 95% CI 0.78-0.90 and aOR=0.81; 95% CI 0.75-0.88).

Three of the four LRoB analyses of anaemia and SPPH reported statistically significant associations after adjustment for other factors. Two of these analyses were from a relatively small study, (112) with fewer than 900 births in each population, and reported that among women who had a pre-labour CS, haemoglobin levels ≤9.9 g/dL were associated with an aOR of 2.80 (95% CI 1.05-7.50), compared with haemoglobin ≥11. Among women who had an intrapartum CS, the odds of SPPH tripled for those with a pre-delivery haemoglobin of ≤9.9 (aOR=2.99; 95% CI 1.29-6.92) and more than doubled for women who had a haemoglobin level of 10-10.9, aOR=2.6 (95 CI 1.38-4.9), compared with haemoglobin ≥11. Similarly, Nyflot et al 2017a (45) found that anaemia at the start of pregnancy (Hb ≤ 9.0 g/dL) was associated with a four-fold increase in the risk of SPPH, compared with no anaemia at the start of pregnancy (aOR=4.27; 95% CI 2.79-6.54).

Most studies that explored this risk factor were relatively small. The largest study (136) (N=37,334) was considered HRoB, but found no significant association between antenatal anaemia and PPH at the univariable level.

Rating: Unclear – Less than 50% of LRoB analyses reported a significant association.

Table 2.19 Included studies investigating anaemia as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Biguzzi, 2011	Haemoglobin one month before delivery (1 g/dL increment): 0.84 (0.78-0.90)	aOR	Sig	VB	**PPH:** EBL ≥500mL	6,011	Low
Biguzzi, 2014	Haemoglobin (1 g/dL increment) one month before delivery: 0.81 (0.75-0.88)	aOR	Sig	VB	**PPH:** EBL ≥500mL	3,219	Low
Butwick, 2017	**Pre-labour CS:** Pre-delivery haemoglobin (g/dL): ≤9.9: 2.80 (1.05-7.50) 10-10.9: 1.11 (0.55-2.24) ≥11: ref **Intrapartum CS:** Pre-delivery haemoglobin (g/dL): ≤9.9: 2.99 (1.29-6.92) 10-10.9: 2.6 (1.38-4.9) ≥11: ref	aOR aOR	Sig Sig	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Firmin, 2019	Anaemia in pregnancy PPH: 39% CTL: 34.7% p=0.373	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Firmin, 2019	Anaemia at birth: 1.44 (0.97-2.12)	uOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Kaufner, 2016	Haemoglobin, pre-partum (g/L) ≤11: 4.57 (0.80-26.04) >11-12: 2.00 (0.38-10.64) >12-13: 1.33 (0.25-7.10) >13: ref	aOR	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Koopmans, 2014	Antepartum Haematocrit (L/L x 10): 0.65 (0.34-1.2)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Koopmans, 2014	Antepartum Haemoglobin (mmol/L): 0.84 (0.64-1.1)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Miller, 2017	PPH: Pre-delivery hB (g/dl): 12.3 (1.2) CTL: Pre-delivery hB (g/dl): 12.4 (1.2)	Mean (SD)	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Nyflot, 2017a	Anaemia in start of pregnancy (Hb ≤ 9.0 g/dL): 4.27 (2.79-6.54)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	Anaemia in start of pregnancy: 3.56 (2.32-5.49)	uOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low
Stones, 1993	Antenatal anaemia: 1.24 (0.82-1.89)	uRR (99% CI)	NS	VB, CS	**PPH:** EBL ≥1000mL	37,334	High

2.4.6 Obstetric history

2.4.6.1 Previous caesarean birth

Previous caesarean was explored as a risk factor for PPH/SPPH by 19 studies, 18 of which were considered to be LRoB. Most studies that investigated previous caesarean analysed this variable as a dichotomous yes/no, however two studies categorised previous caesarean by number of previous sections. For all analyses, 'no previous caesarean' was the reference group. Of the 17 analyses of previous caesarean and PPH, five reported a statistically significant association at the multivariable level, with previous caesarean mostly being associated with a higher risk of PPH. One study (121) that analysed modes of birth separately reported that previous CS was associated with higher odds of PPH among women having a subsequent vaginal birth, but protective for women having a subsequent caesarean, however the reference group for this analyses was vaginal birth without prior caesarean, so interpretation is difficult. One of the studies (111) that reported a significant association was conducted across two countries, Canada and France, and in both analyses included large populations (N=205,842 and N=146,781, respectively). Another Canadian study (12) was also large (N=103,726) while, the other studies reporting this association were relatively small (N=1,032 and N=786).

Of the seven analyses of SPPH, across five studies, three were significant at the multivariable level. In a large Australian study (114), women who had two or more previous caesarean were 34% more likely to have a SPPH (aOR=1.34; 95% CI 1.2-1.5), compared with multiparous women with no previous caesarean, while women who had had one previous caesarean had similar odds to the reference group. In the same study, among women who experienced labour, having one previous caesarean was associated with a 36% increase in the odds of SPPH, after adjustment for other variables (aOR=1.36; 95% CI 1.2-1.6). By contrast, the other study (112) found a statistically significant association with SPPH, reported that among women who had a caesarean after labour, having one previous caesarean was protective for SPPH (aOR=0.43; 95% CI 0.21-0.91). While the two studies had the same definition of SPPH, the former (114) included both vaginal and caesarean births, while the later (112) included only caesarean births.

With only 33% of analyses reporting a significant association at the adjusted level, and with contrasting directions of the effect across studies, it is unclear whether previous caesarean is an independent risk factor for PPH/SPPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association. Significant results were in conflicting directions.

Table 2.20 Included studies investigating previous caesarean as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Briley, 2013	Multipara previous CS: 0.96 (0.61-1.51) Multipara no previous CS: 0.79 (0.56-2.11)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Bonnet, 2013	**Canada:** Primiparous: 1.45 (1.37-1.53) Multiparous without previous CS: ref Multiparous with previous CS: 1.16 (1.01-1.33) **France:** Primiparous: 1.32 (1.16-1.50) Multiparous without previous CS: ref Multiparous with previous CS: 1.75 (1.35-2.26)	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	Low
Butwick, 2017	**Pre-labour CS:** Number of previous CS: 0: ref 1: 0.65 (0.34-1.22) 2: 0.67 (0.29-1.54) ≥3: 0.66 (0.17-2.55) **Intrapartum CS:** Number of previous CS: 0: ref 1: 0.43 (0.21-0.91) ≥2: 0.49 (0.16-1.49)	aOR aOR	NS Sig	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Combs, 1991a	Previous CS: 1.03 (0.56-1.88) none: ref	aOR	NS	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Previous CS: 1.72 (0.84-3.53)	aOR	NS	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Davey, 2019	**All women:** No prior birth: 1.08 (1.0-1.2) Prior birth, no prev CS: ref Prior birth, 1 prev CS: 0.93 (0.8-1.0) Prior birth, 2 or more prev CS: 1.34 (1.2-1.5) Not reported: 0.59 (0.4-0.8)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
	Women who experienced labour: No prior birth: 1.15 (1.1-1.2) Prior birth, no prev CS: ref Prior birth, 1 prev CS: 1.36 (1.2-1.6) Prior birth, 2 or more prev CS: 1.31 (0.9-2.0) Not reported: 0.63 (0.5-0.9)	aOR	Sig				

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Endo-Kawamura, 2016	**Mid-pregnancy blood test:** Previous CS: 2.91 (1.27-6.18) **Pre-delivery blood test:** Previous CS: 2.77 (1.31-5.83)	aOR aOR	Sig Sig	VB	**PPH:** EBL ≥700mL	1,032	Low
Hiersch, 2016	**PPH:** Previous single CS: 9.5% **CTL:** Previous single CS: 9.8% p=1.0	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Previous CS: 1.0 (0.9-1.0)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Kramer, 2011	**PPH:** Previous CS: 1.4 (1.2-1.6) **SPPH:** Previous CS: 3.1 (1.0-10.0)	aOR aOR	Sig NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lisonkova, 2016	Vaginal delivery without prior CS: ref Vaginal delivery with prior CS: 3.70 (1.08-12.7) CS without prev CS: 0.53 (0.32-0.88) CS with prior CS: 0.47 (0.24-0.95)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Mehrabadi, 2013	Previous CS: 0.97 (1.91-1.04)	aOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Miller, 2017	**PPH:** Trial of labour after caesarean: 5 (3.1%) **CTL:** Trial of labour after caesarean: 11 (3.5%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Noguchi, 2017	Prior CS: 1.8 (no CI) p=0.01	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500g	4,829	High
Nyflot, 2017a	Previous CS: 1.12 (0.88-1.41)	uOR	NS	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	Previous CS: 1.26 (0.92-1.72)	uOR	NS	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low
Rossen, 2010	**VB** Previous CS: 1.4 (1.0-1.9) **CS** Previous CS: 1.0 (0.7-1.4)	aOR aOR	NS NS	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Sheiner, 2009	**PPH 1:** Previous CS: 2.2% **PPH 2:** Previous CS: 9.4% **PPH 3:** Previous CS: 19.6% **CTL:** Previous CS: 10.5%	%	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645	Low
Suzuki, 2012	**Singletons:** Previous CS: 0.88 (0.51-1.5) **Twins:** Previous CS: 1.23 (0.16-9.6)	uOR uOR	NS NS	CS	**PPH:** PPH requiring transfusion	**Singletons:** 17,405 **Twins:** 916	Low

2.4.6.2 Previous Postpartum haemorrhage

Previous PPH was investigated as a risk factor for PPH/SPPH by eight studies, six of which were considered LRoB. All four LRoB studies that investigated previous PPH and PPH found previous PPH to be associated with a statistically significantly higher risk of subsequent PPH, after adjustment for other factors. These studies reported generally moderate to high effect sizes, with aORs ranging from 2.22 to 3.55. The two HRoB studies did not report statistical significance.

Of the two LRoB studies examining SPPH, one (45) reported a statistically significant association between previous severe PPH and subsequent severe PPH, with women who had a previous severe PPH being almost nine times as likely to have a subsequent SPPH, after adjustment for other factors (aOR=8.97; 95% CI 5.25-15.33). The study that did not report a statistically significant association after adjustment for other factors, reported a significant association at the univariable level (aOR=7.93; 95% CI 4.27-14.72). These two studies were conducted in similar populations in Norway.

Of the six LRoB analyses, five (83%) reported a significant association between previous PPH and subsequent PPH/SPPH. Previous PPH is therefore considered very likely to be an independent risk factor for PPH/SPPH.

Rating: Very likely - More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Table 2.21 Included studies investigating previous postpartum haemorrhage as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Briley, 2013	Previous PPH 2.75 (1.40-5.44)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Combs, 1991b	Previous PPH: 3.55 (1.24-10.19)	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Firmin, 2019	Previous PPH: 3.36 (1.65-6.87)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Magan, 2005b	Previous PPH: 2.22 (1.7-2.9)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Noguchi, 2017	**PPH:** Previous PPH: 3 **CTL:** Previous PPH: 174	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829	High
Nyflot, 2017a	Previous PPH: 8.97 (5.25-15.33)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	Previous PPH: 7.93 (4.27-14.72)	uOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Salkeld, 2008	**PPH:** Number of previous PPH: 0: 2326 (94.6%) 1: 126 (5.1%) 2: 8 (0.3%) 3: 0 **CTL:** Number of previous PPH: 0: 23534 (98.3%) 1: 1401 (1.7%) 2: 6 (0.0%) 3: < 5 (suppressed)	%	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High

2.4.6.3 Previous uterine surgery

Previous uterine surgery was investigated as a potential risk factor by seven studies, six of which were considered LRoB. Six studies categorised this variable as a dichotomous Yes/No for previous uterine surgery and one investigated 'uterine scarring' Yes/No. Of the three studies that assessed the relationship between previous uterine surgery/scarring and PPH, none reported a significant association at the adjusted level. Two of the three studies (117) (121) were relatively small (N=462 and N=786, respectively) and one was relatively large (N=103,726)(12).

Of the four LRoB studies that investigated previous uterine surgery and SPPH, one (12) reported a significant association, with women who had a previous uterine surgery having higher risk of SPPH, compared with those who did not (aOR=4.6; 95% CI 1.2-17.7). This study found no significant association between previous uterine surgery and PPH. The three other studies (45, 63, 104) that explored this risk factor were relatively small (N=201, N=506 and N=3,123, respectively). One study rated as HRoB for confounding reported a significant association for SPPH at the multivariable level (aOR=1.9; no CI provided, p=0.01).

With only 14% of analyses of PPH or SPPH being significant at the adjusted level, it is unclear whether previous uterine surgery is an independent risk factor for PPH/SPPH.

Rating: Unclear - Less than 50% but more than 0% of LRoB analyses found a significant association.

Table 2.22 Included studies investigating previous uterine surgery as a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Firmin, 2019	Uterine scarring PPH: 13% CTL: 16.9% p=0.276	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Kramer, 2011	**PPH:** History of uterine surgery: 1.4 (0.8-2.3) **SPPH:** History of uterine surgery: 4.6 (1.2-17.7)	aOR aOR	NS Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lee, 2017	Previous uterine surgery: 0.00 (0.00-0.00)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210	Low
Lee, 2018	Previous uterine surgery: 1.46 (0.58-3.70)	uOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506	Low
Lisonkova, 2016	**PPH:** Prior uterine surgery: 28 (7.57%) **CTL:** Prior uterine surgery: 33 (8.62%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Noguchi, 2017	Prior uterine surgery: 1.9 (no CI) p=0.01	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500g	4,829	High
Nyflot, 2017a	Previous uterine surgery: 3.38 (1.60-7.14)	uOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low

2.4.7 Pregnancy factors

2.4.7.1 Parity

Parity was explored as a risk factor by 36 studies, 26 of which were considered LRoB. Most studies examined parity as a dichotomous variable (previous birth Yes/No), but some categorised the number of previous pregnancies. There were 29 LRoB analyses of parity and PPH, of which nine reported that nulliparity was associated with a significantly higher risk of PPH after adjustment for other factors, while one found that previous birth was associated with a significantly higher risk of PPH, compared with nulliparity, after adjustment for other factors (aOR=1.66; 95% CI 1.41-1.96). The study (109) that found nulliparous women at lower risk than parous women was relatively small (N=3,219) and the incidence of PPH was relatively high (24%).

Five LRoB studies examined parity and SPPH, and none found a significant association at the multivariable level. Of the ten HRoB studies, three reported higher odds of PPH among nulliparous women and one reported higher odds of PPH among women who had more than three previous births.

Given that most studies that investigated parity did not report a significant association with PPH/SPPH, and that the direction of the effect was inconsistent across studies that did find an association, it is unclear whether parity is an independent risk factor for PPH/SPPH.

Rating: Unclear – Less than 50% of LRoB analyses found a significant association, and significant results were in conflicting directions.

Table 2.23 Included studies investigating parity as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Allen, 1988	Normal vaginal birth and para 1: 4.1% Normal vaginal birth and para 4 or more: 4.2%	% (incidence of PPH by category)	NS	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Biguzzi, 2014	Parous: 1.66 (1.41-1.96) Nulliparous: ref	aOR	Sig	VB	**PPH:** EBL ≥500mL	3,219	Low
Bonnet, 2013	**Canada:** Primiparous: 1.45 (1.37-1.53) Multiparous without previous CS: ref Multiparous with previous CS: 1.16 (1.01-1.33)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	Low
	France: Primiparous: 1.32 (1.16-1.50) Multiparous without previous CS: ref Multiparous with previous CS: 1.75 (1.35-2.26)	aOR	Sig				
Butwick, 2017	**Pre-labour CS:** SPPH: 1 [0-2] CTL: 1 [0-2] p=0.78	Median [IQR]	NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550	Low
	Intrapartum CS: SPPH: 0 [0-1] CTL: 0 [0-1] p=0.72		NS			**Intrapartum CS** **SPPH:** 278 **CTL:** 572	

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Combs, 1991a	Nulliparous: 1.27 (0.75-2.15) Parous: ref	aOR	NS	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Nulliparous: 1.45 (1.05-2.00) Parous: ref	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Endo-Kawamura, 2016	**Nulliparous:** PPH: 62 (60%) n=104 no-PPH: 505 (54%) n=928	%	NS	VB	**PPH:** EBL ≥700mL	1,032	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Eto, 2016	**Primiparous** PPH 1: 7.9% CTL: 20.3% **Multiparous** PPH 1: 16.9% CTL: 55.0% p=0.006	%	Sig	VB	**PPH 1:** EBL ≥500g **PPH 2:** EBL ≥800g **PPH 3:** EBL >1000g	**CTL:** 2,524 **PPH 1:** 524 **PPH 2:** 147 **PPH 3:** 158	High
	Primiparous PPH 2: 2.9% CTL: 25.3% **Multiparous** PPH 2: 6.2% CTL: 65.6% p=0.176		NS				
	Primiparous PPH 3: 1.4% CTL: 26.7% **Multiparous** PPH 3: 3.3% CTL: 68.6% p=0.524		NS				

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Firmin, 2019	**PPH:** 1: 20.1% 2-4: 39.6% 5-7: 26% 8+: 14.3% **CTL:** 1: 22.1% 2-4: 39.9% 5-7: 23.4% 8+: 14.6%	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Ford, 2007	**1994-1995** 0: 1.02 (0.91-1.13) 1-4: ref ≥: 1.02 (0.95-1.09) **2002** 0: 0.87 (0.74-1.02) 1-4: ref ≥: 1.01 (0.93-1.09)	aOR aOR	NS NS	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Gilbert, 1987	**All deliveries** **PPH:** Primiparous: 60 (70%) Multiparous: 26 (30%) **CTL:** Primiparous: 116 (33%) Multiparous: 235 (67%) **Spontaneous deliveries** Primiparous: 24 (73%) Multiparous: 9 (27%) **CTL:** Primiparous: 78 (26%) Multiparous: 222 (74%)	%	Sig Sig	VB	**PPH:** EBL ≥500mL	**PPH:** 86 **CTL:** 351	High
Henry, 2005	**CTL:** 0: 63 1: 42 2+: 19 **PPH 1:** 0: 84 1: 23 2+: 17 **PPH 2:** 0: 31 1: 0 2+: 9	n	Sig	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Hiersch, 2016	Nulliparity: 1.43 (0.97-2.12)	aOR	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Hiersch, 2016	**PPH:** 1 (1-1) **CTL:** 1 (1-2) p=0.08	Median (IQR)	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Multiparity: 1.0 (1.0-1.0)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Kaelin Agten, 2017	Primiparity >40 years: 0.09 (0.8-1.1)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Kaufner, 2016	Pimipara: 4.27 (1.32-13.80) 2-4: ref ≥5: 3.22 (0.44-23.65)	aOR	Sig	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low
Khireddine, 2012	**CTL:** Pimiparous: 809 (46.4%) **PPH 1:** Pimiparous: 2678 (59.8) **PPH 2:** Pimiparous: 786 (69.9%)	%	Sig	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Koopmans, 2014	Nulliparity: 1.2 (0.79-1.19)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Koopmans, 2014	Multiparity (para 4+): 0.78 (0.81-0.10-6.1)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Kramer, 2011	**PPH:** 0: 1.5 (1.4-1.7) 1: ref 2-4: 1.3 (1.1-1.5) ≥5: 1.4 (0.9-2.2)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
	SPPH: 0: 2.4 (0.7-8.2) 1: ref 2-4: 1.9 (0.7-5.0) ≥5: 4.5 (0.5-40.3)	aOR	NS				
Lisonkova, 2016	0: ref ≥1: 0.47 (0.24-0.95)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Malabarey, 2011	Parity >2: 1.4 (0.8-2.4)	uOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Malabarey, 2011	Parity >3 2.6 (1.2-5.1)	uOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Miller 2017	0: ref ≥1: 0.84 (0.53-1.33)	aOR	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Noguchi, 2017	**PPH:** Multipara: 72 **CTL:** Multipara: 2440	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829	High
Nyflot, 2016	**SPPH:** First delivery: 622 (58.5%) **CTL:** First delivery: 1007 (48.9%)	%	np	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	Primiparity: 1.20 (0.99-1.44)	aOR	NS	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	Primiparity: 1.14 (0.92-1.34)	aOR	NS	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low
Oberg, 2014a	Pimipara: ref Multipara: 0.78 (0.77-0.80)	uOR	Sig	VB, CS	**PPH:** ICD codes, typically EBL ≥1000mL	583,332	High
Oberg, 2014b	Primiparous: ref Multiparous: 0.76 (0.74-0.79)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Rossen, 2010	**VB** Nulliparous: 1.2 (1.0-1.4)	aOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Salkeld, 2008	**PPH:** Previous births 0: 1026 (41.7%) 1: 869 (35.3%0 2: 392 (15.9%) 3: 115 (4.7%) 4: 43 (1.7%) 5: 11 (0.4%) 6: 0.2% 7: 0 8: 0 **CTL:** Previous births 0: 10116 (42.3%) 1: 8604 (35.9%) 2: 3741 (15.6%) 3: 1073 (4.5%) 4: 325 (1.4%) 5: 62 (0.3%) 6: 17 (0.1%) 7: 0 8: 0	%	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High
Sharp, 2014	Nulliparity: 1.47 (1.10-1.98)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	25,322	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Sheiner, 2009	**PPH 1:** 1: 15.3% 2-4 56.9% >5: 27.7% **PPH 2:** 1: 17.9% 2-4: 44.8% >5: 37.3% **PPH 3:** 1: 18.1% 2-4: 44.2% >5: 37.7% **CTL:** 1: 19.9% 2-4: 47.6% >5: 32.5%	%	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645	Low
Stones, 1993	Para 4+: 1.09 (0.56-2.14)	uRR (99% CI)	NS	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Suzuki, 2007	Nulliparity: 1.19 (0.59-2.41)	uOR	NS	CS	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 131	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Suzuki, 2012	**Singletons:** Nulliparity: ref Multiparity: 2.43 (1.4-4.3)	uOR	Sig	CS	**PPH:** PPH requiring transfusion	Singletons: 17,405 Twins: 916	Low
	Twins: Nulliparity: ref Multiparity: 1.12 (0.44-2.8)	uOR	NS				
van Stralen, 2016	0: 1.27 (1.25-1.28) 1-4: ref ≥5: 0.99 (0.92-1.06)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	**Total cohort:** 0: 1.36 (1.34-1.39) 1-4: ref ≥5: 0.95 (0.87-1.05)	aOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low
	Non-induced spontaneous delivery: 0: 1.48 (1.45-1.51) 1-4: ref ≥5: 0.85 (0.75-0.97)	aOR	Sig				

2.4.7.2 Gestational age

Gestational age was evaluated as a potential risk factor for PPH/SPPH in 30 studies, 25 of which were considered LRoB. There was a wide range of categorisations and cut-offs for gestational age, with some studies dichotomising based on pre-term or post-term gestations, while others used three or four categories of gestational age. Across the studies, there were conflicting results in terms of whether later or earlier gestational age, or both, were risk factors compared with being born at or near term.

Twenty-eight LRoB analyses explored gestational age and risk of PPH, with 11 of these reporting a significant association. Five LRoB reported older gestational age to be associated with higher odds of PPH, three reported younger gestation was associated with higher odds, and three reported both younger and older than term were associated with higher odds of PPH, after adjustment for other factors. Mostly, the magnitude of the effect of older gestational ages were small to moderate, however one small study of twin vaginal births only (137) reported a four-fold increase in the odds of PPH among those with babies born at or after 39 weeks' gestation, compared with babies born at 37-38 weeks' gestation.

The five HRoB studies that explored gestational age and PPH reported similar results as the LRoB studies, reporting that both low gestational age and high gestational age were associated with increased odds of PPH, without adjustment for potential confounders.

Five studies explored the association between gestational age and SPPH, with one reporting a significant association. This was the largest study to examine gestational age and SPPH, (N=364,701) and reported that among all women, birth at any gestational age other than 37-41 weeks, was associated with an increased risk of SPPH, after adjustment for confounding factors. This study reported that among women who experienced labour, birth at 20-27 weeks or after 41 weeks was associated with increased risk of SPPH, with a small to moderate effect.

Overall the association between PPH/SPPH and gestational age was conflicting. Less than 50% of LRoB analyses reported a significant association at the adjusted level. Therefore, it is unclear whether gestational age is an independent risk factor for PPH/SPPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.24 Included studies investigating as gestational age a potential risk factor for postpartum haemorrhage

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Allen, 1988	Multiple pregnancy: Normal vaginal delivery: 14.4% CS: 27.1%	%	Sig	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Bais, 2004	**PPH 1:** 2.60 (1.06-6.39) **PPH 2:** 1.00 (0.13-7.49)	aOR uOR	Sig NS	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Bonnet, 2013	**Canada:** Multiple: 3.34 (2.74-4.06) Singleton: ref **France:** Multiple: 2.33 (1.47-3.70) Singleton: ref	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	Low
Briley, 2013	Multiple pregnancy: 2.02 (0.82-5.00)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Butwick, 2017	**Pre-labour CS:** Multiple pregnancy: 8.0 (4.25-15.04) Singleton: ref **Intrapartum CS:** Multiple pregnancy: 3.25 (1.67-6.31) Singleton: ref	aOR	Sig	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Choe, 2016	Multiple gestation: 2.87 (2.23-3.70)	aOR	Sig	VB, CS	**PPH:** ICD-10 code O72.0-O72.3 or transfusion	65,479	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Combs, 1991a	Twins/triplets PPH: 6 (3.1%) CTL: 19 (3.2%)	%	NS	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Twins: 3.31 (1.03-10.60)	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Davey, 2019	**All women:** Multiple pregnancy: 2.83 (2.4-3.3) Singleton: ref **Women who experienced labour:** Multiple pregnancy: 2.84 (2.3-3.5) Singleton: ref	aOR aOR	Sig Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
Kaelin Agten, 2017	Twin pregnancy: 2.5 (2.2-2.7)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Lisonkova, 2016	**PPH:** Multiple pregnancy: 15 (3.92%) **CTL:** Multiple pregnancy: 8 (2.09%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Magan, 2005b	Multiple pregnancy: 2.2 (1.5-3.2)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Mehrabadi, 2013	Multiple pregnancy: 3.77 (3.45-4.12)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Merriam, 2018	**PPH 1:** Multiple pregnancy: 2.32 (2.25-2.39) **PPH 2:** 2.37 (2.29-2.45)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Miller 2017	Multiple pregnancy: 0.96 (0.42-2.19)	aOR	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Nyflot, 2016	Multiple pregnancy: 1.61 (1.05-2.47)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	Multiple pregnancy: 2.11 (1.39-3.22)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	Multiple pregnancy: 4.55 (2.86-7.25)	uOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low
Oberg, 2014b	Multiple pregnancy: 2.92 (2.55-3.34)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Rossen, 2010	**VB** Multiple pregnancy: 6.8 (5.0-9.2) **CS** Multiple pregnancy: 3.7 (2.4-5.8)	aOR aOR	Sig Sig	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low

Author, year	*Effect size & definitions*	*Stat*	*Sig*	*Birth mode*	*Definition of PPH*	*Number of women*	*RoB*
Salkeld, 2008	**PPH:** Multiple pregnancy: 54 (2.2%) **CTL:** Multiple pregnancy: 204 (0.9%)	%	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High
Stones, 1993	Multiple pregnancy: 4.46 (3.01-6.61)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
van Stralen, 2016	Multiple pregnancy: 2.85 (2.77-2.93)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	**Total cohort:** Multiple pregnancy: 2.88 (2.77-3.00) **Non-induced spontaneous delivery:** Multiple pregnancy: 2.36 (2.18-2.54)	aOR aOR	Sig Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.7.3 Multiple pregnancy

Twenty-five studies analysed the association between multiple pregnancy and PPH/SPPH, with 20 of these being LRoB. Of the 17 LRoB analyses, across 14 studies, 13 (76%) found a positive association between multiple pregnancy and PPH.

Five studies examined multiple pregnancy and SPPH, with three reporting a significant association at the adjusted level.

Multiple pregnancy was consistently associated with higher odds of PPH, compared with singleton pregnancy. The magnitude of effect for multiple birth varied at the multivariable level, but was generally higher than observed for other risk factors, ranging from aOR=2.33 (95% CI 1.47-3.70) in a large French study (111), to aOR=6.8 (95% CI 5.0-9.2) among vaginal births in a large Norwegian study (132). A similar trend was observed for SPPH, with the aOR ranging from 1.61 (95% CI 1.05-2.47) (128) to 8.0 (4.25-15.04) (112). The five HRoB studies that investigated multiple pregnancy reported similar results, all observing a higher risk of PPH among multiple births. With 70% of LRoB anlayses reporting a significant association at the adjusted level, multiple pregnancy is considered very likely to be an independent risk factor for PPH/SPPH.

Rating: Very likely - More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Table 2.25 Included studies investigating multiple pregnancy as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Allen, 1988	Multiple pregnancy: Normal vaginal delivery: 14.4% CS: 27.1%	%	Sig	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Bais, 2004	**PPH 1:** 2.60 (1.06-6.39) **PPH 2:** 1.00 (0.13-7.49)	aOR uOR	Sig NS	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Bonnet, 2013	**Canada:** Multiple: 3.34 (2.74-4.06) Singleton: ref **France:** Multiple: 2.33 (1.47-3.70) Singleton: ref	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	Low
Briley, 2013	Multiple pregnancy: 2.02 (0.82-5.00)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Butwick, 2017	**Pre-labour CS:** Multiple pregnancy: 8.0 (4.25-15.04) Singleton: ref **Intrapartum CS:** Multiple pregnancy: 3.25 (1.67-6.31) Singleton: ref	aOR	Sig	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Choe, 2016	Multiple gestation: 2.87 (2.23-3.70)	aOR	Sig	VB, CS	**PPH:** ICD-10 code O72.0-O72.3 or transfusion	65,479	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Combs, 1991a	Twins/triplets PPH: 6 (3.1%) CTL: 19 (3.2%)	%	NS	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Twins: 3.31 (1.03-10.60)	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Davey, 2019	**All women:** Multiple pregnancy: 2.83 (2.4-3.3) Singleton: ref **Women who experienced labour:** Multiple pregnancy: 2.84 (2.3-3.5) Singleton: ref	aOR aOR	Sig Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
Kaelin Agten, 2017	Twin pregnancy: 2.5 (2.2-2.7)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Lisonkova, 2016	**PPH:** Multiple pregnancy: 15 (3.92%) **CTL:** Multiple pregnancy: 8 (2.09%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Magan, 2005b	Multiple pregnancy: 2.2 (1.5-3.2)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Mehrabadi, 2013	Multiple pregnancy: 3.77 (3.45-4.12)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Merriam, 2018	**PPH 1:** Multiple pregnancy: 2.32 (2.25-2.39) **PPH 2:** 2.37 (2.29-2.45)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Miller, 2017	Multiple pregnancy: 0.96 (0.42-2.19)	aOR	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Nyflot, 2016	Multiple pregnancy: 1.61 (1.05-2.47)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	Multiple pregnancy: 2.11 (1.39-3.22)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	Multiple pregnancy: 4.55 (2.86-7.25)	uOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1755	Low
Oberg, 2014b	Multiple pregnancy: 2.92 (2.55-3.34)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Rossen, 2010	**VB** Multiple pregnancy: 6.8 (5.0-9.2) **CS** Multiple pregnancy: 3.7 (2.4-5.8)	aOR aOR	Sig Sig	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Salkeld, 2008	**PPH:** Multiple pregnancy: 54 (2.2%) **CTL:** Multiple pregnancy: 204 (0.9%)	%	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High
Stones, 1993	Multiple pregnancy: 4.46 (3.01-6.61)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
van Stralen, 2016	Multiple pregnancy: 2.85 (2.77-2.93)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	**Total cohort:** Multiple pregnancy: 2.88 (2.77-3.00) **Non-induced spontaneous delivery:** Multiple pregnancy: 2.36 (2.18-2.54)	aOR aOR	Sig Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.7.4 Placenta praevia

Seventeen studies looked at placenta praevia as a potential risk factor for PPH/SPPH, of which 13 were considered to be LRoB. Among 11 LRoB analyses of placenta praevia and PPH, six (55%) found a positive association, with women who had placenta praevia being consistently more likely to have a PPH. One of the LRoB studies reported 100% of the 26 women with placenta praevia having a PPH, which meant that it was not possible to perform statistical analyses but seems to reflect the general trend that placenta praevia is associated with higher risk of PPH.

Of the seven LRoB analyses that investigated SPPH, all found a significant positive association. The magnitude of effect was generally high for placenta praevia with aOR ranging from 2.88 to 10.9 for PPH and from 1.93 to 17.1 for SPPH.

Of the three HRoB studies, all reported a higher risk of PPH among women who had placenta praevia.

Placenta praevia is considered a very likely risk factor for PPH/SPPH.

Rating: Very likely - More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Table 2.26 Included studies investigating placenta praevia as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Allen, 1988	Placenta praevia and CS: 36.6%	Incidence of PPH (%)	Sig	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Briley, 2013	100% of 26 placenta praevia had PPH	aOR	*	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Butwick, 2017	**Pre-labour CS:** Placenta praevia: 6.33 (3.4-11.760 **Intrapartum CS:** na	aOR	Sig	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Davey, 2019	**All women:** Placenta praevia: 10.3 (8.9-11.9) **Women who experienced labour:** Placenta praevia: 3.92 (2.7-5.7)	aOR aOR	Sig Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
Kaelin Agten, 2017	Placenta praevia: 4.9 (4.3-5.6)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Kramer, 2011	**PPH:** Placenta previa or low-lying placenta: 3.5 (2.7-4.5) **SPPH:** Placenta previa or low-lying placenta: 17.1 (6.2-46.7)	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lee, 2018	Placenta praevia: 1.93 (1.05-3.54)	aOR	Sig	CS	**SPPH:** intraoperative blood loss ≥2000mL	506	Low
Lisonkova, 2016	**PPH:** Placenta previa: 8 (2.09%) **CTL:** Placenta previa: 1 (0.26%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Magan, 2005a	**Elective CS:** PPH: 6.65 (3.24-13.09) SPPH: 8.06 (2.98-21.81) **Emergency CS:** PPH: 6.00 (2.08-16.72) SPPH: 11.21 (3.51-35.79)	aOR aOR	Sig Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837	Low
Mehrabadi, 2013	Placenta previa: 10.9 (10.0-12.0)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Merriam, 2018	**PPH 1:** 2.88 (2.74-3.02) **PPH 2:** 5.12 (4.89-5.36)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Nyflot, 2016	**SPPH:** Placenta praevia: 56 (5.3%) **CTL:** Placenta praevia: 3 (0.1%)	%	np	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Oberg, 2014b	Placenta praevia: 5.95 (3.85-9.20)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Salkeld, 2008	**PPH:** Placenta previa: 38 (1.5%) **CTL:** Placenta previa: 72 (0.3%)	%	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High
Sheiner, 2009	**PPH 1:** Placenta previa: 0 **PPH 2:** Placenta previa: 0 **PPH3:** Placenta previa: 3.5% **CTL:** Placenta previa: 0.4%	%	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Stones, 1993	Praevia with bleeding: 13.1 (7.47-23.0)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Stones, 1993	Praevia with no bleeding: 11.3 (3.36-38.1)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Suzuki, 2012	**Singletons:** Placenta previa: 16.1 (9.4-28) **Twins:** Placenta previa: 5.88 (0.63-55)	uOR aOR	Sig NS	CS	**PPH:** PPH requiring transfusion	Singletons: 17,405 Twins: 916	Low

2.4.7.5 Uterine fibroids

Twelve studies examine the relationship between uterine fibroids and PPH/SPPH, nine of which were considered LRoB. Of the seven LRoB analyses, across five studies, only one (125) reported a significant association, for both types of PPH (PPH and PPH with transfusion) examined in a study of over 55,000,000 women in the USA. The magnitude of the effect in this study was small.

Six LRoB studies examined uterine fibroids and SPPH, with three reporting a higher odds of SPPH among women with uterine fibroids, compared with those without. The magnitude of the effect was high with aOR from 2.71 (95% CI 1.69-4.35) to 11.0 (95% CI 3.01-40.00).

Of the three HRoB studies, all three found that fibroids were associated with increased risk of PPH/SPPH. Given that only one third of the analyses of PPH or SPPH found a significant association at the adjusted level, it is unclear whether uterine fibroids are a risk factor for PPH/SPPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.27 Included studies investigating uterine fibroids as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Kramer, 2011	**PPH:** Fibroids: 0.8 (0.6-1.1) **SPPH:** Fibroids: 4.40 (1.4-11.4)	aOR aOR	NS Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lee, 2017	Uterine fibroids: 2.12 (0.42-10.82)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210	Low
Lisonkova, 2016	**PPH:** Uterine fibroids: 8 (2.09%) **CTL:** Uterine fibroids: 5 (1.31%)	%	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Magan, 2005a	**Elective CS:** PPH: 3.52 (0.92-10.64) SPPH: 11.0 (3.01-40.00)	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837	Low
Merriam, 2018	**PPH 1:** 1.46 (1.39-1.53) **PPH 2:** 1.39 (1.33-1.47)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Noguchi, 2017	Uterine myoma: 2.0 (no CI) p <0.01	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500g	4,829	High

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Nyflot, 2016	**SPPH:** Uterine fibromas: 52 (4.9%) **CTL:** Uterine fibromas: 38 (1.9%)	%	np	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	Uterine fibroma: 2.71 (1.69-4.35)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	Uterine fibroids: 2.51 (1.36-4.65)	uOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low
Oberg, 2014a	Uterine fibroids: 2.43 (1.99-2.97)	uOR	Sig	VB, CS	**PPH:** ICD codes, typically EBL ≥1000mL	583,332	High
Oberg, 2014b	Uterine fibroids: 2.79 (1.46-5.33)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Suzuki, 2012	**Singletons:** Myoma ≥6cm: 1.81 (0.93-3.5) **Twins:** Myoma ≥6cm: 0.67 (0.09-5.1)	uOR uOR	Sig NS	CS	**PPH:** PPH requiring transfusion	Singletons: 17,405 Twins: 916	Low

2.4.7.6 Chorioamnionitis

Chorioamnionitis was examined as a risk factor for PPH by 12 studies, ten of which were LRoB. Of the nine studies that explored PPH and chorioamnionitis, four (44%) reported a significant association, after adjustment for confounding variables. All reported similar effect sizes, ranging from 1.77 to 2.69. One of the studies that examined the relationship between chorioamnionitis and PPH found that all ten women with chorioamnionitis had a PPH, so it was not possible to perform statistical tests of the association.

One study examined SPPH and chorioamnionitis and found a significant association, after adjustment for other variables. The magnitude of effect reported in this relatively small, US study was aOR=1.76 (1.13-2.75). Three studies examined chorioamnionitis and PPH without adjusting for potential confounding variables, two of which found a significant association.

With 50% of LRoB studies reporting significantly increased odds of PPH/SPPH for women with chorioamnionitis, it is considered likely that this is an independent risk factor.

Rating: Likely - Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.

Table 2.28 Included studies investigating chorioamnionitis as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Briley, 2013	All 10 with Chorioamnionitis had PPH	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Butwick, 2017	**Pre-labour CS:** na **Intrapartum CS:** Chorioamnionitis: 1.76 (1.13-2.75)	aOR	Sig	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Combs, 1991a	Amnionitis: 2.69 (1.44-5.03)	aOR	Sig	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Amnionitis: 0.66 (0.26-1.70) None: ref	aOR	NS	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Kaelin Agten, 2017	Chorioamnionitis: 1.0 (0.8-1.4)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	739,444	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Lisonkova, 2016	**PPH:** Chorioamnionitis: 16 (4.28%) **CTL:** Chorioamnionitis: 6 (1.58%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Magan, 2005b	Chorioamnionitis: 1.3 (1.1-1.7)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Malabarey, 2011	Chorioamnionitis: 1.6 (1.1-2.3)	uOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Mehrabadi, 2013	Chorioamnionitis: 2.66 (2.38-2.97)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Merriam, 2018	**PPH 1:** 2.17 (2.09-2.25) **PPH 2:** 1.77 (1,67-1.87)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Miller, 2017	Chorioamnionitis: 1.02 (0.47-2.97)	aOR	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Oberg, 2014b	Chorioamnionitis: 1.33 (0.76-2.32)	uOR	NS	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High

2.4.7.7 Placental abruption

Twelve studies analysed the association between placental abruption and PPH/SPPH, nine of which were considered LRoB. Three out of eight studies reported a significant association between placental abruption and PPH, with aOR ranging from 1.67 (95% CI 1.61-1.74) to 13.5 (95% CI 6.7-27).

One study investigated placental abruption and SPPH and reported a seven-fold higher the odds of SPPH, among both women who laboured and women who did not.

Three HRoB studies investigated placental abruption and PPH with one reporting a significantly higher risk of PPH at the univariable level.

While all studies that found a significant association reported that placental abruption was associated with a higher risk of PPH, most studies that investigated this risk factor found no significant association.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.29 Included studies investigating as placental abruption a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Buzaglo, 2014	PPH: 0.2% CTL: 0.3%	%	NS	VB	**PPH:** EBL ≥500mL	56,394	Low
Davey, 2019	**All women:** Placental abruption: 7.85 (6.2-10.0) **Women who experienced labour:** Placental abruption: 7.51 (5.4-10.5)	aOR aOR	Sig Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
Hiersch, 2016	**PPH:** Placental abruption: 1.0% CTL: Placental abruption: 0.5% p=0.38	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, hemoglbon drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Placental abruption: 1.8 (1.7-2.0)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Lisonkova, 2016	**PPH:** Placental abruption: 3 (0.79%) **CTL:** Placental abruption: 2 (0.52%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Mehrabadi, 2013	Placental abruption: 3.02 (2.71-3.35)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Merriam, 2018	**PPH 1:** Placental abruption: 1.67 (1.61-1.74) **PPH 2:** Placental abruption: 4.18 (4.05-4.30)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Oberg, 2014b	Placental abruption: 1.26 (0.62-2.57)	uOR	NS	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Salkeld, 2008	**PPH:** Placental abruption: 77 (3.1%) **CTL:** Placental abruption: 358 (1.5%)	%	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High
Sheiner, 2009	**PPH 1:** Placental abruption: 0 **PPH2:** Placental abruption: 0 **PPH 3:** Placental abruption: 2.5% **CTL:** Placental abruption: 0.8%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Stones, 1993	Proven abruption: 12.6 (7.61-20.9)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Suzuki, 2012	**Singletons:** Placental abruption: 13.5 (6.7-27)	uOr	Sig	CS	**PPH:** PPH requiring transfusion	Singletons: 17,405 Twins: 916	Low
	Twins: Placental abruption: na	uOR	Sig				

2.4.7.8 Polyhydramnios

Nine studies examined polyhydramnios and PPH/SPPH, all of which were considered LRoB. Eight studies investigated polyhydramnios and PPH and three of these found a small but significant association between polyhydramnios and PPH at the multivariable level. All three were relatively large studies. The aOR ranged from 1.15 (95% CI 1.10-1.21) to 1.47 (95% CI 1.19-1.81).

Two studies investigated polyhydramnios and SPPH and neither reported a significant association at the multivariable level.

With only 33% of the analyses of polyhydramnios reporting statistically significant associations after adjustment for confounding factors, it is unclear whether polyhydramnios is an independent risk factor for PPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.30 Included studies investigating as polyhydramnios a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Combs, 1991b	Hydramnios: 1.28 (No CI)	uOR	NS	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Hiersch, 2016	**PPH:** 1.0% **CTL:** 1.7% p=0.58	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, hemoglbon drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Polyhydramnios: 1.3 (1.2-1.6)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Kramer, 2011	**PPH:** Normal: ref Polyhydramnios: 1.3 (1.0-1.7) **SPPH:** Normal: ref Polyhydramnios: 1.2 (0.2-5.9)	aOR aOR	NS NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lisonkova, 2016	**PPH:** Polyhydramnios: 6 (1.57%) **CTL:** 3 (0.79%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Mehrabadi, 2013	Polyhydramnios: 1.47 (1.19-1.81)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Merriam, 2018	**PPH 1:** 1.15 (1.10-1.21) **PPH 2:** 1.19 (1.11-1.26)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Nyflot, 2017a	Polyhydramnios: 2.6 (1.23-5.52)	uOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Sheiner, 2009	**PPH 1:** Hydramnios: 5.1% **PPH 2:** Hydramnios: 4.2% **PPH 3:** Hydramnios: 3.0% **CTL:** Hydramnios: 4.1%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645	Low

2.4.7.9 Assisted conception

Eight studies investigated assisted conception and risk of PPH/SPPH and seven were considered LRoB.

Four studies examined assisted conception and PPH, two of which were conducted in Japan, one in the UK and one in Israel. The Israeli study examined 'fertility treatments' and PPH and found almost double the odds after adjustment for other factors (aOR=1.9; 95% CI 1.3-2.7). One of the studies conducted in Japan (118) found assisted conception was associated with more than three times the odds of PPH, compared with no assisted conception (aOR=3.48; 1.47-8.24). The other study from Japan (137) found no association between IVF and PPH. The UK study that examined 'assisted conception' and PPH reported no significant association at the multivariable level.

The one HRoB study that examined assisted conception and SPPH found more than double the risk of SPPH among women who had an embryo transfer, without adjustment for confounding factors. Four studies examined assisted conception and SPPH. Three of these, all conducted within the same population in Norway, were LRoB and found a significant association after adjustment for other factors.

Most LRoB analyses (56%) of assisted conception reported a significant association, with all reporting that it was assorted with increased odds of PPH/SPPH. Assisted conception is therefore considered a likely risk factor for PPH.

Rating: Likely - Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.

Table 2.31 Included studies investigating assisted conception as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Briley, 2013	Assisted conception: 2.10 (0.83-5.33)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Buzaglo, 2014	Fertility treatments: 1.9 (1.3-2.7)	aOR	Sig	VB	**PPH:** EBL ≥500mL	56,394	Low
Fukami, 2019	Assisted conception: 3.48 (1.47-8.24)	aOR	Sig	VB	**PPH:** CBL ≥1000mL	1,608	Low
Noguchi, 2017	Embryo transfer: 2.6 (no CI) p <0.001	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500g	4,829	High
Nyflot, 2016	ART: 1.58 (1.12-2.24) ART x multiple pregnancy: 7.00 (2.70-18.12) ART x singleton pregnancy: 1.58 (1.12-2.24)	aOR aOR	Sig Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	IVF/ICDI: 1.88 (1.33-2.65)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	IVF/ICDI-pregnancy: 2.72 (1.93-3.85)	uOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1755	Low
Suzuki, 2007	Singletons IVF: 2.23 (0.71-7.6) Twins IVF: 0.83 (1.36-2.1)	uOR uOR	NS NS	CS	**PPH:** PPH requiring transfusion	Singletons: 17,405 Twins: 916	Low

2.4.7.10 Antepartum haemorrhage

Eight studies included analyses of antepartum haemorrhage (APH) and PPH/SPPH, six of which were considered LRoB. Three LRoB studies investigated APH and PPH. A large American study of over 55,000,000 births (125) found APH increased the relative risk of PPH by 50% and of PPH with transfusion four fold, after adjustment for other factors. An Australian study (123) of nearly 5,000 births reported that APH was associated with almost three times the odds of PPH among emergency caesarean births and more than four times the odds among elective caesarean birth, after controlling for confounding factors. However, a UK study (56) of nearly 10,000 births found no significant association between either APH or 'warning APH' and PPH.

Of the four LRoB studies that analysed APH and SPPH, three reported higher odds of SPPH among women with antepartum haemorrhage. One of the two HRoB studies that investigated APH and PPH reported a significant increase in the risk, compared with those without APH, without adjustment for potential confounders.

Most studies that investigated the relationship between APH and PPH/SPPH reported a significant association, with APH being consistently associated with an increased risk of PPH/SPPH. It is therefore considered very likely that APH is an independent risk factor for PPH/SPPH.

Rating: Very likely – More than 60% of LRoB analyses found a significant association. All significant results were in the same direction.

Table 2.32 Included studies investigating antepartum haemorrhage as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Allen, 1988	APH unknown cause and normal vaginal delivery: 7.0%	% (incidence PPH)	Sig	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Briley, 2013	APH: 1.27 (0.65-2.51)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Briley, 2013	Warning APH: 1.92 (0.19-19.3)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Davey, 2019	**All women:** Antepartum haemorrhage: 1.76 (1.5-2.0) **Women who experienced labour:** Antepartum haemorrhage: 3.92 (2.7-5.7)	aOR aOR	Sig Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
Lee, 2017	Antepartum haemorrhage: 0.92 (0.16-5.51) No antepartum haemorrhage: ref	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210	Low
Lee, 2018	Antepartum haemorrhage: 4.76 (2.01-11.02)	aOR	Sig	CS	**SPPH:** intraoperative blood loss ≥2000mL	506	Low
Magan, 2005a	**Elective CS:** PPH: 4.33 (2.36-7.69) SPPH: 4.91 (2.10-11.51) **Emergency CS:** PPH: 2.92 (1.90-4.45) SPPH: 3.64 (2.00-6.60)	aOR aOR	Sig Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Merriam, 2018	**PPH 1:** 1.51 (1.10-1.64) **PPH 2:** 4.10 (3.88-4.33)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Stones, 1993	Indeterminate APH: 1.67 (0.82-3.44)	uRR (99% CI)	NS	VB, CS	**PPH:** EBL ≥1000mL	37,334	High

2.4.7.11 Gravidity

Five studies investigated gravidity and PPH and all were considered LRoB. The method of categorising and analysing gravidity varied between studies, however, none reported a significant association between number of previous pregnancies and PPH. Therefore, gravidity is not considered to be an independent risk factor for PPH.

Rating: Not a risk factor - No LRoB analyses found a significant association.

Table 2.33 Included studies investigating gravidity as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Buzaglo, 2014	PPH: 1: 84.1% 2-4: 15.2% 5+: 0.7% CTL: 1: 83.9% 2-4: 15.8% 5+: 0.3%	%	NS	VB	**PPH:** EBL ≥500mL	56,394	Low
Hiersch, 2016	PPH: 1 (1-2) CTL: 1 (1-2) p=0.001	Median (IQR)	Sig	VB (vacuum only)	**PPH:** EBL ≥500mL, hemoglbon drop ≥3 g/dL	1,154	Low
Kaufner, 2016	CTL: 22 (1-3) PPH: 1 (1-2) p=0.197	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low
Lisonkova, 2016	**PPH:** 1 (primigravida): 190 (49.74%) 2-3: 135 (35.34%) ≥4: 57 (14.92%) **CTL:** 1 (primigravida): 104 (27.37%) 2-3: 212 (55.79%) ≥4: 64 (16.84%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Sheiner, 2009	**PPH 1:** 1: 20.4% 2-4: 57.7% >5: 21.9% **PPH 2:** 1: 22.7% 2-4: 47.9% >5: 29.4% **PPH 3:** 1: 22.6% 2-4: 49.2% >5: 28.1% **CTL:** 1: 23.7% 2-4: 50.9% >5: 25.4%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH 1:** 137 **PPH 2 :** 330 **PPH 3:** 199 **CTL:** 153, 645	Low

2.4.8 Labour factors

2.4.8.1 Labour onset and induction

Induction of labour was investigated as a potential risk factor for PPH/SPPH by 40 studies, 31 of which were considered LRoB. Most studies investigated the association between induction of labour as a dichotomous variable, comparing induced with spontaneous labour, but some studies included analyses of the method of induction. Thirty-four studies compared induced labour with spontaneous labour, all of which used spontaneous labour as the reference group and none of which reported a protective or negative effect of induction of labour. There were 28 LRoB analyses that explored any induction of labour compared with spontaneous labour, of which 14 (50%) reported significantly higher odds of PPH associated with induction, after adjustment for other variables. Most studies reported a small to moderate effect of induction, with aORs ranging from 1.2-2.6.

Eight HRoB studies assessed induction of labour and PPH, with six finding significantly higher odds of PPH among women who had labour induced, compared with spontaneous labour, without adjustment for potential confounding factors. Five LRoB studies explored induction and SPPH, with two (40%) reporting a significant association at the adjusted level. The magnitude of the effect was moderate with aOR ranging from 1.69 to 1.95. Both of these studies were based on similar or overlapping populations of women in Norway.

Six studies explored the association between oxytocin for induction and PPH/SPPH. Of the six LRoB analysis that investigated oxytocin for induction of labour, four (67%) reported a significant increase in the risk of PPH among women who had oxytocin for induction, compared with those who did not. The magnitude of the effect was moderate, ranging from aOR 1.52 to 2.86. Of the other specific methods of induction investigated, only cervical ripening and artificial rupture of membranes were found to be significantly associated with PPH after adjustment for other factors#

Rating: Likely - Between 50% and 60% of LRoB analyses found a significant association. All significant results were in the same direction.

Table 2.34 Included studies investigating labour onset as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Allen, 1988	Induction: Normal vaginal delivery: 6.2%	% (incidence of PPH by category)	Sig	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Bais, 2004	**PPH 1:** Induction of labour: 1.42 (1.14-1.76) No induction: ref **PPH 2:** Induction of labour: 1.93 (1.31-2.86) No induction: ref	uOR uOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Biguzzi, 2011	Induction: 1.11 (0.94-1.10) no induction: ref	aOR	NS	VB	**PPH:** EBL ≥500mL	6,011	Low
Bonnet, 2013	**Canada:** Induced: 1.34 (1.27-1.42) Not induced: ref **France:** Induced: 1.23 (1.07-1.41) Not induced: ref	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	Low
Briley, 2013	Induction: 0.75 (0.39-1.46)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Briley, 2013	Prostin for induction: 1.04 (0.53-2.02)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Briley, 2013	Syntocinon for induction: 1.44 (0.95-2.16)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Butwick, 2017	**Intrapartum CS:** **CTL:** Spontaneous labour: 368 (64.3%) Induction: 204 (35.7%) **SPPH:** Spontaneous labour: 172 (61.9%) Induction: 106 (38.1%)	%	NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Buzaglo, 2014	Induced labour: 1.2 (0.9-1.4)	aOR	NS	VB	**PPH:** EBL ≥500mL	56,394	Low
Choe, 2016	Induction of labour: 1.20 (1.03-1.41)	aOR	Sig	VB, CS	**PPH:** ICD-10 code O72.0-O72.3 or transfusion	65,479	Low
Combs, 1991a	Induced labour: 0.83 (0.67-1.63) Spontaneous: ref	aOR	NS	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Induction: 1.31 (0.83-2.08)	aOR	NS	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Davey, 2019	Oxytocin for induction: 1.19 (1.1-1.3)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Dionne, 2015	**PPH 1:** Induction of labour: 1.23 (0.96-1.56) **PPH 2:** Induction of labour: 1.15 (0.85-1.56)	aOR aOR	NS NS	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048	Low
Farina, 2017	**Induction of labour** **PPH:** 80% **CTL:** 86.7% **p=**0.456	%	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390	High
Firmin, 2019	Labour induced with oxytocin: 2.03 (1.03-3.99) Spontaneous unmanaged labour: ref	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Firmin, 2019	Spontaneous unmanaged labour: ref Spontaneous managed labour: 1.32 (0.74-2.34) Labour induced without oxytocin: 1.45 (0.73-2.88) Labour induced with oxytocin: 2.86 (1.52-5.35)	uOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Fukami, 2019	**CTL:** Labour induction/augmentation by oxytocin: 32.6% No: 67.4% **PPH:** Labour induction/augmentation by oxytocin: 35.5% No: 64.5%	%	NS	VB	**PPH:** CBL ≥1000mL	1,608	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Gilbert, 1987	**All deliveries** **PPH:** Amniotomy/oxytocin: 21 (24%) Prostaglandin pessaries: 9 (10%) Spontaneous: 56 (56%) **CTL:** Amniotomy/oxytocin: 19 (5%) Prostaglandin pessaries: 16 (5%) Spontaneous: 316 (90%) **Spontaneous deliveries** **PPH:** Amniotomy/oxytocin: 6 (18%) Prostaglandin pessaries: 3 (9%) Spontaneous: 24 (73%) **CTL:** Amniotomy/oxytocin: 14 (5%) Prostaglandin pessaries: 14 (5%) Spontaneous: 272 (90%)	% Sig	Sig Sig	VB	**PPH:** EBL ≥500mL	**PPH:** 86 **CTL:** 351	High
Henry, 2005	**PPH 1:** Induced: ref Spontaneous: 1.16 (0.65-2.07) **PPH 2:** Induced: ref Spontaneous: 1.14 (0.53-2.43)	uOR uOR	NS NS	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Hiersch, 2016	**PPH:** Amniotomy: 46.8% **CTL:** Amniotomy: 40.0% p=0.04	%	Sig	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Hiersch, 2016	Induced labour: 1.42 (1.01-2.10)	aOR	Sig	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Induction of labour: 1.3 (1.2-1.3)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Kaufner, 2016	Induced: 1.65 (0.74-3.68)	uOR	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low

Khireddine, 2012	**All women** **PPH 1:** Spontaneous without augmentation: ref Spontaneous with augmentation: 1.17 (1.00-1.37) Induction with cervical ripening: 1.21 (0.97-1.51) Induction with oxytocin: 1.52 (1.19-1.93) **PPH 2:** Spontaneous without augmentation: ref Spontaneous with augmentation: 1.35 (1.07-1.70) Induction with cervical ripening: 1.42 (1.04-1.94) Induction with oxytocin: 1.57 (1.11-2.20) **Pimiparas** **PPH 1:** Spontaneous without augmentation: ref Spontaneous with augmentation: 1.18 (0.93-1.50) Induction with cervical ripening: 1.46 (1.06-2.00) Induction with oxytocin: 1.43 (0.98-2.11) **PPH 2:** Spontaneous without augmentation:	aOR	Sig Sig Sig Sig	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
	ref Spontaneous with augmentation: 1.39 (1.01-1.91) Induction with cervical ripening: 1.71 (1.13-2.56) Induction with oxytocin: 1.35 (0.81-2.24)						
Khireddine, 2012	**All women** **PPH 1:** Spontaneous: ref Induced labour: 1.22 (1.04-1.42)	aOR	Sig	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125	Low
	PPH 2: Spontaneous: ref Induced labour: 1.20 (0.97-1.48)	aOR	NS				
	Pimiparas **PPH 1:** Spontaneous: ref Induced labour: 1.27 (1.34-1.58)	aOr	Sig				
	PPH 2: Spontaneous: ref Induced labour: 1.22 (0.93-1.61)	aOR	NS				

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Koopmans, 2014	Induction of labour: 1.01 (0.68-1.5) Spontaneous: ref	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Kramer, 2011	**PPH:** Induced labour: 1.2 (1.1-1.4) **SPPH:** Induced labour: 0.8 (0.2-2.7)	aOR aOR	Sig NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lisonkova, 2016	**PPH:** Spontaneous onset of labour: 178 (46.6%) **CTL:** Spontaneous onset of labour: 213 (55.61%)	%	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Lisonkova, 2016	Artificial rupture of membranes: 2.50 (1.22-5.14)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Lisonkova, 2016	Labour induction with oxytocin: 1.62 (1.05-2.51)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Looft, 2017	**All:** Induction of labour: 9904 No induction: 47363 **PPH:** Induction of labour: 3358 No induction: 12196	n	NA	VB	**PPH:** EBL ≥500mL	57,267	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Magan, 2005b	Induction: 1.5 (1.2-1.7)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Malabarey, 2011	Induction of labour with oxytocin: 1.2 (0.9-1.6)	uOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Malabarey, 2011	Induction with prostaglandins: 3.6 (2.4-5.0)	uOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Mehrabadi, 2013	Induction of labour: 1.31 (1.25-1.38)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Merriam, 2018	**PPH 1:** Induction of labour: 1.34 (1.26) **PPH 2:** Induction of labour: 1.02 (1.00-1.04)	aRR aRR	Sig NS	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Miller, 2017	Spontaneous: ref Induced: 1.40 (0.86-2.30)	aOR	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Nyflot, 2016	**SPPH:** Induction of labour: 349 (32.8%) **CTL:** Induction of labour: 402 (19.5%)	%	np	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	Labour induction: 1.69 (1.39-2.05)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Nyflot, 2017b	Induction of labour: 1.95 (1.62-2.36)	aOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 17,55	Low
Oberg, 2014b	Induction: 1.59 (1.51-1.66)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Rossen, 2010	**VB** Induction of labour: 2.2 (1.9-2.6) **CS** Induction of labour: 1.3 (0.9-1.9)	aOR aOR	Sig NS	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
Sheiner, 2009	Induction of labour PPH: 1.4 (1.1-1.7)	aOR	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645	Low
Stones, 1993	Induction with oxytocin: 1.67 (1.67-2.95)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Suzuki, 2007	Induction: 2.62 (1.08-6.36)	aOR	Sig	CS	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 139	Low
van Stralen, 2016	Induction of labour: 1.48 (1.46-1.50)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	Non-induced labour: ref Induced labour: 1.52 (1.49-1.55)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.8.2 Analgesia/anaesthesia

Twenty-nine studies investigated the potential association between analgesia/anaesthesia and PPH/SPPH, and 27 of these were considered LRoB. A wide range of analgesics/anaesthetics were investigated, the most commonly investigated being epidural. Twenty-three studies included epidural in their analysis. Generally, when epidural use was compared with no epidural use, a higher risk of PPH was associated with epidural at the univariable level, however, all three studies that reported a significant association at the multivariable level found a lower risk of PPH among women who had an epidural. These three studies were conducted in France, Australia and Canada. While the Australian and Canadian studies were quite large (N=754,374 and 2,193,425, respectively), the French study was smaller (N=5,662).

Four studies that were considered HRoB included epidural in their analysis, two of which reported a significant association, with epidural being associated with a higher risk of PPH at the univariable level. One study investigated epidural and/or spinal anaesthesia and SPPH and reported a significant association at the univariable level, but not after adjustment for other factors.

Three LRoB studies investigated the association between general anaesthesia and PPH, with all three reporting a higher risk of PPH, but only one of these was at the multivariable level.. One study reported a significant association between general anaesthetic and SPPH, for both intrapartum CS and pre-labour CS, with markedly different effect sizes between these two groups (aOR=22.25; 95% CI 4.95-99.89 and aOR=5.44; 95% CI 1.73-17.12, respectively). Combined spinal and epidural was also significant at the multivariable level in this study, while epidural was not, compared with spinal.

Three studies examined analgesia generally and PPH, with only one reporting a statistically significant association at the multivariable level. This study, conducted in Canada and France, found that regional anaesthesia was associated with lower odds of PPH compared with no regional anaesthesia in Canada only. Two studies investigated spinal analgesia and PPH, neither reporting a statistically significant

association at the multivariable level. The heterogeneity of categorisation makes comparison across all studies difficult and with only 23% of analyses of PPH/SPPH significant at the multivariable level, it is unclear whether type of analgesia is an independent risk factor for PPH/SPPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.35 Included studies investigating as analgesia/anaesthesia a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Allen, 1988	Epidural analgesia Normal vaginal delivery: 7.0% Instrumental delivery: 18.6% CS: 15.4% P <0.001	% (incidence of PPH by category)	Sig	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Allen, 1988	General anaesthesia CS: 17.2%	% (incidence of PPH by category)	Sig	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Biguzzi, 2011	Analgesia: 0.94 (0.81-1.10) no analgesia: ref	aOR	NS	VB	**PPH:** EBL ≥500mL	6,011	Low
Bonnet, 2013	**Canda:** Regional anaesthesia for delivery: 0.79 (0.75-0.83) **France:** Regional anaesthesia for delivery: 1.00 (0.88-1.14)	aOR aOR	Sig NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	Low
Briley, 2013	Spinal anaesthesia: 0.87 (0.51-1.49)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Briley, 2013	Epidural analgesia: 1.08 (0.71-1.65)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Butwick, 2017	**Pre-labour CS:** Mode of anaesthesia: Spinal: ref CSE: 3.13 (1.71-5.71) Epidural: 2.54 (0.56-11.44) General: 22.25 (4.95-99.89) **Intrapartum CS:** Mode of anaesthesia: Spinal: ref CSE: 2.31 (0.91-5.85) Epidural: 2.06 (0.99-4.31) General: 5.44 (1.73-17.12)	aOR aOR	Sig Sig	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** **SPPH:** 269 **CTL:** 550 **Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Combs, 1991a	Anesthesia General: 2.94 (1.94-4.46) Epidural: ref	aOR	Sig	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Epidural: 0.87 (0.59-1.28) No epidural: ref	aOR	NS	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Combs, 1991b	Local anaesthesia: 0.79 (0.55-1.13) No local: ref	aOR	NS	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Dionne, 2015	**PPH 1:** Epidural: 0.85 (0.64-1.13) **PPH 2:** Epidural: 0.67 (0.47-0.97)	aOR aOR	NS Sig	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048	Low
Farina, 2017	**Epidural analgesia** **PPH:** 40% **CTL:** 43.1% **p=**0.813	%	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390	High
Ford, 2007	**1994-1995** Epidural: 0.91 (0.85-0.97) **2002** Epidural: 0.91 (0.85-0.99)	aOR aOR	Sig Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Gilbert, 1987	**All deliveries** **PPH:** None/N20: 20 (23%) Narcotics: 7 (8%) Epidural: 58 (69%) **CTL:** None/N20: 171 (49%) Narcotics: 51 (15%) Epidural: 129 (37%) **Spontaneous deliveries** **PPH:** None/N20: 15 (45%) Narcotics: 5 (15%) Epidural: 13 (39%) **CTL:** None/N20: 168 (56%) Narcotics: 50 (17%) Epidural: 82 (27%)	% <

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Hiersch, 2016	Epidural anaesthesia: 1.48 (0.82-2.65)	aOR	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, hemoglbon drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Epidural: 1.0 (0.9-1.0)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Khireddine, 2012	**CTL:** Epidural: 1297 (74.4%) **PPH 1:** Epidural: 3568 (79.7%) **PPH 2:** Epidural: 878 (78.0%)	%	Sig	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125	Low
Koopmans, 2014	Pethidine/promethazone/ nubain: 0.78 (0.43-1.4) No Pethidine/promethazone/ nubain: ref	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Koopmans, 2014	Epidural/spinal analgesia: 1.50 (0.96-2.3) No epidural/spinal analgesia: ref	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Koopmans, 2014	Other pain relief: 1.42 (0.64-3.1) Pethidine/promethazone/ nubain or Epidural/spinal analgesia: ref	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Kramer, 2011	**PPH:** None: 2.3% Narcotic: 2.1% Other: 1.7% **SPPH:** None: 0.20% Narcotic:0.00% Other: 0.00%	PPH/SPPH rate (%)	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Kramer, 2011	**PPH:** None: 2.5% Spinal: 2.5% Epidural: 2.1% Combined spinal/epidural: 2.1 Other: 2.2% **SPPH:** None: 0.39% Spinal: 0.62% Epidural: 0.05% Combined spinal/epidural: 0.23% Other: 0.0%	PPH/SPPH rate (%)	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lisonkova, 2016	**PPH:** Epidural analgesia: 277 (73.87%) **CTL:** Epidural analgesia: 224 (60.70%)	%	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Lisonkova, 2016	PPH: Spinal analgesia: 34 (9.14%) CTL: Spinal analgesia: 67 (18.21%)	%	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Lisonkova, 2016	**PPH:** General anaesthesia: 14 (3.73%) **CTL:** General anaesthesia: 8 (2.17%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Lisonkova, 2016	PPH: Analgesia medication during labour: 180 (47.0%) CTL: Analgesia medication during labour: 152 (39.90%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Looft, 2017	**All:** Epidural analgesia: 35466 No epidural: 21801 **PPH:** Epidural analgesia: 1,0327 No epidural: 6227	n	NA	VB	**PPH:** EBL ≥500mL	57,267	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Magan, 2005a	**General anaesthesia** **Elective CS:** PPH: 4.81 (2.34-9.35) SPPH: 4.05 (1.49-10.99) **Emergency CS:** PPH: 2.79 (1.88-4.10) SPPH: 4.50 (2.707.52)	aOR	Sig Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837	Low
Magan, 2005b	Epidural: 1.3 (1.0-1.6)	aOR	NS	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Malabarey, 2011	Regional analgesia: 0.7 (0.5-0.9)	uOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Mehrabadi, 2013	Epidural: 0.84 (0.80-0.87)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Miller, 2017	**PPH:** None: 36 (22.6%) Epidural: 79 (49.7%) Spinal or CSE: 44 (27.7%) **CTL:** None: 58 (18.2%) Epidural: 160 (50.3%) Spinal or CSE: 100 (31.5%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Nyflot, 2016	**SPPH:** Epidural: 455 (42.8%) **CTL:** Epidural: 727 (35.3%)	%	np	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Rossen, 2010	**VB** Epidural: 1.0 (0.9-1.2)	aOR	NS	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
Suzuki, 2012	**Singletons:** General anaesthesia: 69.5 (4.3-1100) **Twins:** na	uOR	Sig	CS	**PPH:** PPH requiring transfusion	Singletons: 17405 Twins: 916	Low
van Stralen, 2016	None: ref Opiates: 1.34 (1.32-1.37) Epidural vaginal: 1.66 (1.63-1.69) Epidural/spinal CS: 0.99 (0.97-1.01) General anaesthesia: 1.87 (1.79-1.94)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
von Schmidt, 2013	No/primary care medication: ref Opioid analgesics: 1.28 (1.24-1.31) Epidural during labour: 1.27 (1.24-1.31) Spinal or epidural at CS: 0.73 (0.73-0.77) General anaesthesia: 1.32 (1.24-1.40)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.8.3 Augmentation of labour

The association between augmentation of labour and PPH/SPPH was investigated in 20 studies, of which 19 were considered LRoB. Most studies compared augmentation with no augmentation, while some compared different augmentation methods, timing or dosage. Oxytocin was the most commonly analysed specific method of augmentation. Three (38%) of eight studies that investigated oxytocin use specifically found oxytocin for augmentation was associated with a higher risk of PPH (aOR ranging from 1.2 to 1.4), but one small US study found that women who had 1-7 hours of oxytocin administration were at lower risk of PPH, compared with women who had none (aOR=0.53; 95% CI 0.30-0.92).

Five studies analysed augmentation and SPPH and two (40%) found a significant association. Both these studies were based on the same or overlapping cohort of women, with data collected from one region of Norway between 2008 and 2011. Adjusted analyses reported a modest increase in the risk of SPPH, with aOR ranging from 1.59 for labour augmentation (45) to 1.89 for oxytocin augmentation (129).

The HRoB study that explored Syntocinon for augmentation did not report whether the association was statistically significant.

With nine (41%) of the 22 analyses of augmentation of labour being statistically significant at the adjusted level, it is unclear whether augmentation is an independent risk factor for PPH/SPPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.36 Included studies investigating as augmentation of labour a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Allen, 1988	Syntocinon augmentation of labour Normal vaginal delivery: 5.6% Intrumental delivery: 17.4% CS: 16.9%	% (incidence of PPH by category)	NA	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Bais, 2004	**PPH 1:** Augmentation: 1.23 (0.92-1.66) No augmentation: ref **PPH 2:** Augmentation: 0.89 (0.47-1.66) No augmentation: ref	uOR uOr	Sig NS	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Briley, 2013	Augmentation of labour: 0.83 (0.42-1.64)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Butwick, 2017	**Intrapartum CS:** Oxytocin augmentation: 0.78 (0.47-1.31)	aOR	NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Intrapartum CS** **SPPH:** 278 **CTL:** 572	Low
Buzaglo, 2014	Oxytocin treatment during delivery: PPH: 43.2% CTL: 37.9%	%	Sig	VB	**PPH:** EBL ≥500mL	56,394	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Combs, 1991a	Augmented labour: 0.67 (0.35-1.25) Spontaneous: ref	aOR	NS	CS	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Augmented labour: 1.66 (1.23-2.25)	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Davey, 2019	**Women who experienced labour:** Oxytocin infusion in labour: 1.20 (1.1-1.3)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
Dionne, 2015	**Total dose of Oxytocin (IU)** **PPH 1:** 0: ref 0-0.57: 1.16 (0.89-1.52) 0.57-1.38: 1.26 (0.97-1.64) >1.68: 1.58 (1.19-2.10) **PPH 2:** 0: 1.21 (0.85-1.72) 0-0.57: 1.23 (0.87-1.74) 0.57-1.38: 1.82 (1.27-2.60) >1.68: 0.67 (0.47-0.97)	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048	Low
Hiersch, 2016	Oxytocin augmentation: 0.99 (0.68-1.43)	aOR	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Labour augmentation, using oxytocin: 1.2 (1.2-1.3)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Lisonkova, 2016	**PPH:** Augmentation: 130 (33.94%) **CTL:** Augmentation: 101 (26.44%)	%	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Lisonkova, 2016	**PPH:** Oxytocin augmentation: 126 (33.07%) **CTL:** Oxytocin augmentation: 93 (24.80%)	%	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Lisonkova, 2016	**PPH:** Prostaglandin: 64 (16.84%) Manual - Foley catheter: 10 (2.61%) Manual sweet of membranes: 4 (1.04%) Manual ARM: 46 (12.01%) **CTL:** Prostaglandin: 42 (10.99%) Manual - Foley catheter: 8 (2.09%) Manual sweet of membranes: 3 (0.78%) Manual ARM: 18 (4.80%)	%	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Looft, 2017	**All:** Oxytocin in first stage: 26312 No oxytocin in first stage: 30955 **PPH:** Oxytocin in first stage: 8377 No oxytocin in first stage: 8177	n	NA	VB	**PPH:** EBL ≥500mL	57,267	Low
Miller, 2017	**PPH:** Oxytocin augmentation: 95 (59.8%) **CTL:** Oxytocin augmentation: 203 (63.8%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Miller, 2017	Duration of oxytocin augmentation (hr) 0: ref 1-7: 0.53 (0.30-0.92) ≥7.1: 0.80 (0.45-1.44)	aOR	Sig	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Nyflot, 2016	**SPPH:** Augmentation: 587 (55.2%) **CTL:** Augmentation: 797 (38.7%)	%	np	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	Labour augmentation: 1.59 (1.32-1.91)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Nyflot, 2017b	Oxytocin augmentation: 1.89 (1.56-2.29)	aOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1755	Low
Rossen, 2010	**VB** Augmentation of labour: 1.2 (1.0-1.5)	aOR	NS	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
Sheiner, 2009	Oxytocin augmentation PPH: 1.4 (1.2-1.7)	aOR	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645	Low
Suzuki, 2007	Oxytocin use during labour: 2.86 (1.27-6.48)	uOR	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 140	Low
von Schmidt, 2013	Augmentation of labour: 1.52 (1.50-1.55)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.8.4 Duration of second stage

The duration of the second stage of labour was evaluated as a potential risk factor for PPH by 20 studies, 16 of which were considered low risk of bias. There was a wide range of methods used to categorise or measure this risk factor, but most studies compared longer second stage to shorter durations of the second stage, with shorter durations being the reference group. No studies examined duration of second stage and SPPH.

Of the 18 LRoB analyses, across 16 studies, 13 (72%) reported a significant association between duration of the second stage of labour and PPH, at the multivariable level, with all significant associations indicating higher odds of PPH associated with increased duration of second stage. One study (122) looked specifically at 'pushing time' within the second stage of labour, and reported that pushing time of 30 minutes or longer was associated with a small increase in the risk of PPH. Two studies looked at the progression of the second stage with one study (113), conducted in Israel, reporting that 'non-progressive labour in the second stage' was associated with more than twice the odds of PPH, after adjustment for other factors (aOR=2.6; 95% 1.8-3.7). The other study that examined progression, reported more than three times the odds of PPH associated with 'failure to progress second stage', after adjustment for other factors (aOR=3.4; 95% CI 2.4-4.7). 'Prolonged second stage' was investigated as a risk factor in three studies but was only significant at the adjusted level in one study. The other studies that reported a significant association between duration of second stage and PPH used varying cut offs of length of second stage in minutes and used different reference groups but followed the general trend that increased duration was associated with an increased risk of PPH.

Rating: Very likely - More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Table 2.37 Included studies investigating as duration of second stage of labour a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Bais, 2004	Duration second stage **PPH 1:** ≤30 mins: 0.68 (0.32-0.83) 31-59 min: ref ≥60 mins: 1.33 (0.89-1.96) **PPH 2:** ≤30 mins: 0.52 (0.55-0.84) 31-59 min: ref ≥60 mins: 1.3 (1.08-1.59)	uOR uOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Buzaglo, 2014	Non-progressive labour - 2nd stage: 2.6 (1.8-3.7)	aOR	Sig	VB	**PPH:** EBL ≥500mL	56,394	Low
Combs, 1991a	Prolonged second stage: 1.26 (0.63-2.50)	aOR	NS	CS	**PPH:** Haematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991a	Arrest of descent 1.90 (1.23-2.94)	aOR	Sig	CS	**PPH:** Haematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Arrest of descent: 2.91 (1.59-5.32)	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Dionne, 2015	**Duration second stage (mins)** **PPH 1:** ≤18: ref 18-27: 1.17 (0.92-1.48) 27-37: 1.31 (0.99-1.76) >37: 1.39 (0.99-1.96) Missing: 0.62 (0.47-0.83) **PPH 2:** ≤18: ref 18-27: 1.37 (1.02-1.85) 27-37: 1.41 (0.99-2.02) >37: 1.59 (1.06-2.39) Missing: 0.62 (0.43-0.90)	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048	Low
Farina, 2017	**Duration (mins)** **PPH:** 105 (37) **CTL:** 94 (32) **p=**0.227	Mean (SD)	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390	High

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Gilbert, 1987	**All deliveries** **PPH:** <1 h: 31 (36%) >1 h: 55 (64%) **CTL:** <1 h: 259 (74%) >1 h: 92 (26%) **Spontaneous deliveries** **PPH:** <1 h: 21 (64%) >1 h: 12 (36%) **CTL:** <1 h: 248 (83%) >1 h: 52 (17%)	%	Sig	VB	**PPH:** EBL ≥500mL	**PPH:** 86 **CTL:** 351	High
Henry, 2005	**PPH 1:** <60 mins: ref ≥60 mins: 2.68 (1.27-5.64) **PPH 2:** <60 mins: ref ≥60 mins: 5.76 (1.89-17.19)	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low
Hiersch, 2016	Second stage (min): 1.003 (1.001-1.006)	aOR	Sig	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Prolonged second stage: 1.5 (1.5-1.6)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Koopmans, 2014	Duration of bearing down stage (min): 1.00 (1.0-1.0)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Lisonkova, 2016	PPH: Prolonged second stage (>2 hrs): 82 (22.84%) CTL: Prolonged second stage (>2 hrs): 39 (10.96%)	%	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Looft, 2017	Pushing time (mins) 0-14: 0.98 (0.94-1.03) 15-29: ref 30-44: 1.08 (1.04-1.12) 45-59: 1.11 (1.06-1.16) ≥60: 1.20 (1.15-1.25)	aOR	Sig	VB	**PPH:** EBL ≥500mL	57,267	Low
Magan, 2005b	Prolonged second stage of labour: 1.6 (1.1-2.1)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Malabarey, 2011	Second stage >2h: 1.7 (1.3-2.30	uOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Malabarey, 2011	Second stage > 3h: 2.0 (1.4-2.8)	uOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Miller, 2017	Duration second stage (hr) 0-1.9: ref 2-2.9: 1.17 (0.58-2.37) ≥ 3: 2.32 (1.16-4.63)	aOR	Sig	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Rossen, 2010	**VB** Second stage > 30 mins: 1.3 (1.1-1.5)	aOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Sheiner, 2009	Failure to progress second stage PPH: 3.4 (2.4-4.7)	aOR	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645	Low
van Stralen, 2016	Second stage ≥1hr: 1.51 (1.48-1.53)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	Expulsive phase <60 min: ref Expulsive phase ≥60 mins: 1.52 (1.49-1.55)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.8.5 Overall duration of labour

Overall duration of labour was investigated as a potential risk factor of PPH/SPPH by 15 studies, nine of which were considered LRoB. This risk factor was captured and categorised in a range of different ways, with some studies reporting mean number of hours, others on the basis of 'prolonged labour' or 'obstructed labour' and others comparing categories of labour duration. Seven LRoB studies investigated duration of labour and PPH, with two reporting a significant association after adjustment for other factors, both observing a small increase in the odds of PPH for women who had longer or 'Prolonged labour' compared with those who did not. Three LRoB studies analysed duration of labour and SPPH, with two finding a significant increase in the odds of SPPH for women who had labour ≥12 hours (aOR=2.44; 95% CI 1.69-3.53), and women who had labour 12-24 hours (aOR=1.12; 95% CI 1.03-1.2) compared with shorter durations.

Five HRoB studies explored duration of labour, with three of these finding a significant association and, similar to the LRoB studies, reporting a small to moderate increase in the odds of PPH with increased durations of labour, at the univariable level.

Generally, studies that found a significant association for this risk factor, observed that increased duration of labour was associated with an increased risk of PPH/SPPH, but most studies that investigated duration of labour and PPH/SPPH did not report a significant association at the adjusted level.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.38 Included studies investigating duration of labour as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Davey, 2019	**Women who experienced labour:** <2 hr: 0.96 (0.8-1.1) 2-4 hr: 0.85 (0.8-0.9) 4-12 hr: ref 12-24hr: 1.12 (1.03-1.2) ≥ 24hr: 1.07 (0.8-1.4) Not reported: 1.02 (0.7-1.4)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
Davey, 2019	**All women** Obstructed labour: 1.14 (0.8-1.6) **Women who experienced labour** Obstructed labour 1.44 (0.9-2.3)	uOR uOR	NS NS	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
Eto, 2016	**Duration (hours)** **PPH:** 9.6 (8.7) **CTL:** 8.4 (7.1) p < 0.001 **PPH2:** 10.6 (10.2) **CTL:** 8.5 (7.2) p < 0.001 **PPH3:** 11.1 (11.5) **CTL:** 8.6 (7.3) p=0.007	Mean (SD)	Sig	VB	**PPH 1:** EBL ≥500g **PPH 2:** EBL ≥800g **PPH 3:** EBL >1000g	**CTL:** 2,524 **PPH 1:** 524 **PPH 2:** 147 **PPH 3:** 158	High

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Ford, 2007	**Prolonged labour:** **1994-1995** 1.24 (1.13-1.36) **2002** 1.63 (1.44-1.86)	aOR aOR	Sig Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low
Ford, 2007	**1994-1995** Obstructed labour: 1.38 (1.27-1.50) **2002** Obstructed labour: 1.29 (1.16-1.44)	aOR aOR	Sig Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low
Kaufner, 2016	Duration of birth: ≤12 h: ref >12 h: 1.45 (0.61-3.44)	uOR	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Khireddine, 2012	**Duration of active phase of labour (Percentiles based on % of CTLs)** **CTL:** <50: 833 (49.5%) P50-P75: 425 (25.3%) P75-90: 262 (15.6%) ≥90: 161 (9.6%) Missing: 62 **PPH 1:** <50: 1514 (35.2%) P50-P75: 1093 (25.4%) P75-90: 919 (21.4%) ≥90: 778 (18.05%) Missing: 173 **PPH 2:** <50: 355 (33.4%) P50-P75: 238 (22.4%) P75-90: 242 (22.85%) ≥90: 228 (21.4%) Missing: 62	%	Sig	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Kramer, 2011	**PPH:** Duration of labour >12 hours: 1.0 (0.9-1.2) **SPPH:** Duration of labour >12 hours: 1.9 (0.7-5.6)	aOR aOR	NS NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Looft, 2017	Time from retracted cervix to birth (h) <1: ref ≥: 1.18 (1.15-1.22) 1 to <2: ref ≥2: 1,13 (0.09-1.16) 2 to <3: ref ≥3: 1.16 (1.11-1.20) 3 to <4: ref ≥4: 1.19 (1.05-1.16)	aOR	Sig	VB	**PPH:** EBL ≥500mL	57,267	Low
Nyflot, 2017b	Duration of labour ≥12 hours: 2.44 (1.69-3.53)	aOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low
Oberg, 2014b	Weak/prolonged labour: 1.63 (1.56-1.70)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Salkeld, 2008	**PPH:** Obstructed labour: 221 (9.0%) **CTL:** Obstructed labour: 1227 (5.1%)	%	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Salkeld, 2008	**PPH:** Prolonged labour: 127 (5.2%) **CTL:** Prolonged labour: 773 (3.2%)	%	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High
Stones, 1993	Labour >12 hrs: 1.98 (1.37-2.87)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Suzuki, 2007	Duration of labour: <3 hours: 0.76 (0.29-2.00)	uOR	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 143	Low
Suzuki, 2007	Duration of labour: ≥24 hours: 2.55 (1.15-5.62)	uOR	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 144	Low

2.4.8.6 Premature rupture of membranes

Pre-labour rupture of membranes (PROM) was investigated as a risk factor by twelve studies. There was a variety of categorisations of this factor, from a dichotomous Yes/No for diagnosis of PROM, to classification based on number of hours (including 6, 12, 18 and 24 hours). Only one LRoB study (113) reported a significant association between PROM and PPH after adjustment for other factors (aOR=1.4; 95% CI 1.0-1.7).

One HRoB study reported significantly higher odds of PPH for women with rupture of membranes longer than 18 hours, compared with 18 hours or less (uOR=1.7; 95% CI 1.2-2.4).

One study reported a significant association between PROM and SPPH, however this was unadjusted for confounding factors.

With only one LRoB study reporting a significant association at the adjusted level, it is unclear whether PROM is independently associated with increased risk of PPH/SPPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.39 Included studies investigating pre-labour rupture of membranes as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Briley, 2013	ROM > 2 hours before onset: 0.95 (0.64-1.41)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Briley, 2013	ROM > 6 hours before onset: 1.35 (0.90-2.02)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Briley, 2013	ROM not recorded: 1.03 (0.60-1.77)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Buzaglo, 2014	PROM: 1.4 (1.0-1.7)	aOR	Sig	VB	**PPH:** EBL ≥500mL	56,394	Low
Hiersch, 2016	PPH: PROM: 10.2% CTL: PROM: 11.5% p=0.59	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Lisonkova, 2016	**PPH:** PROM: 55 (14.445) **CTL:** PROM: 49 (12.86%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Lisonkova, 2016	**PPH:** PROM for ≥24 hours: 18 (4.76%) **CTL:** PROM for ≥24 hours: 2.87 (0.17%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Malabarey, 2011	ROM > 18h: 1.7 (1.2-2.4) ≤18 hours: ref	uOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Nyflot, 2016	SPPH: PROM: 127 (12.0%) CTL: PROM: 169 (8.2%)	%	np	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	PROM: 1.51 (1.19-1.93)	uOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Suzuki, 2007	PROM: 1.29 (0.56-2.97)	uOR	NS	CS	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 138	Low
von Schmidt, 2013	Rupture of membranes <12 hrs: ref Rupture of membranes ≥12 hrs: 1.35 (1.32-1.37)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.8.7 Duration of first stage

Eleven studies investigated the association between length of first stage of labour and PPH, and nine of these were considered LRoB. While most studies examined the risk factor in relation to the duration of labour (in minutes/hours), 'prolonged first stage' and 'failure to progress first stage' were also explored. Nine LRoB studies examined duration of first stage and PPH, with three studies (33%) reporting a significant association between longer duration of first stage and PPH at the multivariable level. One Swiss study (n=739,000) reported that a 'prolonged first stage of labour' was associated with a 20% increase in the odds of PPH (aOR=1.2; 95% CI 1.1-1.3). A study conducted in Norway reported a 40% increase in the odds of PPH among women who had vaginal births with a first stage of labour >10 hours, compared with first stage ≤10 hours (aOR=1.4; 95% CI 1.1-1.8). One French study reported a significant association between the duration of all labour prior to expulsive efforts, with the risk increasing 4% per hour of labour (aOR=1.04; 95% CI 1.10-1.08).

Two HRoB studies explored duration of first stage, with one reporting no significant difference in the mean duration of labour between women who had a PPH and controls, and the other reporting a significant difference, with cases more likely to have longer duration of first stage of labour.

With only 33% of LRoB analyses that investigated some aspect of length of first stage finding a significant association, it is unclear whether this is an independent risk factor of PPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.40 Included studies investigating duration of first stage of labour as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Buzaglo, 2014	Non-progressive labour Stage 1: PPH: 0.00% CTL: 0.01%	%	NS	VB	**PPH:** EBL ≥500mL	56,394	Low
Combs, 1991a	Prolonged latent stage: 1.12 (0.67-1.86)	aOR	NS	CS	**PPH:** Haematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Dionne, 2015	**Duration of labour prior to expulsive efforts (for one hour)** **PPH 1:** 1.04 (1.01-1.08) **PPH 2:** 1.04 (1.00-1.09)	aOR aOR	Sig NS	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	**CTL:** 762 **PPH 1:** 3,852 **PPH 2:** 1,048	Low
Farina, 2017	**PPH:** 257 (65) **CTL:** 252 (50) **p=**0.165	Mean dif	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390	High

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Gilbert, 1987	**All deliveries** **PPH:** <2 h: 2 (2%) 2-8 h: 37 (43%) 8-12 h: 27 (31%) > 12 h: 20 (23%) **CTL:** <2 h: 25 (7%) 2-8 h: 236 (67%) 8-12 h: 61 (17%) > 12 h: 29 (8%) **Spontaneous deliveries** **PPH:** <2 h: 2 (6%) 2-8 h: 17 (52%) 8-12 h: 7 (21%) > 12 h: 7 (21%) **CTL:** <2 h: 25 (8%) 2-8 h: 219 (73%) 8-12 h: 37 (12%) > 12 h: 19 (6%)	%	Sig	VB	**PPH:** EBL ≥500mL	**PPH:** 86 **CTL:** 351	High
Kaelin Agten, 2017	Prolonged first stage: 1.2 (1.1-1.3)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Koopmans, 2014	Duration of dilation stage (h): 1.07 (1.0-1.1)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Magan, 2005b	Prolonged first stage of labour: 1.6 (1.0-1.6)	aOR	NS	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Miller, 2017	Duration 1st stage (hr) <11: ref 11-15.9: 1.14 (0.73-3.31) ≥ 16: 1.55 (0.73-3.31) Missing: 1.04 (0.61-1.78)	aOR	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Rossen, 2010	**VB** First stage >10 hours: 1.4 (1.1-1.8) **CS** First stage >10 hours: 1.7 (1.0-2.8)	aOR aOR	Sig NS	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
Sheiner, 2009	**PPH 1:** Failure to progress first stage: 1.5% **PPH 2:** Failure to progress first stage: 0 **PPH 3:** Failure to progress first stage: 2.5% **CTL:** Failure to progress first stage: 1.9%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **SPPH:** 199 **CTL:** 153,645	Low

2.4.8.8 Duration of third stage

The association between the duration of the third stage of labour and PPH was investigated by eight studies, seven of which were LRoB. No studies investigated duration of third stage and SPPH. There was a range of categorisations for this variable, but generally longer duration of third stage was associated with increased risk of PPH. Four LRoB studies found increased risk of PPH for duration of labour longer than 30 minutes, compared with shorter durations. Of the studies that analysed duration based on minutes as a continuous variable, one found that the odds of PPH increased 2% for each minute of the third stage, while the other reported no statistically significant difference in the duration of the third stage in minutes between cases and controls.

One HRoB study assessed length of third stage and PPH and reported an increased risk of PPH with increased duration of third stage.

With six (86%) of the seven LRoB studies examining duration of third stage and PPH finding an increased risk associated with longer duration, it is considered very likely that prolonged third stage of labour is an independent risk factor for PPH.

Rating: Very likely - More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Table 2.41 Included studies investigating duration of third stage of labour as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Bais, 2004	**Third stage ≥30 mins** **PPH 1:** 2.61 (1.83-3.72) **PPH 2:** 4.90 (2.89-8.32)	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Combs, 1991b	Prolonged third stage ≥30 mins: 7.56 (4.32-13.53)	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Eto, 2016	**Third stage duration (mins)** **PPH 1:** 13.2 (12.6) **CTL:** 11.0 (6.8) p < 0.001 **PPH 2:** 13.9 (15.2) **CTL:** 11.3 (7.6) p=0.006 **PPH 3:** 14.8 (17.5) **CTL:** 11.3 (7.9) p=0.023	Mean(SD)	Sig	VB	**PPH 1:** EBL ≥500g **PPH 2:** EBL ≥800g **PPH 3:** EBL >1000g	**CTL:** 2,524 **PPH 1:** 524 **PPH 2:** 147 **PPH 3:** 158	High
Firmin, 2019	15 minutes or less: ref >15-30 mins: 1.54 (0.79-3.02) > 30 mins: 10.92 (2.17-54.99)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Henry, 2005	**PPH 1:** <30 mins: ref ≥ 30 mins: 2.92 (0.90-9.41) **PPH 2:** <30 mins: ref ≥ 30 mins: 7.56 (2.25-25.45)	uOR uOR	NS Sig	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Hiersch, 2016	Duration third stage (mins) 1.02 (1.01-1.04)	aOR	Sig	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Magan, 2005b	Prolonged third stage of labour: 6.2 (4.6-8.2)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Miller, 2017	Duration third stage (min) PPH: 5 (3-8) CTL: 5 (3-7) p=0.58	Median (IQR)	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low

2.4.8.9 Maternal pyrexia in labour

Fever in labour was examined as a potential risk factor for PPH/SPPH by seven studies. Six of these were considered LRoB. Four LRoB studies examined the association between fever in labour and PPH, with three of these studies finding an increased risk after adjustment for other variables. The magnitude of the increased risk varied from aOR 1.6 to 5.26.

Two studies examined fever and SPPH, both reporting a significantly higher risk, after adjustment for other variables.

The one HRoB study reported a significant association between pyrexia and PPH, but did not adjust for potential confounding factors.

With five of the six LRoB studies reporting an increased risk of PPH/SPPH associated with fever in labour, after adjustment for other variables, it is considered very likely that this in an independent risk factor for PPH/SPPH.

Rating: Very likely - More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Table 2.42 Included studies investigating fever in labour as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Briley, 2013	Raised temperature (per degree > 37°C): 2.62 (1.24-5.52) Temperature not recorded; 0.75 (0.50 - 1.11)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Hiersch, 2016	**PPH:** Intrapartum fever: 3.7% **CTL:** Intrapartum fever: 2.0%	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Fever during labour >38°C: 1.6 (1.4-1.9)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Lisonkova, 2016	Intrapartum fever: 5.26 (1.75-15.7)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Nyflot, 2017a	Fever in labour: 1.88 (1.28-2.75)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Nyflot, 2017b	Fever during labour: 1.88 (1.29-2.74)	aOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low
Stones, 1993	Pyrexia: 2.02 (1.03-3.97)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High

2.4.8.10 Third stage management

Third stage management was explored, in varying ways, by five studies, four of which were considered LRoB. Two studies examined the management of third stage, generally, with one reporting no significant difference at the adjusted level between physiological and active management, the other reporting that 'No management of third stage' was associated with more than double the odds of PPH, compared with management, after adjustment for confounding factors (aOR=2.22; 95% CI 1.41-3.86). One study (115) reported that prophylactic oxytocin administration was associated with significantly lower odds of PPH, after adjustment for confounding factors. Two studies analysed Syntometrine use, with one (56) reporting that Syntometrine intramuscular and syntometrine 40/50 IU infusion were associated with significantly lower odds of PPH, at the multivariable level, while the other (119) reported that Syntometrine was more commonly used among controls than cases and Oxytocin was more commonly used in cases of PPH, however this study was considered HRoB and did not present adjusted statistics. This same study also reported that controlled cord traction was more common among cases than controls, though these results were not adjusted for confounding factors.

The high degree of heterogeneity in terms of how this factor was assessed makes it difficult to draw conclusions across studies, however, regardless of which aspect of third stage management was selected, there appears to be a be a significant independent relationship between how third stage of labour is managed and risk of PPH.

Rating: Likely - Between 50% and 60% of LRoB analyses found a significant association.

Table 2.43 Included studies investigating as third stage management a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Briley, 2013	Physiological management: 1.48 (0.80-2.77) Active: ref	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Briley, 2013	Syntometrine intramuscular: 0.55 (0.33-0.91) No Syntometrine intramuscular: ref	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Briley, 2013	Syntocinon intravenous bolus: 0.58 (0.27-1.25) No Syntocinon intravenous bolus: ref	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Briley, 2013	Syntocinon 40/50 IU infusion: 0.61 (0.38-0.99) No Syntocinon 40/50 IU infusion: ref	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Dionne, 2015	**Prophylactic postpartum oxytocin administration** **PPH 1:** 0.48 (0.39-0.59) **PPH 2:** 0.44 (0.34-0.57)	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048	Low
Firmin, 2019	No management of third stage: 2.33 (1.41-3.86) Managed third stage: ref	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Firmin, 2019	No post-natal PPH prevention (prophylactic administration of oxytocin or misoprostol after the birth) performed: 2.33 (1.41-3.86) Post-natal PPH prevention: ref	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Gilbert, 1987	**All deliveries** **PPH:** Controlled cord traction: 80 (93%) Spontaneous: 6 (7%) **CTL:** Controlled cord traction: 254 (72%) Spontaneous: 97 (28%) **Spontaneous deliveries** **PPH:** Controlled cord traction: 28 (85%) Spontaneous: 5 (15%) **CTL:** Controlled cord traction: 203 (68%) Spontaneous: 97 (32%)	% <

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Gilbert, 1987	**All deliveries** **PPH:** Syntometrine: 73 (85%) Oxytocin: 13 (15%) **CTL:** Syntometrine: 341 (97%) Oxytocin: 10 (3%) **Spontaneous deliveries** **PPH:** Syntometrine: 28 (85%) Oxytocin: 5 (15%) **CTL:** Syntometrine: 292 (97%) Oxytocin: 8 (3%)	% <

2.4.9 Birth factors

2.4.9.1 Mode of birth

Birth mode was investigated as a risk factor for PPH/SPPH by 40 studies, 33 of which were considered LRoB. While some studies restricted their population based on mode of birth, most studies included both vaginal and caesarean births. Most examined a sub-group of either vaginal or caesarean births, typically investigating the association between instrumental birth or emergency caesarean and risk of PPH/SPPH, compared with spontaneous vaginal birth.

There were 29 LRoB analyses of instrumental birth and PPH. Nineteen of these analyses found instrumental birth to be associated with a higher risk of PPH after adjustment for other factors, compared with non-instrumental birth. The magnitude of the effect varied from small (aOR=1.1, 95% CI 1.1-1.2) for 'operative vaginal birth', in a large Swiss study, to very large (aOR=6.56; 95% CI 2.55-16.86) for 'forceps birth' in a small Australian study. There were five LRoB analyses of instrumental birth and SPPH, with all five reporting significantly higher odds of SPPH among with women who had an instrumental birth.

Eighteen LRoB analyses compared vaginal and caesarean birth in terms of risk for PPH/SPPH, with 12 (67%) reporting a significant association. Seven analyses that compared caesarean birth with vaginal birth reported an increased risk of PPH/SPPH among women who had a caesarean, whether planned or unplanned. However, five LRoB analyses reported that planned caesarean birth was associated with a lower risk of PPH/SPPH compared with vaginal birth, after adjustment for other variables. One study reported that emergency caesarean was protective for PPH, compared with spontaneous vaginal birth. Four LRoB studies compared emergency/in-labour caesarean with planned caesarean and none reported a significant association with PPH/SPPH at the multivariable level.

Eight HRoB studies examined mode of birth, reporting generally similar findings to the LRoB studies, with instrumental and caesarean birth being associated with a higher risk of PPH/SPPH compared with spontaneous vaginal birth, without adjustment for potential confounders.

Most (70%) LRoB analyses that analysed instrumental birth as a risk factor for PPH/SPPH reported a significant association, after adjustment for confounding variables. Therefore, instrumental birth is considered a likely risk factor for PPH/SPPH. Given that the direction of effect for planned and unplanned caesarean was inconsistent, it is unclear whether type of caesarean is an independent risk factor PPH.

Rating: Instrumental birth: Very likely - More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Rating: Caesarean birth: Unclear - Between 50% and 80% of LRoB analysis found a significant association but in conflicting directions.

Table 2.44 Included studies investigating birth mode as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Allen, 1988	Normal vaginal birth: 3.9% Instrumental: 13.7% CS: 15.4% p <0.01	% (incidence of PPH by category)	Sig	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Bais, 2004	Instrumental delivery **PPH:** 1.89 (1.61-2.29) **SPPH:** 1.70 (1.17-2.45)	uOR uOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Biguzzi, 2011	Vacuum: 1.45 (1.13-1.87) No vacuum: ref	aOR	Sig	VB	**PPH:** EBL ≥500mL	6,011	Low
Biguzzi, 2014	Vacuum: 2.11 (1.61-2.77) No vacuum: ref	aOR	Sig	VB	**PPH:** EBL ≥500mL	3,219	Low
Bonnet, 2013	**Canada:** Operative vaginal delivery: 1.62 (1.52-1.72) **France:** Operative vaginal delivery: 1.43 (1.22-1.68)	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	Low
Briley, 2013	Spontaneous vaginal: ref Instrumental vaginal: 3.50 (2.21-5.24) Elective CS: 24.4 (5.53-108.00) Emergency CS: 40.5 (16.30-101.00)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	9,937	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Buzaglo, 2014	Vacuum-assisted birth: PPH: 15.4% CTL: 9.1%	%	Sig	VB	**PPH:** EBL ≥500mL	56,394	Low
Choe, 2016	Caesarean: 2.05 (1.82-2.30) Vaginal: ref	aOR	Sig	VB, CS	**PPH:** ICD-10 code O72.0-O72.3 or transfusion	65,479	Low
Combs, 1991a	Caesarean with no labour: ref Caesarean after labour: 1.11 (0.67-1.84)	aOR	NS	CS	**PPH:** Haematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Forceps/vacuum: 1.66 (1.06-2.60) Spontaneous: ref	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Davey, 2019	**All women:** Unassisted vaginal: ref Forceps: 2.09 (1.9-2.3) Vacuum: 1.36 (1.2-1.5) Unplanned CS (pre-labour): 0.61 (0.4-0.9) Planned CS (pre-labour): 0.72 (0.6-0.8) Unplanned CS (in labour): 1.22 (1.1-1.3) Planned CS (in labour): 1.67 (1.5-1.9)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
	Women who experienced labour: Unassisted vaginal: ref Forceps: 2.04 (1.8-2.3) Vacuum: 1.26 (1.1-1.4) Planned CS (in labour): 0.61 (0.3-1.1) Unplanned CS (in labour): 1.06 (1.0-1.2)	aOR	Sig				
Dionne, 2015	**PPH 1:** Spontaneous: ref Forceps: 1.58 (1.24-2.02) Vacuum: 0.83 (0.59-1.76)	aOR	Sig	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048	Low
	PPH 2: Spontaneous: ref Forceps: 1.98 (1.47-2.66) Vacuum: 0.75 (0.45-1.15)	aOR	Sig		**PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL		

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Flood, 2019	**PPH:** Unassisted vaginal: 22346 (28.1%) Forceps: 7003 (8.8%) Vacuum: 5358 (6.7%) CS: 44730 (56.3%) **SPPH:** Unassisted vaginal: 2314 (45.2%) Forceps: 644 (12.9%) Vacuum: 484 (9.5%) CS: 1678 (32.8%) **All confinements** Unassisted vaginal: 197179 (54.1%) Forceps: 23111 (6.3%) Vacuum: 30069 (8.2%) CS: 114215 (31.3%)	%	NA	VB, CS	**PPH:** EBL ≥500mL **SPPH:** EBL ≥1500mL	Total: 364,574 **PPH:** 79,437 **SPPH:** 5120	High

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Ford, 2007	**1994-1995** Spontaneous onset, vaginal: ref Spontaneous onset, Instrumental: 1.30 (1.17-1.44) Spontaneous onset, CS: 0.66 (0.57-0.76) Induced/augmented, vaginal: 1.34 (1.27-1.43) induced/augmented, Instrumental: 1.76 (1.60-1.94) induced/augmented, CS: 0.66 (0.56-0.76) no labour, CS: 0.55 (0.47-0.62)	aOR	Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low
	2002 Spontaneous onset, Vaginal: ref Spontaneous onset, Instrumental: 1.07 (0.93-1.24) Spontaneous onset, CS: 0.43 (0.35-0.52) Induced/augmented, Vaginal: 1.19 (1.11-1.29) Induced/augmented, instrumental: 1.25 (1.10-1.42) Induced/augmented, CS: 0.54 (0.46-0.64) no labour, CS: 0.46 (0.40-0.52)	aOR	Sig				

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Fukami, 2019	**CTL:** Assisted vaginal delivery: 8.0% No: 92.0% **PPH:** Assisted vaginal delivery: 9.7% No: 90.3%	%	NS	VB	**PPH:** CBL ≥1000mL	1,608	Low
Gilbert, 1987	**All deliveries** **PPH:** Spontaneous: 33 (38%) Forceps, oulet: 33 (38%) Forceps, rotational: 20 (23%) **CTL:** Spontaneous: 300 (85%) Forceps, oulet: 30 (9%) Forceps, rotational: 21 (6%)	%	Sig	VB	**PPH:** EBL ≥500mL	**PPH:** 86 **CTL:** 351	High
Henry, 2005	**PPH 1:** Vaginal: ref Ventouse: 2.40 (0.64-8.84) Forceps: 3.47 (1.35-8.91) **PPH 2:** Vaginal: ref Ventouse: 2.10 (0.48-9.27) Forceps: 6.56 (2.55-16.86)	aOR uOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low
Kaelin Agten, 2017	Spontaneous vaginal: ref Operative vaginal: 1.1 (1.1-1.2) Elective CS: 0.4 (0.4-0.5) Emergency CS: 0.6 (0.5-0.6)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Kaufner, 2016	Uncomplicated vaginal: ref Instrumental vaginal: 0.87 (0.22-3.49) Urgent CS: 2.77 (1.00-7.67)	aOR	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low
Khireddine, 2012	**CTL:** Spontaneous vaginal: 1422 (81.5%) Instrumental vaginal: 207 (11.9%) Emergency CS: 115 (6.6%) **PPH 1:** Spontaneous vaginal: 3251 (72.6%) Instrumental vaginal: 955 21.3% Emergency CS: 271 (6.1%) **PPH 2:** Spontaneous vaginal: 697 (62.0%) Instrumental vaginal: 321 (28.55) Emergency CS: 107 (9.5%)	%	Sig	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125	Low
Koopmans, 2014	Spontaneous: ref Vaginal instrumental delivery: 1.7 (1.03-2.7) Caesarean delivery: 1.4 (0.85-2.3)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Kramer, 2011	**PPH:** Spontaneous vaginal: ref Forceps or vacuum: 1.5 (1.3-1.7) Caesarean section: 1.3 (1.1-1.5) **SPPH:** Spontaneous vaginal: ref Forceps or vacuum: 1.9 (0.2-16.1) Caesarean section: 4.8 (1.4-16.0)	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lee, 2017	Emergent CS: 3.13 (0.82-12.02) Non-emergent: ref	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210	Low
Lee, 2018	Emergency CS: 0.60 (0.24-1.48) non-emergency CS: ref	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506	Low
Lisonkova, 2016	PPH: Caesarean section: 87 (22.72%) CTL: Caesarean section: 111 (28.98%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Lisonkova, 2016	PPH: Emergency CS: 66 (17.23%) CTL: Emergency CS: 57 (14.88%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Lisonkova, 2016	Forceps delivery: 2.38 (1.04-5.45)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Looft, 2017	**All:** Non-instrumental: 46569 Instrumental: 10698 **PPH:** Non-instrumental: 12583 Instrumental: 3971	n	NA	VB	**PPH:** EBL ≥500mL	57,267	Low
Magan, 2005b	Forceps after unsuccessful vacuum delivery: 1.9 (1.1-3.2)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Malabarey, 2011	Operative delivery: 1.5 (0.97-2.3)	uOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Malabarey, 2011	Caesarean section: 0.9 (0.5-1.2) Vaginal birth: ref	uOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Mehrabadi, 2013	Instrumental delivery: 1.98 (1.87-2.10)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Mehrabadi, 2013	CS: 1.39 (1.32-1.47)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Merriam, 2018	**PPH 1:** Primary CS: 0.59 (0.56-0.62) Repeat CS: 0.47 (0.44-0.49) Operative vaginal: 1.26 (1.23-1.30) Non-operative vaginal: ref **PPH 2** Primary CS: 2.78 (2.72-2.85) Repeat CS: 2.45 (2.39-2.52) Operative vaginal: 1.95 (1.90-2.01) Non-operative vaginal: ref	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Miller, 2017	**PPH:** Spontaneous vaginal: 139 (87.4%) Instrumental: 20 (12.6%) **CTL:** Spontaneous vaginal: 288 (90.6%) Instrumental: 30 (9.4%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Nyflot, 2016	Spontaneous vaginal: 0.53 (0.45-0.62)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	Spontaneous vaginal: ref Instrumental vaginal: 1.50 (1.17-1.93) In-labour CS: 1.95 (1.53-2.47) Elective CS: 1.66 (1.22-2.24)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low
Rossen, 2010	**VB** Operative vaginal delivery: 1.0 (0.9-1.3)	aOR	NS	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Salkeld, 2008	**PPH:** CS: 386 (15.7%) Vaginal: 2074 (84.3%) **CTL:** CS: 3414 (14.3%) Vaginal: 33603 (85.6%)	%	np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High
Sharp, 2014	CS: 8.20 (6.19-10.86)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	25,322	Low
Sharp, 2014	Instrumental delivery: 0.42 (0.27-0.66)	uOR	Sig	VB, CS	**PPH:** EBL ≥500mL	25,322	Low
Sheiner, 2009	**PPH 1:** CS: 8.8% **PPH 2:** CS: 0.6% **PPH 3:** CS: 14.6% **CTL:** CS: 11.1%	%	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645	Low
Sheiner, 2009	Instrumental delivery **PPH:** 2.3 (1.6-3.4)	aOR	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Stones, 1993	Emergency CS: 2.24 (1.43-3.53) Elective CS: ref	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Stones, 1993	Emergency CS: 3.71 (2.54-5.42) Operative vaginal: ref	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Stones, 1993	Emergency CS: 8.84 (6.74-11.6) Spontaneous vaginal: ref	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Stones, 1993	Elective CS: 3.94 (2.52-6.17) Spontaneous vaginal: ref	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Stones, 1993	Elective CS: 1.65 (0.98-2.78) Operative vaginal: ref	uRR (99% CI)	NS	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Stones, 1993	Operative vaginal: 2.39 (1.64-3.48) Spontaneous vaginal: ref	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Suzuki, 2007	Vacuum/forceps: 1.59 (0.90-2.83)	uOR	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 141	Low
Suzuki, 2012	**Singletons:** Emergency CS: 1.55 (0.93-2.6) **Twins:** Emergency CS: 0.58 (2.3) (CI as provided)	uOR	NS	CS	**PPH:** PPH requiring transfusion	Singletons: 17,405 Twins: 916	Low
van Stralen, 2016	Spontaneous: ref Assisted vaginal: 1.31 (1.29-1.33) Planned CS: 1.21 (1.18-1.24) Emergency CS: 1.10 (1.08-1.13)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	Spontaneous: ref Assisted delivery: 1.49 (1.46-1.52) Elective CS: 0.98 (0.95-1.08) Emergency CS: 0.72 (0.72-0.74)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.9.2 Genital tract trauma

Genital tract trauma and/or laceration was investigated as a risk factor for PPH/SPPH by 31 studies and 29 of these were considered LRoB. There was a wide range of definitions and classifications for this variable but most studies compared more severe with less severe tearing and lacerations, and generally it was reported that the more severe categories were associated with a higher risk of PPH/SPPH.

Sixteen studies analysed lacerations and perineal tears generally, without reporting on the degree of the trauma, and 14 of these were considered LRoB. Of the 14 LRoB analyses of PPH, 10 reported a statistically significant association after adjustment for other factors. Women with perineal tears or lacerations were consistently more likely to have a PPH, although the magnitude of this effect varied from a 10% increase in odds to more than seven fold.

Of the five HRoB studies, three reported a significant increase in the odds of PPH among women who had perineal/genital tract trauma, compared with those without, with moderate to large effect sizes.

Comparisons of the degree of tearing were performed in seven studies, six of which reported a significant increase in risk of PPH in the more severe categories compared with the less severe categories of tear.

Four studies examined cervical tearing and PPH or SPPH, with three reporting significantly increased risk among women who had cervical tearing. The study that did not report a significant increase was small (N=786) with only 5 cases and 2 controls having cervical lacerations. The two studies that reported statistically significant increases after adjustment for other factors were both large but reported markedly different magnitudes of effect among women with cervical lacerations (aOR=4.0; 95% CI 2.3-7.0 and 26.7; 95% CI 23.6-30.1).

There was a high degree of heterogeneity in the way perineal trauma was categorised, but given that most analyses (76%) found a significantly higher risk of PPH/SPPH with increased degree of

perineal/cervical trauma after adjustment for other variables, it is considered very likely that this is an independent risk factor for PPH/SPPH.

Rating: Very likely - More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Table 2.45 Included studies investigating as perineal status a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Bais, 2004	**PPH 1:** Laceration ≥ first degree: 1.40 (1.04-1.87) No or first degree laceration: ref **PPH 2:** Laceration ≥ first degree: 2.55 (1.57-4.18) No or first degree laceration: ref	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Bais, 2004	**PPH 1:** Tear ≥ second degree: 1.45(1.10-1.90) No or first degree laceration: ref **PPH 2:** Tear ≥ second degree: 1.84(1.08-3.12) No or first degree laceration: ref	uOR uOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Biguzzi, 2011	Genital tract lacerations: 1.65 (1.32-2.07) no genital tract laceration: ref	aOR	Sig	VB	**PPH:** EBL ≥500mL	6,011	Low
Biguzzi, 2014	Genital tract lacerations: 2.08 (1.47-2.94) No lacerations: ref	aOR	Sig	VB	**PPH:** EBL ≥500mL	3,219	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Buzaglo, 2014	Cervical tear: PPH: 8.7% CTL: 0.4%	%	Sig	VB	**PPH:** EBL ≥500mL	56,394	Low
Buzaglo, 2014	Perineal tear: Grade 2: 2.5 (1.9-3.3) Grade 3: 5.2 (2.5-10.6)	aOR	Sig	VB	**PPH:** EBL ≥500mL	56,394	Low
Combs, 1991a	Cervical/vaginal laceration: 4.20 (0.73-7.91) none: ref	aOR	Sig	CS	**PPH:** Haematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588	Low
Combs, 1991b	Cervical/vaginal/perineal laceration: 2.05 (1.45-2.90) none: ref	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Davey, 2019	**All women:** 3rd or 4th degree perineal laceration: 2.42 (2.1-2.8) **Women who experienced labour:** na	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Dionne, 2015	**Perineal tears** **PPH 1:** 1.63 (1.29-2.06) **PPH 2:** 2.09 (1.53-2.86)	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048	Low
Ford, 2007	**Perineal trauma** **1994-1995** 1.10 (1.04-1.16) **2002** 1.13 (1.05-1.21)	aOR aOR	Sig Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low
Fukami, 2019	Severe vaginal/perineal laceration: No: ref 1.98 (1.12-3.31)	aOR	NS	VB	**PPH:** CBL ≥1000mL	1,608	Low
Henry, 2005	**PPH 1:** Sutures: 3.00 (1.59-5.66) No: ref **PPH 2:** Sutures: 2.92 (1.21-7.07) No: ref	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Hiersch, 2016	**Degree of perineal tear** **PPH:** I: 0.7% II: 10.5% III: 2.4% IV: 0% **CTL:** I: 6.2% II:8.6% III: 1.0% IV: 0% p < 0.001	%	Sig	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Vaginal/perineal laceration: 7.6 (6.9-8.3)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low
Kaufner, 2016	laceration: 0.99 (0.44-2.221) No: ref	uOR	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217	Low
Khireddine, 2012	**CTL:** Perineal tears: 501 (28.7%) **PPH 1:** Perineal tears: 1345 (30.05) **PPH 2:** Perineal tears: 317 (28.2%)	%	NS	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Koopmans, 2014	No rupture: ref First or second degree: 0.80 (0.52-1.5) Third or fourth: 1.06 (0.24-4.8) Episiotomy: 1.5 (0.95-2.4)	aOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014	Low
Kramer, 2011	**PPH:** None: ref Uterine: 3.8 (2.4-6.2) Cervical: 4.0 (2.3-7.0) Other (vaginal, perineal): 1.1 (1.0-1.2) **SPPH:** None: ref Uterine, Cervical, Other (vaginal, perineal): 0.7 (0.2-2.8)	aOR aOR	Sig NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lisonkova, 2016	**PPH:** Perineal tear (3rd/4th): 29 (7.92%) Cervical laceration: 5 (1.31%) **CTL:** Perineal tear (3rd/4th): 12 (3.20%) Cervical laceration: 2 (0.52%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Magan, 2005a	**Emergency CS:** PPH: 4.80 (1.41-13.74) SPPH: 4.53 (0.90-22.70)	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837	Low
Magan, 2005b	Genital tract trauma at delivery: 1.7 (1.4-2.1)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Mehrabadi, 2013	High vaginal laceration: 5.27 (4.52-6.14)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Mehrabadi, 2013	Cervical laceration: 26.7 (23.6-30.1)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Mehrabadi, 2013	Perineal tear (3rd/4th): 2.35-2.34)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Miller, 2017	**PPH:** Genital tract laceration: 117 (73.6%) **CTL:** Genital tract laceration: 240 (75.5%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Rossen, 2010	**VB** Sphincter rupture: 1.6 (1.2-2.0)	aOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
Salkeld, 2008	**PPH:** Perineal laceration or other gynaecologic laceration: 966 (39.3%) **CTL:** Perineal laceration or other gynaecologic laceration: 8421 (35.2%)	%	Np	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943	High
	PPH: Other obstetric trauma: 86 (3.5%) **CTL:** Other obstetric trauma: 275 (1.1%)	%	Np				
Sharp, 2014	Genital trauma or episiotomy: 9.61 (2.15-42.02)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	25,322	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Sheiner, 2009	**PPH 1:** Lacerations: 24.8% **PPH 2:** Lacerations: 28.2% **PPH 3:** Lacerations: 32.7% **CTL:** Lacerations: 14.6%	%	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **SPPH:** 199 **CTL:** 153,645	Low
Sheiner, 2009	Lacerations PPH: 2.4 (2.0-2.8)	aOR	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645	Low
Stones, 1993	Perineal tears: 1.41 (0.01-2.18)	uRR (99% CI)	NS	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
van Stralen, 2016	Rupture >2nd degree: 1.71 (1.66-1.76)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
von Schmidt, 2013	No episiotomy, no perineal tear: ref No episiotomy, perineal tear: 1.92 (1.83-2.01) Episiotomy, no perineal tear: 1.69 (1.66-1.71) Episiotomy, perineal tear: 2.68 (2.46-2.92)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.9.3 Episiotomy

Episiotomy was evaluated as a potential risk factor for PPH in 16 studies, 14 of which were considered LRoB. No studies evaluated episiotomy and SPPH. Of 16 LRoB analyses, across 14 studies, 11 (69%) found a significant association. Nine LRoB analyses found a higher risk of PPH among women who had an episiotomy, compared with those who did not, after adjustment for confounding factors, but the remaining two analyses found episiotomy to be protective for PPH. Both of these studies included a large population, one in Switzerland the other in Canada (aOR=0.9; 95% CI 0.8-0.9 and 0.93; 95% CI 0.87-0.99, respectively). Two HRoB studies examined episiotomy at the univariable level and both reported a statistically significantly higher risk of PPH among women who had an episiotomy, compared with those who did not. The magnitude of the effect of episiotomy varied but was generally modest, ranging from aOR 1.3 to 2.6. Considering that most studies reported an increased risk of PPH but that two found a protective effect, after adjustment for other variables, it is unclear whether episiotomy is a risk factor for PPH.

Rating: Unclear: Between 50% and 80% of LRoB analysis found a significant association, but in conflicting directions.

Table 2.46 Included studies investigating episiotomy as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Bais, 2004	**PPH 1:** No or first degree laceration: ref Episiotomy: 2.18 (1.69-2.81) **PPH 2:** No or first degree laceration: ref Episiotomy: 2.01 (1.26-3.22)	aOR uOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Biguzzi, 2011	No episiotomy: ref midline episiotomy: 1.35 (1.01-1.81) midlateral episiotomy: 2.48 (1.95-3.17)	aOR	Sig	VB	**PPH:** EBL ≥500mL	6,011	Low
Biguzzi, 2014	Episiotomy: 2.66 (1.94-3.64) No episiotomy: ref	aOR	Sig	VB	**PPH:** EBL ≥500mL	3,219	Low
Bonnet, 2013	**Canada:** Episiotomy: 0.93 (0.87-0.99) no episiotomy: ref **France:** Episiotomy: 1.39 (1.23-1.57) no episiotomy: ref	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	Low
Buzaglo, 2014	Episiotomy PPH: 39.6% CTL: 49.2%	%	Sig	VB	**PPH:** EBL ≥500mL	56,394	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Combs, 1991b	Mediolateral: 4.67 (2.59-8.43) None/midline: ref	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Combs, 1991b	Midline: 1.58 (1.12-2.23) none/mediolaternal: ref	aOR	Sig	VB	**PPH:** Hematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 374 **CTL:** 1,122	Low
Dionne, 2015	**PPH 1:** Episiotomy: 1.74 (1.38-2.18) no episiotomy: ref	aOR	Sig	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048	Low
	PPH 2: Episiotomy: 2.62 (1.91-3.59) no episiotomy: ref	aOR	Sig		**PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL		
Hiersch, 2016	Episiotomy: 1.25 (0.81-1.93)	aOR	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Episiotomy: 0.9 (0.8-0.9)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Khireddine, 2012	**CTL:** Episiotomy: 551 (31.6%) **PPH 1:** Episiotomy: 2027 (45.3%) **PPH 2:** Episiotomy: 611 (54.3%)	%	Sig	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125	Low
Magan, 2005a	**Emergency CS:** **Vaginal/cervical operation** PPH: 2.66 (1.29-5.08) SPPH: 0.77 (1.21-2.85)* *Note: incompatible OR and CI are reported in the study. Unable to verify results.	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837	Low
Miller, 2017	Episiotomy: 1.80 (0.77-4.21)	aOR	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318	Low
Rossen, 2010	**VB** Episiotomy: 1.3 (1.1-1.5)	aOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Sheiner, 2009	**PPH 1:** Episiotomy: 31.2% **PPH 2:** Episiotomy: 23.9% **PPH 3:** Episiotomy: 27.6% **CTL:** Episiotomy: 23.6%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645	Low
Stones, 1993	Episiotomy: 2.06 (1.36-3.11)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
van Stralen, 2016	Episiotomy: 1.64 (1.62-1.66)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High

2.4.9.4 Presentation

Ten studies explored the association between the baby's presentation and PPH/SPPH, all of which were considered LRoB. There were different categorisations of this risk factor between studies but generally studies compared vertex/cephalic presentation to non-vertex/cephalic presentation. Of the nine LRoB analyses of presentation and PPH, two (22%) found a statistically significant association at the multivariable level. One of these (52) investigated 'compound presentation' and found a higher risk of PPH compared with non-compound presentation (aOR=3.0; 95% CI 1.1-7.3). The other study (12) reported that compound and transverse presentations were associated with a higher risk of PPH (aOR=1.9; 95% CI 1.03-3.3 and 3.4; 95% 2.3-5.1, respectively), while breech presentation was associated with a lower risk of PPH (aOR=0.7; 95% CI 0.5-0.9), after adjustment for confounding factors.

Of the three LRoB studies that examined presentation and SPPH, two found a significant association at the multivariable level, with one reporting that transverse presentation was associated with a higher risk of SPPH compared with cephalic presentation (aOR=7.3; 95% CI 1.8-30.0) and the other reporting that non-cephalic presentation was associated with a twelve-fold increase in the odds of SPPH (aOR=12.48; 95% 1.29-121.24). The latter study only included women with incomplete placenta praevia and included just 210 patients in South Korea. With just four (33%) of the twelve LRoB analyses finding a significant association at the adjusted level, it is unclear whether presentation is a risk factor for PPH/SPPH.

Rating: Unclear - Less than 50% of LRoB analyses found a significant association.

Table 2.47 Included studies investigating presentation as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Hiersch, 2016	**PPH:** Persistent occiput posterior: 22.4% **CTL:** Persistent occiput posterior: 22.5% p=1.074	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kramer, 2011	**PPH:** Cephalic: ref Breech: 0.7 (0.5-0.9) Transverse: 3.4 (2.3-5.1) Compound: 1.9 (1.03-3.3) Oblique: 1.2 (0.4-4.0) Other: 0.6 (0.1-2.5) **SPPH:** Transverse: 7.3 (1.8-30.0) All other presentations: ref	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low
Lee, 2017	Non-cephalic presentation: 12.48 (1.29-121.24) Cephalic presentation: ref	aOR	Sig	CS	**SPPH:** intraoperative blood loss ≥2000mL	210	Low
Lee, 2018	Non-cephalic presentation: 3.41 (1.40-8.30)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Lisonkova, 2016	**PPH:** Cephalic: 358 (96.5%) Breech: 8 (2.16%) Transverse: 4 (1.08%) Compound: 0 Oblique: 1 (0.27%) **CTL:** Cephalic: 351 (95.38%) Breech: 16 (4.08%) Transverse: 1 (0.27%) Compound: 1 (0.27%) Oblique: 0	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Magan, 2005b	Compound presentation: 3.0 (1.1-7.3)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Rossen, 2010	**VB** Occiput posterior position: 1.1 (0.6-1.4)	aOR	NS	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
Rossen, 2010	**VB** Breech: 0.9 (0.6-1.4) **CS** Breech: 0.8 (0.5-1.2)	aOR aOR	NS NS	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Sheiner, 2009	**PPH 1:** Non-vertex presentation: 7.3% **PPH 2:** Non-vertex presentation: 3.9% **PPH 3:** Non-vertex presentation: 5.0% **CTL:** Non-vertex presentation: 5.0%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645	Low
Suzuki, 2007	Vertex-vertex presentation: 1.72 (0.70-4.24)	uOR	NS	CS	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 137	Low
von Schmidt, 2013	Vertex: ref Breech: 0.80 (0.77-0.83) Other: 1.54 (1.42-1.66)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.9.5 Retained placenta/manual removal of placenta

Retained placenta or manual removal of placenta (MROP) was explored as a risk factor for PPH in ten studies. No studies examined the association between retained placenta/MROP and SPPH. Of the eight LRoB studies, six reported a higher risk of PPH among women who had a retained placenta or MROP. The magnitude of the effect was very large for most studies with aORs ranging from 3.5 to 21.3. The two LRoB studies that did not report a significant association at the adjusted level reported significant results at the univariable level.

Both HRoB studies reported a significant association with the risk of PPH being markedly higher among women who had a retained placenta (uRR 5.15; 99% CI 3.36-7.87) and MROP uOR 29.30 (95% CI 28.78-29.83) but these were not adjusted for potential confounding factors.

Given that all studies that examined this risk factor found a significant association, it is considered very likely that retained placenta/MROP is an independent risk factor for PPH.

Rating: Very likely - More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Table 2.48 Retained placenta/manual removal of placenta

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Bais, 2004	**PPH 1:** 7.83 (3.78-16.22) **PPH 2:** 11.73 (5.67-24.1)	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Biguzzi, 2011	Retained placenta: 9.21 (5.09-16.68) no retained placenta: ref	aOR	Sig	VB	**PPH:** EBL ≥500mL	6,011	Low
Biguzzi, 2014	Retained placenta: 10.0 (4.34-20.0)	aOR	Sig	VB	**PPH:** EBL ≥500mL	3,219	Low
Briley, 2013	Retained placenta: 21.3 (8.31-54.7)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	9,937	Low
Rossen, 2010	**VB** Retained placenta: 3.9 (3.0-4.9)	aOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
Sheiner, 2009	**PPH 1:** MROP: 1.5% **PPH 2:** MROP: 2.1% **PPH 3:** MROP: 6.0% **CTL:** MROP: 0.5%	%	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Sheiner, 2009	Retained placenta: PPH: 3.5 (2.1-5.8)	aOR	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH 2:** 330 **PPH 3:** 199 **CTL:** 153, 645	Low
Stones, 1993	Retained placenta: 5.15 (3.36-7.87)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
van Stralen, 2016	MROP: 29.30 (28.78-29.83)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	MROP: 33.39 (32.62-34.19)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.10 Baby characteristics

2.4.10.1 Birthweight

Thirty-seven studies examined the relationship between birthweight and PPH/SPPH, 29 of which were considered LRoB. Most studies categorised birthweight dichotomously, comparing larger birthweights with smaller birthweights, albeit with varying cut-offs. A small number of studies compared mean birthweight in grams, while others used three or four categories of birthweight to analyse this risk factor.

Of the 26 LRoB analyses that investigated birthweight and PPH, 18 were significant at the adjusted level with all reporting that higher birthweight, however defined, was associated with a higher risk of PPH, compared with lower birthweight. Typically, 4000g was the highest category of birthweight examined and was associated with higher magnitudes of effect than lower birthweight categories. Two studies reported that low birthweight was associated with increased risk of PPH, but did not adjust for confounding factors.

Three studies examined birthweight for gestational age with one reporting that low birthweight for gestational age was associated with higher odds of PPH, after adjustment for confounding factors (aOR=1.9; 95% CI 1.6-2.4). Because birthweight for gestational age is distinct from birthweight, these three studies were not included in the rating of birthweight as a potential risk factor.

Eight LRoB studies explored the association between birthweight and SPPH, with three finding a significant positive association between larger birthweights and SPPH. One large study (N=364,701) found that macrosomia (birthweight ≥4000g) was associated with an 82% and 88% increase in the odds of SPPH among all women and women who experienced labour, respectively. In a smaller study (N=3,123), birthweight ≥4,500g was associated with a 46% increase in the odds of SPPH, compared with birthweight <4500g, after adjustment for confounding factors (aOR=1.46; 95% CI 1.01-2.12). The

third study reporting a significant association between birthweight and SPPH found more than twice the odds with birthweight >4kg, compared with less than 4kg (aOR=2.26; 95% CI 1.16-4.41).

Rating: Very likely - More than 60% of LRoB analyses found a significant association. All significant results were in in the same direction.

Table 2.49 Included studies investigating birthweight as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Allen, 1988	Normal vaginal delivery: Birthweight ≤ 4000g: 3.6% Birthweight >4000g: 6.1% Instrumental delivery: Birthweight ≤ 4000g: 12.8% Birthweight >4000g: 20.2% CS: Birthweight ≤ 4000g: 14.3% Birthweight >4000g: 22.7%	% (incidence of PPH by category)	Sig	VB, CS	**PPH:** EBL ≥600mL within 24 hours of delivery	34,935	High
Bais, 2004	**PPH 1:** >4kg: 2.11 (1.62-2.76) **PPH 2:** >4kg: 2.55 (1.57-4.18)	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL <1000mL **PPH 2:** EBL ≥1000mL	3,464	Low
Bonnet, 2013	**Canada:** ≤2500g: 0.79 (0.68-0.92) 2501-3999g: ref ≥4000: 1.74 :(1.63-1.86) Missing: 0.82 (0.83-1.02) **France:** ≤2500g: 0.73 (0.54-1.00) 2501-3999g: ref ≥4000: 1.90 (1.54-2.34)	aOR aOR	Sig Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	**France:** 146,781 **Canada:** 205,842	Low
Briley, 2013	Maximum birthweight (kg): 2.19 (1.62-2.99)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	9,937	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Davey, 2019	**All women:** Macrosomia (≥4000g) : 1.82 (1.7-2.0) **Women who experienced labour:** macrosomia (≥4000g): 1.88 (1.7-2.0)	OR aOR	Sig Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701	Low
Dionne, 2015	**PPH 1:** ≤3000: 0.67 (0.54-0.84) 3001-3500: ref 3501-4000: 1.24 (0.99-1.54) 4000: 2.23 (1.37-3.61) **PPH 2:** ≤3000: 0.66 (0.49-0.89) 3001-3500: ref 3501-4000: 1.26 (0.96-1.65) 4000: 2.8 (1.61-4.86)	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048	Low
Eto, 2016	**PPH:** 3241.2 (380.9) **CTL:** 3105.4 (351.9) p < 0.001 **PPH2:** 3294.0 (380.1) **CTL:** 3123.5 (358.7) p < 0.001 **PPH3:** 3335.1 (397.6) **CTL:** 3129.3 (359.5) p <0.001	Mean(SD)	Sig	VB	**PPH 1:** EBL ≥500g **PPH 2:** EBL ≥800g **PPH 3:** EBL >1000g	**CTL:** 2,524 **PPH 1:** 524 **PPH 2:** 147 **PPH 3:** 158	High

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Farina, 2017	**PPH:** 3692g (237) **CTL:** 3387 (425) **p=**0.006	Mean dif	Sig	VB	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390	High
Firmin, 2019	<2500g: 0.37 (0.15-0.92) 2500-4000g: ref >4000g: 6.38 (1.97-20.67)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154	Low
Ford, 2007	**1994-1995** <3500: ref 3500-<4000: 1.49 (1.41-1.57) 4000-<4500: 2.09 (1.95-2.24) ≥4500: 2.74 (2.40-3.12) **2002** <3500: ref 3500-<4000: 1.34 (1.26-1.44) 4000-<4500: 1.82 (1.66-1.99) ≥4500: 2.55 (2.15-3.03)	aOR aOR	Sig Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374	Low
Fukami, 2019	**CTL:** <2499: 21.4% 2500-3499: 69.6% 3500-3999: 7.9 % >4000: 1.0% **PPH:** <2499: 2.2% 2500-3499: 72.0% 3500-3999: 21.5% >4000: 4.3%	%	Sig	VB	**PPH:** CBL ≥1000mL	1,608	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Hiersch, 2016	**PPH:** SGA <10th percentile: 4.7% **CTL:** SGA <10th percentile: 6.3% p=0.39	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Hiersch, 2016	**PPH:** LGA >90th percentile: 10.8% **CTL:** LGA >90th percentile: 6.8% p=0.03	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Kaelin Agten, 2017	Fetal macrosomia: 1.6 (1.6-1.7)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Khireddine, 2012	**CTL:** <3000:350 (20.1%) 3000-3499: 757 (43.%) 3500-3999: 519 (29.8%) ≥4000: 116 (6.7%) **PPH 1:** <3000: 576 (12.9%) 3000-3499: 1747 (39.1%) 3500-3999: 1611 (36.0%) ≥4000: 535 (12.0%) **PPH 2:** <3000: 130 (11.5%) 3000-3499: 439 (39.0%) 3500-3999: 419 (37.2%) ≥4000: 138 (12.3%)	%	Sig	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125	Low
Kramer, 2011	**PPH:** < 2500: 0.6 (0.4-0.8) 2500-3999: ref 4000-4499: 1.8 (1.6-2.1) ≥4500: 2.2 (1.6-2.8) **SPPH:** < 2500: 1.0 (0.2-5.4) 2500-3999: ref ≥4000 1.2 (0.4-3.6)	aOR aOR	Sig NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Lee, 2017	Small for gestational age: 0.92 (0.06-13.39)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210	Low
Lee, 2018	Birthweight (g): 1.00 (1.00-1.01)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506	Low
Lisonkova, 2016	**PPH:** Macrosomic baby (4500g): 16 (4.21%) **CTL:** Macrosomic baby (4500g): 6 (1.60%)	%	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Looft, 2017	**All:** <2500: 598 2500-2999: 6525 3000-3499: 22203 3500-3999: 20509 4000-4499: 6486 ≥4500: 910 Missing: 36 **PPH:** <2500: 95 2500-2999: 1194 3000-3499: 5291 3500-3999: 6699 4000-4499: 2757 ≥4500: 503 Missing: 15	n	NA	VB	**PPH:** EBL ≥500mL	57,267	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Magan, 2005a	**Birthweight > 4kg** **Emergency CS:** PPH: 2.45 (1.60-3.71) SPPH: 2.26 (1.16-4.41)	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837	Low
Magan, 2005b	Birthweight >4kg: 1.8 (1.4-2.3)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868	Low
Malabarey, 2011	PPH: 3375g (400) CTL: 3275g (494) P=0.002	Mean (SD)	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Mehrabadi, 2013	Large fetus: 1.78 (1.60-1.98)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425	Low
Merriam, 2018	**PPH 1:** Suspected macrosomia: 1.57 (1.53-1.61) **PPH 2:** Suspected macrosomia: 1.05 (1.01-1.10)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088	Low
Noguchi, 2017	**PPH:** Low birth weight: 9 **CTL:** Low birth weight: 340	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829	High
Nyflot, 2016	SPPH: 3612g (3196-3966) CTL: 3480g (3152-3840)	Median (IQR)	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82	Low
Nyflot, 2017a	Birthweight >4500g: 1.46 (1.01-2.12)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Nyflot, 2017b	Birthweight: 1.82 (1.21-2.71)	uOR	Sig	VB, CS (unplanned only)	**SPPH:** EBL ≥1500mL	**SPPH:** 859 **CTL:** 1,755	Low
Oberg, 2014b	High birthweight (≥4000g): 1.82 (1.75-1.89)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Rossen, 2010	**VB** ≥4000g: 2.0 (1.8-2.4) **CS** ≥4000g: 1.8 (1.2-2.6)	aOR aOR	Sig Sig	VB, CS	**PPH:** EBL ≥1000mL	41,365	Low
Sharp, 2014	High birthweight (≥4kg): 1.87 (1.27-2.67)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	25,322	Low
Sharp, 2014	Low birthweight (≤2.5kg): 1.11 (0.88-1.39)	uOR	NS	VB, CS	**PPH:** EBL ≥500mL	25,322	Low
Sheiner, 2009	Low for gestational age: PPH: 1.9 (1.6-2.4)	aOR	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645	Low
Stones, 1993	>4kg: 1.9 (1.38-2.6)	uRR (99% CI)	Sig	VB, CS	**PPH:** EBL ≥1000mL	37,334	High
Suzuki, 2007	Twins Combined neonatal birthweight >5,500 g: 2.53 (1.00-6.45)	uOR	Sig	CS	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 142	Low

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Suzuki, 2012	**Singletons:** <2500: 3.22 (1.9-5.5) 2500-3499: ref ≥3500: 1.64 (0.56-4.8) **Twins:** (combined weight) < 4000:0.42 (0.14-1.3) 4000-5499: ref ≥5500: 1.06 (0.33-3.4)	uOR uOR	Sig NS	CS	**PPH:** PPH requiring transfusion	Singletons: 17,405 Twins: 916	Low
van Stralen, 2016	<3000: 1.04 (1.02-1.05) 3000-3999: ref ≥4000: 1.59 (1.56-1.61)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	2,406,784	High
von Schmidt, 2013	≤999g: 2.08 (1.96-2.23) 1000-1999g: 1.48 (1.41-1.56) 2000-2999g: 1.01 (0.99-1.03) 3000-3999g: ref ≥4000g: 1.59 (1.56-1.62)	uOR	Sig	VB, CS	**PPH:** EBL ≥1000mL	1,457,576	Low

2.4.10.2 Sex of the baby

Sex of the baby was explored as a potential risk factor for PPH by five studies. Of these, three were considered LRoB. No LRoB studies reported a significant association between sex of the baby and risk of PPH.

The two HRoB studies both found that female sex was associated with a small increase in the risk of PPH, however, these results were not adjusted for potential confounding factors.

With no LRoB studies reporting a significant association between sex of the baby and PPH, sex is not considered to be an independent risk factor.

Rating: Not a risk factor - No LRoB analyses found a significant association.

Table 2.50 Included studies investigating sex of the baby as a potential risk factor for postpartum haemorrhage

Author, year	Effect size & definitions	Stat	Sig	Birth mode	Definition of PPH	Number of women	RoB
Hiersch, 2016	**PPH:** Male: 59.6% **CTL:** male: 55.6% p=0.24	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154	Low
Lisonkova, 2016	**PPH:** Male: 194 (50.79%) **CTL:** Male: 184 (48.04%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393	Low
Malabarey, 2011	Female: 1.3 (1.03-1.7)	uOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL	15,198	High
Oberg, 2014b	Female: 1.08 (1.04-1.11)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756	High
Sheiner, 2009	**PPH 1:** Male: 54.0% Female: 46.0% **PPH 2:** Male: 47.3% Female: 52.7% **PPH 3:** Male: 48.2% Female: 51.8% **CTL:** Male: 51.2% Female: 48.8%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645	Low

2.5 Discussion

2.5.1 Summary

This systematic review summarised the existing research evidence relating to risk factors for PPH in high-income countries. It highlights the range of definitions of PPH and SPPH used in different contexts and the significant heterogeneity in terms of the definitions, measurement and categorisation of risk factors explored between studies. The incidence of PPH and SPPH varied greatly across studies, which suggests differences in the underlying risk profiles of the populations as well as methodological diagnostic differences between settings.

This review confirms that there is strong evidence for a number of factors that are regarded as well-established risk factors for PPH (35, 43, 44), including previous PPH, multiple pregnancy, instrumental birth, perineal trauma and high birthweight. However, the results also call into question the strength of the evidence for some other factors that may also be regarded as 'known' risk factors for PPH, but for which the evidence was unclear, often with inconsistent associations across different LRoB studies. Factors such as advanced maternal age, obesity or high BMI, augmentation of labour and caesarean birth are commonly referred to as known risk factors for PPH (35, 83). However, these factors were all classified as 'Unclear' in this review because either only a minority of LRoB analyses reported a statistically significant association after adjustment for potential confounders, or statistically significant associations were in opposing directions.

The findings also emphasise the need for further research investigating risk factors for women who might otherwise be considered at low-risk of PPH, including women who plan birth in midwifery units. Almost all studies were conducted in hospital settings highlighting the need for further research into PPH occurring in other birth settings.

2.5.2 Strengths and limitations

A major strength of this systematic review was the thorough approach to searching for relevant articles. The comprehensive search for articles, across three databases, reduced the likelihood that relevant articles were missed by the search. Additionally, two reviewers performed full-text screening, data extraction, and risk of bias assessment, which reduced the potential for errors and research bias at each of these stages of the review.

Another strength was the pragmatic approach to the definition of PPH/SPPH, which enabled the inclusion of a greater number and wider range of studies. Since the definition of PPH/SPPH varies by region and country, including all definitions of PPH/SPPH reduced the chances of biasing the review towards a particular country or region. However, while important for expanding the range of studies eligible for inclusion, the wide range of definitions of PPH contributed to difficulties comparing the findings across studies. It is plausible, for example, that risk factors for PPH defined as blood loss ≥500mL have a different level of magnitude of effect compared with risk factors for PPH ≥1000mL. The decision to combine different definitions as one outcome may have obscured true differences in the magnitude or profile of risk factors related to differences in the severity of the pathology.

Similarly, the pragmatic approach to classifying risk factors was a strength if the study as it enabled synthesis of findings for risk factors that were measured or defined in different ways but examined broadly similar concepts. This allowed a more comprehensive overview of the risk factors than would have been possible with a narrow approach to determining comparability of risk factor categories and definitions.

The structured and transparent method of assessing the strength of the evidence of each risk factor was also a major strength of this study. Using a modified version of the rubric developed by Ende and colleagues (78) enabled a qualitative assessment of the strength of the evidence, without pooling the

magnitude of effect across studies, which was considered inappropriate given the level of heterogeneity in the conduct of studies. Counting only adjusted effect measures was also a strength of this approach as it meant the ratings were more meaningful than also including unadjusted associations. This approach was considered particularly important in light of the correlation of many risk factors for PPH.

Studies also had a range of inclusion/exclusion criteria and it is difficult to determine the impact this may have on the magnitude of effect estimated for each risk factor investigated. It is not possible to determine, therefore, whether the results for a given risk factor may have been different had included studies used different inclusion criteria. The heterogeneity of inclusion criteria, as well as the underlying risk profile of the population and differences in obstetric practices between settings, makes it difficult to compare across studies.

All of the studies included in this review were, due to the nature of the research question, observational and inherent in this study design is the potential for bias and residual confounding (140). While the narrative synthesis aimed to minimise the effect of confounding by including only adjusted results in the 'counting' of significant findings, studies each adjusted for different potential confounding variables and it is not possible to determine the impact this, or the effect of unmeasured variables, had on the observed effect measures.

The potential for publication bias should also be acknowledged as a possible limitation and this was not formally examined. However, given the nature of the study designs and the research questions addressed by the included studies in this review, publication bias seems likely to be limited. Almost all of the included studies were designed to explore the association between a range of risk factors and the occurrence of PPH. This is a product of the review inclusion criteria specifying that studies analyse risk factors for PPH by comparing women who had a PPH with women who did not. It is likely that

studies with this design investigating multiple potential risk factors would identify some significant associations and would therefore be likely to be published. This stands in contrast to study designs that examine the association between a single exposure and outcome, for which a non-significant association might be more likely (given only one hypothesis is being tested) and therefore more likely to result in non-publication.

A further limitation is the exclusion of studies that were not published in English, which was necessary given the language skills of the reviewers and the resources available. This exclusion likely contributed to bias towards English-speaking countries and institutions. It may not be possible, therefore, to generalise the results of this systematic review to non-English-speaking countries.

Finally, midwifery and obstetric practices, for example, the management of the third stage of labour, would have differed between study settings and over time. Unfortunately, it was not possible to capture this information for each study and therefore this information could not be considered in the context of identified risk factors.

2.6 Conclusions

This systematic review of 53 published articles provides a comprehensive synthesis of the evidence about risk factors for PPH in high-oncome countries. The results reveal considerable heterogeneity between studies in terms of the definitions and measurement of PPH and SPPH, and the investigation and categorisation of risk factors. This heterogeneity was reflected in the high degree of inconsistency of results for many factors, including those that have been previously regarded as well-established risk factors for PPH. Several risk factors emerged as likely or very likely to be independently associated with PPH and the strength of this evidence is considered high in light of the high degree of heterogeneity.

The majority of studies were based in obstetric settings and by necessity included a high proportion of higher risk women. These findings underscore the importance of further research into risk factors for PPH among women who are considered low-risk, including those who give birth in midwifery units. Addressing this gap, the next chapter of this thesis presents a case-control study investigating risk factors for PPH among women who give birth in midwifery units in the UK.

Chapter 3: Incidence and risk factors for postpartum haemorrhage in midwifery units in the UK: a case-control study

3.1 Introduction

Women who plan to give birth in midwifery units (MUs) are less likely to develop complications during labour and birth, including PPH (141). However, women who plan birth in MUs can still experience PPH; some after transfer to obstetric care prior to birth and some after giving birth in an MU (92, 141). For women who give birth in MUs, there may be a delay in access to medical treatments for PPH, such as blood products or an operating theatre, particularly in FMUs where transfer to obstetric care requires traveling to a different location. Currently, there is limited evidence about the incidence of PPH occurring in MUs, the risk factors associated with PPH among women who give birth in MUs, and the outcomes for women who experience PPH in these settings. To ensure the safety of birth in MUs, it is crucial to identify women who may be at a higher risk of experiencing PPH and promptly diagnose and manage any cases that arise. Such evidence would be valuable in guiding decision-making for women who are considering or planning to give birth in an MU and for the healthcare professionals responsible for their care.

3.2 Researcher roles

This study was designed by Rachel Rowe (RR) and the UKMidSS Steering Group (see Appendix B.1 for members) prior to the involvement of the author. The data collection form was also developed by RR, in consultation with the UKMidSS Steering Group. Email reminders and data queries were coordinated by the UKMidSS Research Midwife, Alessandra Morelli (AM). The author developed the data analysis plan, cleaned the dataset, conducted the data analysis, interpreted the data and wrote up the findings.

3.3 Aims and objectives

The aim of this study was to estimate the occurrence and outcomes of PPH occurring in MUs in the UK and requiring transfer to obstetric care (referred to below as 'PPH requiring transfer'), to inform

midwifery care policy and practice and ultimately improve outcomes for women planning birth in MUs and their babies. The objectives were to:

Estimate the incidence of PPH requiring transfer, occurring in MUs

Investigate and identify the pre-existing factors, as well as aspects of labour progress, care and management, associated with PPH requiring transfer among women giving birth in MUs

Identify aspects of labour progress, care and management of PPH that are associated with poor and good outcomes for mothers, and their babies, following PPH requiring transfer in MUs

3.4 Methods

3.4.1 Study design

This was a national population-based case-control study of all women who gave birth in an MU in the UK between September 2019 and February 2020 and who experienced a PPH requiring transfer to obstetric care. A case-control design was chosen because of the relative rarity of PPH among women giving birth in MUs (141). The study was intended to run for 12 months, however, due to the onset of the COVID-19 pandemic, and following guidance from the funder, data collection was terminated in March 2020 after six months.

3.4.2 Data collection

Anonymised information from AMUs and FMUs across the UK was collected using the UK Midwifery Study System (UKMidSS), a national research infrastructure established in 2015 and designed to support national observational studies of relevance to midwifery-led care (142). All 127 AMUs and all 79 FMUs in the UK were invited to collect data for the study. The UKMidSS comprises a network of midwife 'reporters' in all UK MUs, who report monthly data about admissions, births and 'cases' for UKMidSS studies, and a secure web-based administrative and data entry system, facilitating anonymised data entry by reporters directly from medical records.

Midwife reporters identified cases and corresponding controls from their birth registers, medical records or electronic systems. Each month, reporters provided the number of cases meeting the eligibility criteria that occurred that month or reported a nil value if no cases were identified. This approach enabled non-responding units to be distinguished from units in which there were no cases for that month. Data about the number of births in each MU each month were reported at the same time, for the purpose of calculating the incidence of PPH requiring transfer. Once a case was reported, an electronic data collection form was generated in the secure online data entry system, OpenClinica, and anonymised data were entered about both the case and the control by reporters from women's notes or the hospital electronic patient record system.

Reminder emails were sent to reporters on a monthly basis for any monthly report that was more than 3 months overdue. Following the report of a case, if data entry for both case and control was not completed within 6 weeks, a reminder email was also sent. Monthly status emails were used to summarise monthly reporting and data entry completion and list data queries that were generated automatically in OpenClinica for missing or invalid data. This process was managed by AM.

3.4.3 Data and definitions

Data about maternal socio-demographic and clinical characteristics, care and progress during labour, birth, and maternal and neonatal outcomes were collected through the UKMidSS (Appendix B.1).

3.4.3.1 Cases and controls

Cases were identified as women who gave birth in an MU between 1st September 2019 and 29th February 2020, and who experienced a PPH requiring transfer, where the primary or secondary reason for transfer was PPH. Controls were selected as the women who did not meet the case definition who gave birth in the same MU, immediately before each case. One control was requested for each case.

In the UK, at the time of data collection, the definition of PPH was blood loss ≥500mL and blood loss volume was typically estimated visually (55), which is known to be inconsistent and inaccurate (54, 143). Considering the relatively high prevalence of blood loss ≥500mL and the uncertainty of its

diagnostic accuracy, a pragmatic definition of the primary outcome was chosen. This was intended to reduce the administrative burden on reporting midwives, compared with capturing all cases of blood loss ≥500mL, and to capture a level of severity of PPH that was considered high enough to warrant obstetric care.

3.4.3.2 Description and definition of variables collected

The data that were collected and corresponding definitions and categorisations for analysis are described in Table 3.1.

Table 3.1 Description and definitions of variables collected

Variable	Description and additional information
	Maternal sociodemographic characteristics
Maternal age	Maternal age at birth, provided as an integer and categorised for analysis as: • <20 • 20-24 • 25-29 • 30-34 • 35-49 • 40+
Smoking status	Self-reported smoking status: • Did not smoke during pregnancy • Smoked during pregnancy
Socioeconomic status	Women's and partners' occupations were collected as free-text variables and used to derive a measure of individual socio-economic status using the simplified derivation method (144). Responses were coded by ME using the Office for National Statistics Occupation Coding Tool, which allows users to code occupation titles against the Standard Occupational Classification 2010 (144). The recorded occupation for women and partners, provided as free text, was entered into the search bar in the coding tool and the associated National Statistics Socio-economic Classification (NS-SEC) code was assigned to the record. The three-class version of the NS-SEC was used for analysis (144). Additional categories were added for 'employment status unknown', 'employed, but occupation unrecorded/uncodable' and 'unemployed/student'. If a woman's occupation could not be coded, including those categorised as 'employment status unknown', 'employed, but occupation unrecorded/uncodable' and 'unemployed/student', the partners' NS-SEC was used to determine socioeconomic status. In the case that the partner's occupation was also unable to be categorised, the category assigned to the woman was used.

Variable	Description and additional information
Area-based deprivation	A measure of area-based deprivation, the Children in Low-income Families Measure (CLFM) (145), was derived using women's postcode of usual residence. The CLFM score represents the proportion of children in low-level geographies aged under 16 living in households in receipt of out of work benefits, or tax credits where their reported income is less than 60% of UK median income (145). This measure was chosen as, unlike some measures such as the Indices of Deprivation, it covers all of the UK, which was important for a nation-wide study. In order to ensure that data collected were anonymised, midwives entered women's postcodes into a bespoke 'look-up' website developed for the UKMidSS. This returned the corresponding CLFM score which midwives then copied and pasted into the electronic data collection form. Women were assigned to a quintile based on their CLFM score (1=least deprived and 5=most deprived).

Ethnicity	Ethnicity was provided as the following sub-categories below and categorised into the broader groups listed for the purposes of analysis:
	• White (UK and Ireland)
	  ○ White – English/Welsh
	  ○ White Irish
	• White (other)
	  ○ White – other
	• Asian
	  ○ Indian
	  ○ Pakistani
	  ○ Bangladeshi
	  ○ Chinese
	  ○ Asian - other
	• Black
	  ○ African
	  ○ Caribbean
	  ○ Black – other
	• Other
	  ○ Arab
	  ○ Mixed white and Black
	  ○ Mixed white and Asian
	  ○ Mixed Other
	  ○ Any other ethnic group

Pre-existing clinical and obstetric history characteristics	
BMI	BMI at booking was provided as an integer and categorised into the following: • < 18.5 • 18.5-24.9 • 25-29.9 • 30-35 • >35
Parity	Parity was categorised for the purposes of analysis into the following: • 0 • 1 • 2+

Variable	Description and additional information
Pre-existing medical risk factors	The following pre-existing medical risk factors were collected: • Essential hypertension • Confirmed cardiac disease • Thromboembolic disorder • Atypical antibodies • Hyperthyroidism • Diabetes • Renal disease • Epilepsy • Other[1]

Previous pregnancy complications	The following previous pregnancy complications were collected:
	• Primary postpartum haemorrhage needing treatment or transfusion
	• Previous complications other than PPH, comprising:
	  ○ Retained placenta requiring manual removal
	  ○ Caesarean
	  ○ Uterine surgery (excluding Caesarean)
	  ○ Other†

Pregnancy-related factors	
Current pregnancy problems	The following current pregnancy complications were collected: • BMI at booking >35kg/m^2 • Post-term (>42 weeks) • Anaemia (haemoglobin <105g/litre) • Group B Streptococcus • Antepartum haemorrhage • Pre-eclampsia / pregnancy induced hypertension • Gestational diabetes • Malpresentation (breech or transverse lie) • Other[1]
Sex of baby	Provided as: • Male • Female
Gestational age	Gestational age at the birth was provided as the number of weeks and grouped into the following categories: • 24-31 • 32-36 • 36-37 • 38 • 39 • 40 • 41+
Intrapartum factors	
Stage of labour at start of labour care	Provided in the following categories: • Latent stage • Active 1st stage • Passive 2nd stage • Active 2nd stage
Induction of labour	• Yes • No

Variable	Description and additional information
Maternal complications identified at the start of labour care	• Maternal tachycardia • Essential hypertension • Proteinuria • Maternal pyrexia • Vaginal blood loss • Prolonged rupture of membranes • Reported pain differing from pain normally associated with contractions
Fetal complications identified at the start of labour care	• Significant meconium • Abnormal presentation, including cord presentation • Transverse or oblique lie • High or free-floating head • Suspected fetal growth restriction or macrosomia • Suspected anhydramnios or polyhydramnios • Fetal heart rate abnormality • Deceleration in fetal heart rate • Reduced fetal movements in the last 24 hours
Maternal complications identified during labour (before birth)	• Maternal tachycardia • Hypertension • Maternal pyrexia • Vaginal blood loss • Prolonged rupture of membranes • Reported pain differing from pain normally associated with contractions
Fetal complications identified during labour (before birth)	• Significant meconium • Confirmed/suspected delay in first stage of labour • Confirmed/suspected delay in second stage of labour • Obstetric emergency • Abnormal presentation, including cord presentation • Transverse or oblique lie • High or free-floating head • Fetal heart rate abnormality • Deceleration in fetal heart rate
Labour/birth in water	Provided as Immersion in water for pain in labour (Yes/No) and Birth in water (Yes/No) and categorised for analysis as: • No immersion in water • Immersion in water for labour, land birth • Labour and birth in water
Birth-related factors	
Birth mode	• Spontaneous vertex birth • Vaginal breech • Instrumental (comprises vacuum and forceps)
Duration of 3rd stage of labour	Provided in minutes and categorised as • <60 minutes • ≥60 minutes
Perineal trauma	• <3rd degree tear or no tear • 3rd or 4th degree tear

Variable	Description and additional information
Syntocinon/ Syntometrine for 3rd stage management	• Yes • No
Birthweight	Birthweight was provided in grams and was classified into the following groups: • <3000g • 3000-3499g • 3500-3999g • ≥4000g
Maternal outcomes	
Estimated blood loss	Provided in mL
Major obstetric haemorrhage called	• Yes • No
Blood transfusion received	• Yes • No
Units of blood received	Provided as an integer and categorised as: • 1 • 2 • 3 • 4+
Primary cause of PPH	• Uterine atony • Genital tract trauma • Retained products / morbidly adherent placenta • Other • Not recorded
Management of PPH	Information was collected on the following procedures for PPH management: • Bimanual compression • Catheterisation • Cannulation/IV fluids • First-line uterotonics • Second-line uterotonic[1] • Blood products/ transfusion or iron transfusion • Tranexamic acid • Invasive procedure • Manual removal of placenta • Examination under anesthesia • Sutures • Vaginal pack
Higher level of care received with 48 hours of the birth	• Yes • No
Highest level of care received	• Enhanced maternity care • Intensive care

Variable	Description and additional information
Main reason for higher level care	Main reason for admission to higher level care was provided as a free text response and categorised into the following: • PPH and observation following PPH • Observation (without PPH specified) • Recovery from theatre procedure • Sepsis/pyrexia & Other/not clear
Duration of stay in higher level care	Provided as the number of days and categorised as: • < 1 day • 1 day • 2 days • 3 or more days
Maternal morbidity	• Yes • No
Maternal death	• Yes • No
Neonatal outcomes	
Stillbirth	• Yes • No
Apgar score at 5 minutes	Provided as a number between 0 and 10 and categorised as • <7 • ≥7
Breastfed before discharge	• Yes • No
Admitted to higher level care within 48 hours of birth	• Yes • No
Neonatal morbidity reported	• Yes • No
Neonatal death	• Yes • No

[1] Free text information, including for 'Other' categories, was coded against a coding dictionary created for this study by ME (see Appendix B.3) and checked by RR for errors and internal consistency. The coding dictionary was based on the NICE clinical guideline for Intrapartum care for healthy women and babies (146). The dictionary used the guideline's Tables 6-9 to determine which complications and conditions were considered significant enough to impact decisions about care. Where free-text responses named a condition or complication listed in the NICE guidelines, the use of the 'other' category was retained. Where free text responses named a condition or complication not included in the guidelines, this was deemed not significant to care and so the use of 'other' was replaced with 'null'.

3.4.3.3 Definition of 'Enhanced care or treatment'

As an indicator of maternal outcome following a PPH requiring transfer, a measure of 'enhanced care or treatment' was derived, defined as having either blood transfusion or admission to higher level care (enhanced maternity care or intensive care).

3.4.3.4 Definition of 'low-risk'

Women were defined as being at 'low-risk' of complications if they had none of the following, based on the conditions and complications described in Table 3.1:

- Previous pregnancy complication
- Current pregnancy complication
- Current medical problem
- Induction of labour

3.4.3.5 Definition of severe PPH

Severe PPH was defined as estimated blood loss ≥1500mL.

3.4.4 Data cleaning and management

The OpenClinica database used for data collection has a validation system that automatically raises queries for missing or potentially invalid data based on range checks and logical checks which are programmed at the start of each study. These queries were sent to UKMidSS reporters in monthly emails, as described above. AM also checked the database for inconsistencies that may have been missed by automatic validation and ME cleaned the data further, using visual inspection and cross tabulation of relevant variables. Variables that should align, for example whether or not a woman had previous pregnancies and the stated number of previous pregnancies, were cross-tabulated to identify any logical inconsistencies. Queries were followed up by AM who liaised with the relevant reporter to confirm or amend the submitted data. Where an inconsistency could not be confirmed or amended by a reporter and if no further information was available from the 'notes' field, the data were changed to missing.

As data are collected anonymously, reporting midwives were asked to keep a record of the unique study number assigned to cases and the patient identifiers to prevent submission of duplicate records. The data were also manually checked by ME to identify duplicate records, using duplicate identifiers and visual inspection, and any duplicates were removed.

3.4.5 Statistical analysis

All statistical analysis was conducted using STATA statistical software 15(147).

3.4.5.1 *Incidence, postpartum blood loss, cause and treatment*

The incidence of PPH requiring transfer with 95% confidence intervals (CIs) was calculated by inputting the number of cases reported as the numerator and the total number of births in reporting MUs during the study period as the denominator.

The incidence of PPH requiring transfer in FMUs and AMUs was calculated with 95% CIs, by inputting the number of confirmed cases in each unit type as the numerator and the total number of births in each unit type during the study period as the denominator. A two-sample test of proportions was conducted to compare incidence in the two types of unit.

Data entry completion for each unit type was described by subtracting the total number of confirmed cases (i.e. those with sufficient data to confirm case or control status) from the total number of cases reported by each unit type, excluding ineligible cases, divided by the total number of cases reported, and multiplied by 100 to present case completeness percentages.

Estimated postpartum blood loss (mL) was categorised into groups of blood loss amounts increasing by 250mL. The number of cases and controls in each category was calculated and presented as a histogram.

Cause of PPH and treatments for PPH, including units of blood products received, were described in terms of the number and proportion of cases in each category. Cases were also described in terms of the number and proportion who were classified as having a severe PPH, cross-tabulated against whether a blood transfusion was received.

3.4.5.2 *Factors associated with PPH requiring transfer to obstetric care*

Maternal socio-demographic, pre-existing clinical characteristics, clinical characteristics arising during pregnancy, intrapartum factors and birth-related factors were compared between cases and controls to identify risk factors associated with PPH requiring transfer. Proportions were compared using Pearson's chi-square test and a P-value of <0.05 was considered statistically significant. Univariable unconditional logistic regression was used to investigate associations between potential explanatory variables and PPH requiring transfer, generating ORs with 95% CIs.

For each risk factor, the reference group was the group with the largest number of observations, except where there was a clinical or interpretational reason for presenting an alternative reference group. Robust variance estimation was used to allow for the clustering of women within MUs. Confounding was assessed by stratifying cases and controls and cross-tabulating using the Mantel-Haenszel test for variables that had a plausible relationship to another variable in the model and to PPH. Due to the large number of variables in the dataset, only risk factors with a plausible independent relationship to each other and the outcome were considered and investigated as potential confounders.

Multivariable analysis using logistic regression was conducted, generating aORs with 95% CIs, using a stepwise forward regression approach. Variables with a p-value <0.1 in the univariable analysis, or where there was prior evidence of confounding from the earlier analysis of the literature, were considered for inclusion in the multivariable model. Variables were entered into the regression equation to assess whether the inclusion of the variable would significantly affect the model, with sociodemographic and pre-existing risk factors entered first, followed by pregnancy-related and intrapartum factors. The impact of the inclusion of each variable was visually examined before the next variable was added using Wald tests, and variables for which p<0.05 or where there was evidence of confounding were retained in the model. Variables that were no longer significant, or were not considered confounders, were removed from the regression equation. The Cochran-Armitage test for trend in ordered groups was conducted to determine whether increasing birthweight was associated with increasing odds of PPH.

'Administration of Syntocinon/ Syntometrine for 3rd stage management' was excluded from the multivariable analysis, despite it being statistically significantly associated with PPH in univariable analysis, because it was not possible to determine when during third stage management the drug was

administered, and whether it was used as part of active management, or administered in response to blood loss during the third stage of labour. The final model only included variables that made a significant contribution to the fit of the data (<0.05), or that were considered to be potential confounders.

3.4.5.3 Sub-group analysis

While most women planning birth in MUs are healthy with straightforward pregnancies and therefore at a low risk of complications during labour and birth, including PPH, previous research has shown that approximately 2.5% of women who plan birth in FMUs, and 4.4% of women who plan birth in AMUs, are at a higher risk of complications at the start of care in labour (141). To investigate whether the risk factors for a PPH requiring transfer were different among women who are considered 'low-risk', compared with the main analysis, a sub-group analysis was conducted.

'Low-risk' women were identified as those who had no risk factors that might place them at higher risk for labour and birth complications, according to the NICE intrapartum care for healthy women guideline (2014), defined above. Cases and controls were described in terms of numbers and proportions of women categorised as 'low-risk'. Univariable unconditional logistic regression was used to investigate any association between risk status and PPH requiring transfer, generating an OR with 95% CIs. Maternal socio-demographic, pre-existing clinical characteristics, clinical characteristics arising during pregnancy, intrapartum factors and birth-related factors were compared between cases and controls to identify risk factors associated with PPH requiring transfer among 'low-risk' women using the approach described above for the main analysis.

3.4.5.4 Labour progress, care and management factors associated with PPH requiring 'enhanced care or treatment'

Within the group of women transferred to obstetric care for PPH, the factors associated with receiving 'enhanced care or treatment' were investigated, using logistic regression. 'Cases' for this analysis were those who required 'enhanced care or treatment', as defined above, while controls were women who had a PPH who did not require such care.

Univariable analysis of maternal socio-demographic, pre-existing clinical characteristics and clinical characteristics arising during pregnancy, intrapartum factors and birth-related factors were compared between cases and controls to identify risk factors associated with PPH requiring enhanced care or treatment. Multivariable analyses using logistic regression, generating ORs with 95% CIs, was conducted using a step-wise forward regression model, using the approach described above for the main analysis.

3.4.5.5 Neonatal outcomes

Neonatal outcomes, including Apgar score, admission to higher-level care, neonatal morbidity, and neonatal death, were described in terms of numbers and proportions among cases and controls.

3.4.5.6 Post-hoc analysis of characteristics of women by unit type

To determine whether the characteristics of women giving birth in AMUs were different from those giving birth in FMUs, a post-hoc analysis describing the frequencies and proportions of cases and controls in terms of risk factors for PPH requiring transfer was conducted. Volume of blood loss, categorised in 500mL increments up to 1500mL, was also reported as frequencies and proportions among cases and controls by unit type. For both analyses, chi-squared tests for differences in proportion were used to assess statistical significance.

3.4.5.7 Sample size and power

The study was planned for a 12-month period with an anticipated incidence of PPH requiring transfer of 1% (141).Based on an anticipated 107,000 births in MUs over 12 months, it was estimated that the study would have 80% power at the 5% level of significance to detect ORs of 1.4 or greater and 1.7 or greater, assuming putative risk factors with a prevalence among controls of 15% and 4%, respectively. The power calculations were redone post-hoc in view of the early termination of data collection The actual number of cases and controls identified during the study period gave an 80% power at the 5% level to detect ORs of 1.3 or greater and 1.6 or greater, assuming putative risk factors with a prevalence of 15% (e.g. gestational age >40 weeks) and 4% (e.g. current pregnancy complication), respectively.

In terms of the 'enhanced treatment or care' analysis, there were 370 woman who had 'enhanced treatment or care' and 1131 comparison women. The study therefore had 80% power at the 5% level to detect ORs of 1.6 or greater for variables with 15% prevalence and ORs of 2.1 or greater for variables with a prevalence of 4%.

3.4.5.8 Small numbers and missing data

Table cells with numbers smaller than five were supressed, to avoid deductive disclosure.

Data completeness was high, with most variables having <1% missing. However for variables with ≥1% missing, data were not assumed to be missing at random, based on previous research published about these variables (148), and therefore a 'Missing' or 'Not recorded' category was created for variables with ≥1% missing data. In the multivariable analyses, a complete case analysis was conducted for these variables, meaning records with missing data for these variables were excluded from the analysis. For variables with ≥1% missing data, the 'Missing' category was included in the analysis and therefore records with missing data for these variables were retained in the analysis.

3.4.6 Ethics committee approval

UKMidSS received research ethics committee approval from the National Research Ethics Service (NRES) Committee South West – Frenchay (REC ref. 15/SW/0166) in May 2015, and this study was approved as a substantial amendment to that approval (SA03) in July 2019.

3.5 Results

3.5.1 Response and sample

All 214 MUs in the UK were invited to participate in the study and 209 units (98%) submitted at least one monthly report between September 2019 and February 2020 (Figure 3.1). The overall response to monthly report requests was 95%, with some variation by region. There were 122 AMUs and 78 FMUs that submitted data to the study.

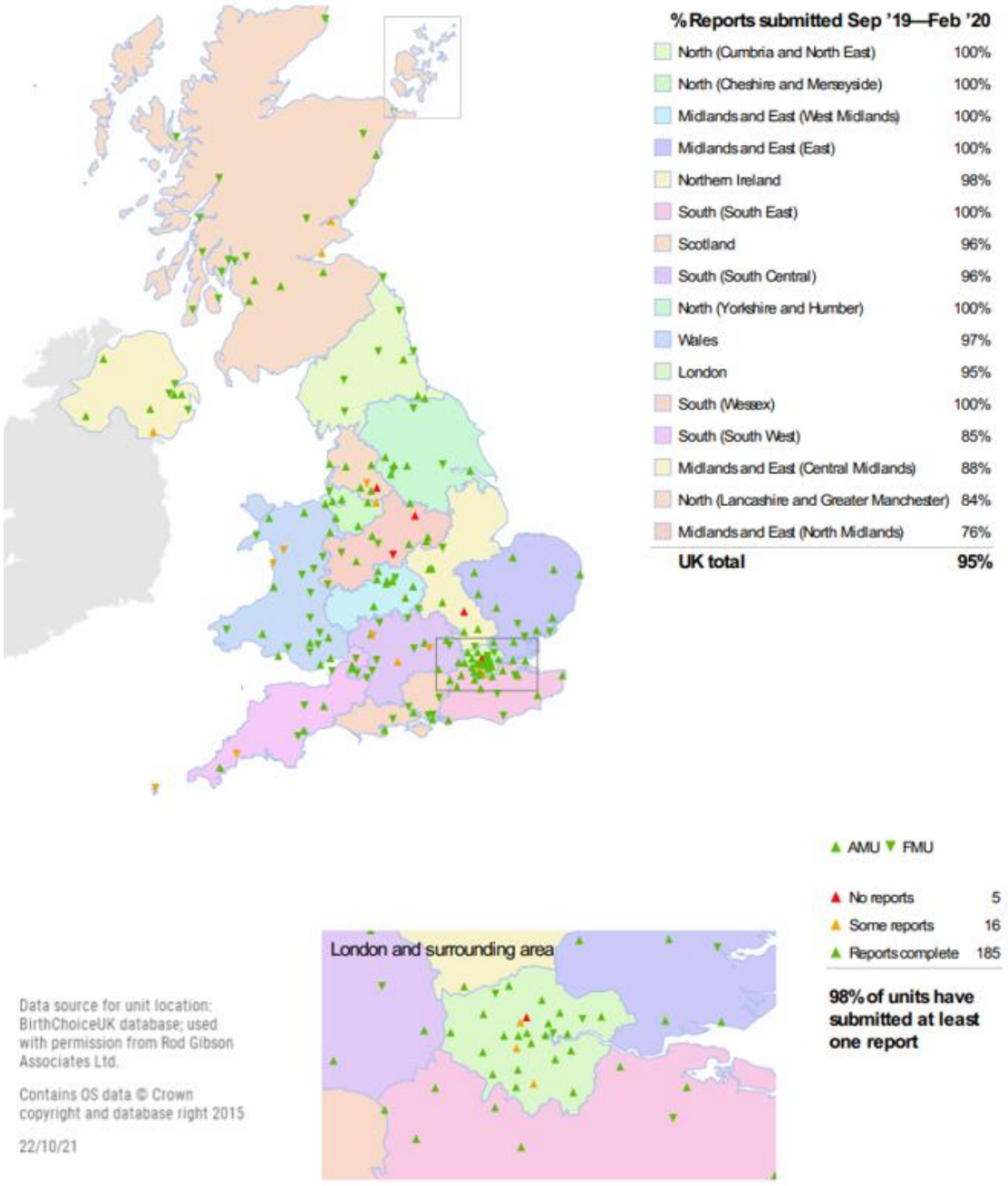


Figure 3.1 Response to monthly report requests by region

Source: UKMidSS administration system

3.5.2 Incidence of postpartum haemorrhage in midwifery units

After data cleaning, there were 1501 cases and 1475 controls included in the analysis (Figure 3.2).

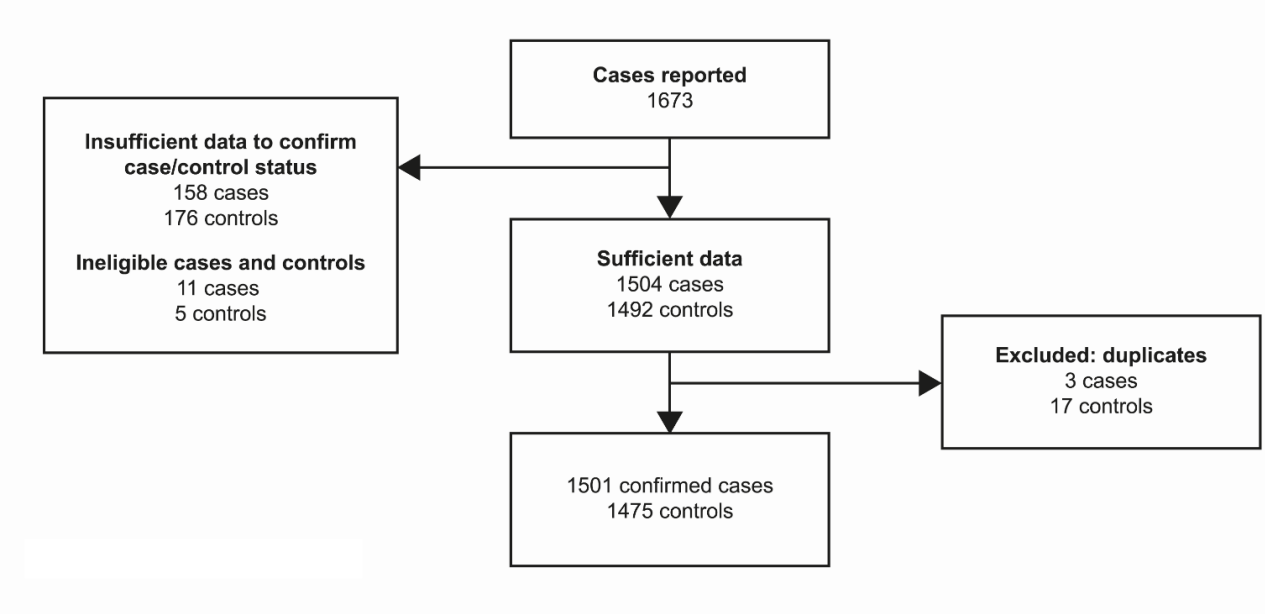


Figure 3.2 Reported and confirmed cases

During the 6-month study period, there were 1501 confirmed cases of PPH requiring transfer from a total of 39,953 reported births in MUs, representing an incidence of 3.7 per 100 women giving birth in an MU (95% CI 3.6-3.9). There were 99 confirmed cases and 3,814 births reported during the study period by FMUs and 1402 confirmed cases and 36,139 births reported during the study period by AMUs. The incidence of PPH requiring transfer was significantly higher in AMUs at 3.9 per 100 births, 95% CI 3.6-4.1, compared with FMUs at 2.6 per 100 births, 95% CI 2.1-3.2 ($p<0.001$).

There were 134 cases reported in AMUs and 24 cases reported in FMUs for which there was insufficient data to determine case status. This represents an 80% completion rate in FMUs and a 91% completion rate in AMUs. The incidence of PPH in each unit type based on reported (rather than confirmed) cases was 4.3% in AMUs (95% CI 4.1-4.5) and 3.2% in FMUs (95% CI 2.7-3.8).

Postpartum blood loss was significantly higher among cases, compared with controls (mean = 1175mL and 289mL respectively, $p < 0.001$). Among controls, 43 (2.9%) had a recorded blood loss of 501-999mL

and three (0.2%) had a recorded blood loss of 1000-1499mL (Table 3.2 and Figure 3.3). These were all confirmed as controls (i.e. not transferred to obstetric care for PPH) through validation questions during data entry. Less than 0.3% of cases lost less than 500mL of blood; these women also were confirmed as cases through data validation. No controls and 363 (24.1%) cases had a blood loss ≥ 1500mL.

Table 3.2 Postpartum blood loss among cases and controls

	Controls n = 1475		Cases n=1501	
	n	%	n	%
Blood loss (mL)				
<500	1377	93.4	<5	<0.3
500	46	3.1	61	4.1
501-999	43	2.9	554	36.9
1000-1499	3	0.2	517	34.4
≥1500	0	0.0	363	24.2
Missing	7	0.5	<5	<0.3

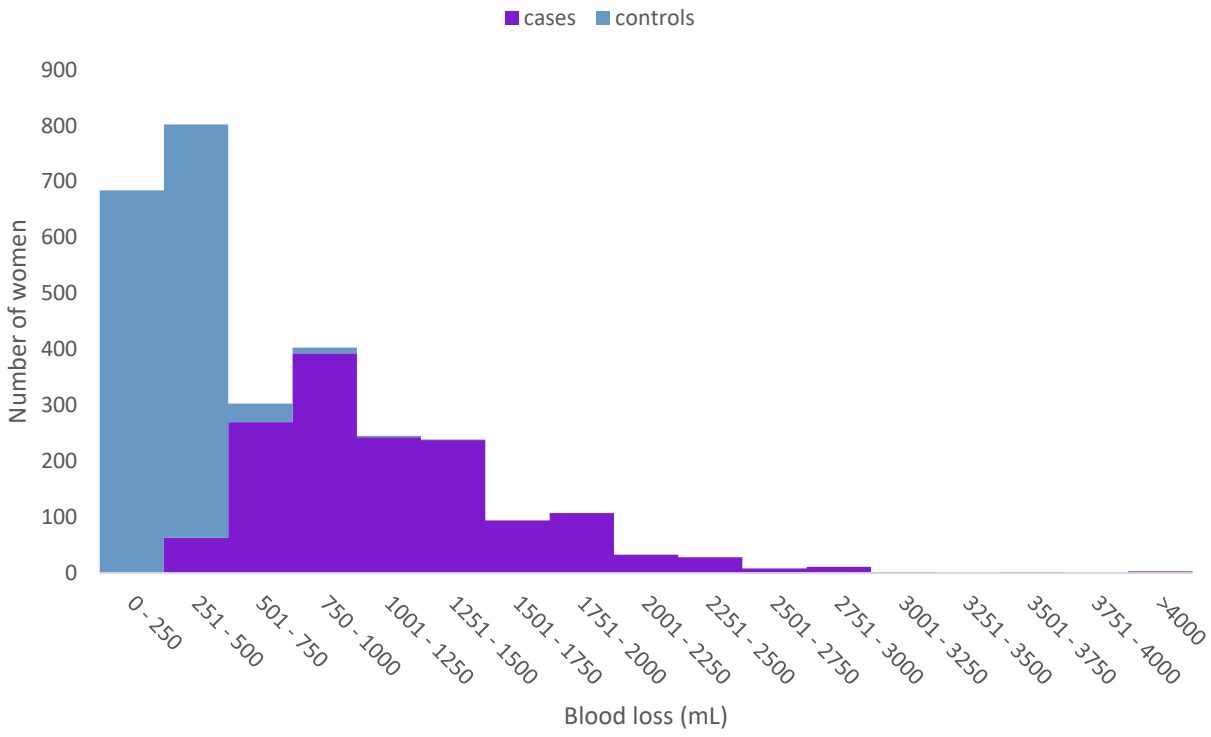


Figure 3.3 Frequency of blood loss volume among cases and controls, in 250mL increments

3.5.3 Risk factors for postpartum haemorrhage requiring transfer to obstetric care

Tables 3.3-3.7 present descriptive statistics and unadjusted ORs for sociodemographic, pre-existing clinical, clinical characteristics arising during pregnancy, labour, and birth-related factors.

3.5.3.1 Univariable analysis of risk factors for PPH requiring transfer

Cases and controls had similar age profiles (Table 3.3). In the unadjusted analysis, socioeconomic status was significantly associated with PPH requiring transfer (p=0.017). Compared with controls, cases were more likely to have 'Higher managerial' occupations (35.1% vs 29.0%) and were less likely to be unemployed or a student (5.3% vs 6.8%). Controls were significantly more likely to have smoked in pregnancy, compared with cases (11.8% vs 8.2%).

Table 3.3 Maternal sociodemographic characteristics among cases and controls

	Controls (n = 1475)		Cases (n = 1501)		Unadjusted ORs		p value
	n	%	n	%	OR	95% CI	
Maternal age							0.69
<20	50	3.4	48	3.2	0.98	(0.66-1.46)	
20-24	216	14.6	205	13.7	0.97	(0.75-1.25)	
25-29	427	28.9	418	28.1	1	.	
30-34	498	33.8	552	36.7	1.13	(0.93-1.38)	
35-40	260	17.6	253	16.6	0.99	(0.77-1.27)	
>40	24	1.6	25	1.6	1.06	(0.61-1.85)	
Smoking status							0.005
Did not smoke during pregnancy	1274	86.4	1351	90.0	1	.	
Smoked during pregnancy	171	11.6	121	8.1	0.67	(0.52-0.85)	
Missing	30	2.0	29	1.9	0.91	(0.621.34)	
Area deprivation quintile							0.13
1st (least deprived)	321	21.9	380	25.5	1	.	
2nd	312	21.3	301	20.2	0.81	(0.67-0.99)	
3rd	297	20.3	270	18.1	0.77	(0.62-0.95)	
4th	276	18.8	274	18.4	0.84	(0.68-1.03)	
5th (most deprived)	260	17.7	265	17.8	0.86	(0.69-1.06)	
Missing	10	.	11	.	.	. .	
Ethnicity							0.94
White (UK and Ireland)	986	66.9	997	66.4	1	.	
White (other)	182	12.3	189	12.6	1.03	(0.82-1.29)	
Asian	156	10.6	171	11.4	1.08	(0.85-1.38)	
Black	64	4.3	64	4.3	1.00	(0.70-1.39)	
Other	87	5.9	80	5.3	0.91	(0.63-1.31)	
Socioeconomic status							0.010
Higher managerial	428	29.0	526	35.0	1	.	
Intermediate	289	19.6	264	17.6	0.75	(0.61-0.91)	
Routine and manual	358	24.3	335	22.3	0.76	(0.64 -0.91)	
Employed, occupation unknown	104	7.1	103	6.9	0.81	(0.60-1.08)	
Unemployed/ student	101	6.8	80	5.3	0.65	(0.47 -0.90)	
Not recorded	195	13.2	193	12.9	0.80	(0.66-0.98)	

Parity was significantly associated with PPH requiring transfer in the unadjusted analysis, with women who had not given birth previously having higher odds of PPH compared with women who had one or more previous births (p<0.001) (Table 3.4). Among multiparous women, those with a previous PPH, and those with problems in a previous pregnancy other than PPH, were more likely to have a PPH requiring transfer (p<0.001 and p=0.004, respectively).

Table 3.4 Pre-existing clinical characteristics among cases and controls

	Controls (n = 1475)		Cases (n = 1501)		Unadjusted ORs		p value
	n	%	n	%	OR	95% CI	
BMI at booking							0.730
< 18.5	48	3.3	42	2.8	0.88	(0.57-1.37)	
18.5-24.9	797	54.0	789	52.6	1	.	
25-29.9	406	27.5	432	28.8	1.07	(0.91-1.27)	
30-35	153	10.4	168	11.2	1.11	(0.88-1.40)	
>35	28	1.9	30	2.0	1.08	(0.62-1.88)	
BMI not recorded	43	2.9	40	2.7	0.94	(0.65-1.37)	
Parity[1]							<.001
0	513	34.8	750	50.0	1.74	(1.50-2.02)	
1	654	44.3	548	36.5	1	.	
2 or more	308	20.8	203	13.5	0.78	(0.64-0.97)	
Missing	0	.	0	.	.	.	
Pre-existing medical risk factors[2]							0.520
No previous complication	1453	98.5	1474	98.2	1	.	
One or more	22	1.5	27	1.8	1.21	(0.67-2.17)	
Missing	0	.	0	.	.	.	
Previous pregnancy complication[3]							<0.001
No previous complication	909	96.1	650	89.8	1	.	
Previous PPH[4]	37	3.9	74	10.2	2.80	(1.77-4.41)	
Previous pregnancy complication other than PPH[5]	16	1.7	27	4.0	2.36	(1.33-4.217)	

[1] Number of previous pregnancies carried to at least 24 completed weeks' gestation
[2] Hypertension, confirmed cardiac disease, thromboembolic disorder, atypical antibodies, hyperthyroidism, diabetes, renal disease, epilepsy. Proportions for each of these categories are presented in Table 3.5
[3] Excludes primiparous women.
[4] Includes all women with a PPH including those with another previous complication.
[5] Complications comprises retained placenta requiring manual removal, caesarean, uterine surgery excluding caesarean, and shoulder dystocia. Proportions for each of these categories are presented in Table 3.5.

The most common previous complication among both cases and controls was PPH (9.9% and 3.5%, respectively) (Table 3.5). Endocrine disorders were the most common pre-existing medical condition

among both cases and controls (1.1% and 0.8%, respectively). The most common current pregnancy complication was Group B Streptococcus (2.9% and 3.5% respectively).

Table 3.5 Complications and medical risk factors among cases and controls

	Controls n = 1475		Cases n = 1501	
	n	**%**	**n**	**%**
Previous pregnancy complication[1]	n=962		n=751	
Primary postpartum haemorrhage needing treatment or transfusion	37	3.8	74	9.9
Previous complication other than PPH[2]				
Retained placenta requiring manual removal	9	0.7	30	3.9
Caesarean or uterine surgery	7	0.6	7	0.7
Shoulder dystocia	<5	<0.5	<5	<0.6
Pre-existing medical condition				
Cardiovascular	4	0.3	6	0.4
Atypical antibodies	4	0.3	0	0.0
Endocrine disorder	12	0.8	16	1.1
Other[3]	<5	<0.3	<5	<0.3
Current pregnancy complication				
BMI at booking >35kg/m^2	29	2.0	30	2.0
Post-term (>42 weeks)	<5	<0.3	<5	<0.3
Anaemia	0	0.0	6	0.4
Group B streptococcus	52	3.5	43	2.9
Antepartum haemorrhage	<5	<0.3	5	0.3
Pre-eclampsia / pregnancy induced hypertension	<5	<0.3	<5	<0.3
Gestational diabetes	6	0.4	9	0.6
Malpresentation (breech or transverse lie)	0	0.0	<5	<0.3
Other[4]	<5	<0.3	<5	<0.3

[1] Includes all women with a PPH including those with another previous complication. Previous complications comprise: retained placenta requiring manual removal and Caesarean. Excludes primiparous women.
[2] Excludes primiparous women.
[3] Low platelets, Factor V Leiden and previous VTE, autoimmune hepatitis, epilepsy and renal disease
[4] Twin pregnancy

In terms of clinical characteristics arising during pregnancy, only gestational age was significantly associated with higher odds of PPH requiring transfer in the unadjusted analysis (Table 3.6). Women who gave birth after 41 weeks' gestation had nearly 50% higher odds of PPH requiring transfer (OR=1.49; 95% CI 1.21-1.83) compared with women who gave birth at 40 weeks' gestation.

Table 3.6 Clinical characteristics arising during pregnancy among cases and controls

	Controls (n = 1475)		Cases (n = 1501)		Unadjusted ORs		p value
	n	%	n	%	OR	95% CI	
Current pregnancy problems[1]							0.60
None	1382	93.7	1403	93.5	1	.	
One or more	93	6.3	98	6.5	1.04	(0.77-1.39)	
Sex of baby							0.93
Male	710	48.3	717	47.9	1.01	(0.88-1.18)	
Female	761	51.7	781	52.1	1	.	
Missing	4	.	3	.	.	.	
Gestational age (weeks)							<0.001
36-37	66	4.5	38	2.5	0.58	(0.37-0.91)	
38	167	11.3	143	9.4	0.86	(0.67-1.10)	
39	399	27.1	358	23.9	0.90	(0.77-1.05)	
40	591	40.1	589	39.2	1	.	
41-42	251	17.0	373	24.9	1.49	(1.21-1.83)	
Missing	2	.	0	.	.	.	

[1] BMI at booking >35, post-term pregnancy (>42 weeks' gestation), anaemia, Group B streptococcus, antepartum haemorrhage, pre-eclampsia/pregnancy-induced hypertension, gestational diabetes, malpresentation (breech or transverse lie), other. Proportions for each of these categories are presented in Table 3.8.

Induction of labour, maternal and fetal complications identified at the start of labour care, and maternal and fetal complications identified during labour (before the birth) were all significantly associated with higher odds of PPH requiring transfer, ($p<0.05$ for all variables) in univariable analysis (Table 3.7).

Table 3.7 Intrapartum factors among cases and controls

	Controls (n = 1475)		Cases (n = 1501)		Unadjusted ORs		
	n	%	n	%	OR	95% CI	p value
Stage of labour at start of care							0.63
Latent stage	276	18.7	270	18.1	0.94	(0.77-1.15)	
Active 1st stage	1030	70.0	1072	71.7	1	.	
Passive 2nd stage	53	3.6	46	3.1	0.83	(0.58-1.20)	
Active 2nd stage	113	7.7	108	7.2	0.92	(0.69-1.22)	
Missing	3	.	5	.	.	.	
Induction of labour							0.02
No	1412	96.2	1410	94.4	1	.	
Yes	56	3.8	84	5.6	1.50	(1.06-2.13)	
Missing	7	.	7	.	.	.	
Maternal complications identified at the start of labour care[1]							0.003
None	1455	98.9	1463	97.5	1	.	
One or more	16	1.1	38	2.5	2.37	(1.33-4.23)	
Missing	4	.	6	.	.	.	
Fetal complications identified at the start of labour care[2]							0.008
None	1447	98.1	1451	96.7	1	.	
One or more	28	1.9	49	3.3	1.75	(1.15-2.64)	
Missing	0	.	0	.	.	.	
Maternal complications identified during labour (before birth)[3]							0.007
None	1451	98.4	1458	97.2	1	.	
One or more	24	1.6	43	2.8	1.78	(1.17-2.73)	
Missing	0	.	0	.	.	.	
Fetal complications identified during labour (before birth)[4]							0.005
None	1376	93.2	1360	90.6	1		
One or more	99	6.8	141	9.4	1.44	(1.12-1.86)	

[1] Maternal tachycardia, hypertension, proteinuria, maternal pyrexia, vaginal blood loss, prolonged rupture of membranes, and reported pain differing from pain normally associated with contractions. Proportions for each of these categories are presented in Table 3.8.

[2] Significant meconium, abnormal presentation, high or free-floating head, suspected anhydramnios or polyhydramnios, fetal heart rate abnormality, deceleration in fetal heart rate, and reduced fetal movements in the last 24 hours. Proportions for each of these categories are presented in Table 3.8.

[3] Maternal tachycardia, hypertension, maternal prexia, vaginal blood loss, prolonged rupture of membranes. Proportions for each of these categories are presented in Table 3.8.

[4] Significant meconium, confirmed/suspected delay in first stage of labour, confirmed\suspected delay in second stage of labour, obstetric emergency, abnormal presentation, fetal heart rate abnormality, and deceleration in fetal heart rate. Proportions for each of these categories are presented in Table 3.8.

Most individual maternal and fetal complications identified at the start of labour care or during labour occurred infrequently, in fewer than 1% of women, in both cases and controls (Table 3.8). Reduced fetal movements in the 24 hours before admission was the most common complication identified at the start of labour care for both cases and controls (1.8% and 0.8%, respectively). The most common

complication identified during labour care (before the birth) was deceleration in the fetal heart rate (4.4% among cases and 2.2% among controls).

Table 3.8 Complications in labour care among cases and controls

	Controls n = 1475		Cases n = 1501	
	n	%	n	%
Maternal complication identified at the start of labour care[1]				
Maternal tachycardia	<5	<0.3	8	0.5
Hypertension	8	0.5	12	0.8
Proteinuria	<5	<0.3	<5	<0.3
Maternal pyrexia	<5	<0.3	<5	<0.3
Vaginal blood loss	<5	<0.3	10	0.6
PROM	<5	<0.3	5	0.3
Pain different from normal contractions	0	0.0	<5	<0.3
Fetal complication identified at the start of labour care[2]				
Significant meconium	5	0.4	<5	<0.3
High or free-floating head	<5	<0.3	<5	<0.3
Suspected FGR	<5	<0.3	13	0.9
Suspected anhydramnios or polyhydramnios	<5	<0.3	<5	<0.3
Fetal heart rate abnormality	<5	<0.3	<5	<0.3
Deceleration in fetal heart rate	<5	<0.3	6	0.4
Reduced fetal movements in the last 24 hours	12	0.8	27	1.8
Maternal complication identified during labour (before birth)[3]				
Maternal tachycardia	7	0.5	14	0.9
Hypertension	8	0.5	6	0.4
Maternal pyrexia	<5	<0.3	<5	<0.3
Vaginal blood loss	<5	<0.3	15	1.0
PROM	<5	<0.3	8	0.5
Reported pain differing from pain normally associated with contractions	0	0.0	<5	<0.3
Fetal complication identified during labour (before birth)[4]				
Significant meconium	28	1.9	36	2.4
Abnormal presentation	<5	<0.3	<5	<0.3
Fetal heart rate abnormality	18	1.2	21	1.4
Deceleration in fetal heart rate	32	2.2	65	4.4
Confirmed/suspected first stage delay	11	0.8	8	0.5
Confirmed/suspected second stage delay	5	0.3	20	1.3
Obstetric emergency	9	0.6	15	1.0

[1] Maternal tachycardia, hypertension, proteinuria, maternal pyrexia, vaginal blood loss, prolonged rupture of membranes, and reported pain differing from pain normally associated with contractions.
[2] Significant meconium, abnormal presentation, high or free-floating head, suspected anhydramnios or polyhydramnios, fetal heart rate abnormality, deceleration in fetal heart rate, and reduced fetal movements in the last 24 hours.
[3] Maternal tachycardia, hypertension, maternal prexia, vaginal blood loss, prolonged rupture of membranes.
[4] Significant meconium, confirmed/suspected delay in first stage of labour, confirmed\suspected delay in second stage of labour, obstetric emergency, abnormal presentation, fetal heart rate abnormality, and deceleration in fetal heart rate.

Women who had an instrumental birth had a higher odds of having a PPH requiring transfer compared with those who had a spontaneous vertex birth (OR 3.51, 95% CI 2.25-5.45) (Table 3.9). Other birth-

related factors associated with a higher odds of having a PPH requiring transfer in univariable analysis were having a third stage of labour lasting 60 minutes or more (OR 4.83, 95% CI 3.43-6.81), 3rd or 4th degree perineal trauma (OR 5.09, 95% CI 3.47-7.44), and Syntocinon/ Syntometrine administered for 3rd stage management (OR 1.47, 95% CI 1.17-1.84). The chances of having a PPH requiring transfer increased for each 500g category of birthweight ($p < 0.001$); with higher odds of PPH requiring transfer for women who gave birth to a baby weighing 3500-3999g (OR 1.64 95% CI 1.37-1.97) or ≥4000g (OR 2.11 95% CI 1.65-2.69), compared with those whose baby weighed 3000-3499g.

Table 3.9 Birth-related factors

	Controls (n = 1475)		Cases (n = 1501)		Unadjusted ORs		p value
	n	%	n	%	OR	95% CI	
Birth/labour in water							0.004
No immersion in water	820	55.7	808	54.0	1	.	
Immersion in water for labour, land birth	217	14.7	263	17.6	1.23	(1.04-1.45)	
Birth in water	435	29.6	425	28.4	0.99	(0.86-1.14)	
Birth mode							<0.001
Spontaneous vertex birth	1459	99.2	1456	97.2	1	.	
Vaginal breech	<5	<0.3	0	0	.	.	
Instrumental	10	0.7	35	2.4	3.51	(2.25-5.43)	
Missing	<5	0.3	10	.	.	.	
Duration of third stage of labour							<0.001
< 60 minutes	1399	94.9	1240	82.6	1	.	
≥ 60 minutes	53	3.6	227	15.1	4.83	(3.43-6.79)	
Missing	23	1.6	34	2.3	.	.	
Perineal trauma							<0.001
<3rd degree tear or no tear	1427	96.9	1290	86.2	1	.	
3rd or 4th degree tear	45	3.1	207	13.8	5.09	(3.49-7.42)	
Missing	3	.	4	.	.	.	
Syntocinon/ Syntometrine for 3rd stage management							0.001
No	278	18.9	205	13.7	1	.	
Yes	1194	81.1	1291	86.3	1.47	(1.17-1.84)	
Missing	4	.	5	.	.	.	
Birthweight (g)							<0.001
<3000	192	13.1	112	7.5	0.74	(0.57-0.96)	
3000-3499	644	43.8	508	33.9	1	.	
3500-3999	485	33.0	628	41.9	1.64	(1.37-1.96)	
≥4000	150	10.2	250	16.7	2.11	(1.66-2.69)	
Missing	4	.	3	.	.	.	

3.5.3.2 *Multivariable analysis of risk factors for PPH requiring transfer*

The results of the multivariable analysis are presented in Table 3.10. Having adjusted for all of the other factors in Table 3.10, smoking during pregnancy was associated with a 27% decrease in the odds of having a PPH requiring transfer (aOR=0.73; 95% CI 0.56-0.94). Compared with living in the least deprived areas, living in areas of highest deprivation was associated with 27% higher odds of having a PPH requiring transfer (aOR=1.27 95% CI 1.00-1.61). Cases were nearly twice as likely to be giving birth for the first time compared with controls (aOR=1.96; 95% CI 1.66-2.30). Among those who had previously given birth, having a previous PPH more than doubled the odds of PPH requiring transfer (aOR=2.67; 95% CI 1.67-4.25), as did having one or more complications in a previous pregnancy other than PPH (aOR=2.40; 95% CI 1.25-4.60). Giving birth at after 41 weeks gestation increased the odds of PPH requiring transfer by 36% (aOR=1.36; 95% CI 1.10-4.69). Women who had an instrumental birth were nearly three times as likely to have a PPH requiring transfer (aOR=2.69 95% CI 1.53-4.72) and those who had a third stage of labour lasting longer than 60 minutes were nearly 6 times as likely (aOR=5.56 95% CI 3.93-7.88). Having a perineal tear was associated with nearly five times the odds of PPH requiring transfer (aOR=4.67 95% CI 3.16-6.90). Giving birth to a baby weighing 3500-3999 was associated with a 71% increase in odds of PPH requiring transfer (aOR=1.71 95% CI 1.42-2.07) while giving birth to a baby weighing 4000g more was associated with more than double the odds of PPH requiring transfer, compared with giving birth to a baby weighing 3000-3499g (aOR=2.31 95% CI 1.78-3.00).

Table 3.10 Factors associated with PPH requiring transfer to obstetric care in MUs[1]

	Controls		Cases		Unadjusted analysis		Adjusted analysis n=2940		
	n	%	n	%	OR	(95% CI)	aOR	(95% CI)	p value
Smoking status									0.031
Did not smoke during pregnancy	1274	86.4	1351	90.0	1	.	1		
Smoked during pregnancy	171	11.6	121	8.1	0.66	(0.52-0.85)	0.73	(0.56-0.94)	
Missing	30	2.0	29	1.9	0.91	(0.62-1.34)	0.80	(0.48-1.31)	
Area-based deprivation quintile									0.019
1st (least deprived)	321	21.9	380	25.5	1	.	1		
2nd	312	21.3	301	20.2	0.81	(0.67-0.88)	0.87	(0.71-1.07)	
3rd	297	20.3	270	18.1	0.77	(0.62-0.95)	0.88	(0.71-1.09)	
4th	276	18.8	274	18.4	0.84	(0.68-1.03)	1.04	(0.83-1.31)	
5th (most deprived)	260	17.7	265	17.8	0.86	(0.69-1.07)	1.27	(1.00-1.61)	
Parity									<0.001
0	513	34.8	750	50.0	1.87	(1.62-2.15)	1.96	(1.66-2.30)	
1	654	44.3	548	36.5	1	.	1		
2+	308	20.8	203	13.5	0.78	(0.64-0.97)	0.81	(0.65-1.01)	
Previous pregnancy complication[2]									
No previous complication	909	94.5	650	86.6	1	.	1	.	
Previous PPH	37	3.9	74	9.9	2.80	(1.77-4.41)	2.67	(1.67-4.25)	<0.001
Previous complication other than PPH	16	1.7	27	3.6	2.36	(1.33-4.17)	2.40	(1.25-4.60)	0.009
Gestational age									0.007
36-37	66	4.5	38	2.5	0.58	(0.37-0.91)	0.69	(0.42-1.14)	
38	167	11.3	143	9.4	0.86	(0.68-1.10)	1.04	(0.80-1.36)	
39	399	27.1	358	23.9	0.90	(0.77-1.05)	0.98	(0.82-1.17)	
40	591	40.1	589	39.2	1	.	1	.	
41-43	251	17.0	373	24.9	1.49	(1.21-1.84)	1.36	(1.10-1.69)	
Birth mode									<0.001
Spontaneous vertex or vaginal breech birth	1461	99.2	1456	97.7	1	.	1	.	
Instrumental birth	10	0.82	35	2.35	2.92	(1.83-4.64)	2.69	(1.53-4.72)	
Duration of third stage of labour									<0.001
< 60 minutes	1399	94.9	1240	82.6	1	.	1	.	
≥ 60 minutes	53	3.6	227	15.1	4.8	(3.42-6.81)	5.56	(3.93-7.88)	
Missing	23	1.6	34	2.3	.	.	.	.	
Perineal tear									<0.001
<3rd degree tear or no tear	1427	96.9	1290	86.2	1	.	1	.	
3rd or 4th degree tear	45	3.1	207	13.8	5.09	(3.49-7.42)	4.67	(3.16-6.90)	
Birthweight (gm)									<0.001
<3000	192	13.1	112	7.5	0.47	(0.57-0.96)	0.78	(0.57-1.06)	
3000-3499	644	43.8	508	33.9	1	.	1	.	
3500-3999	485	33.0	628	41.9	1.64	(1.37-1.96)	1.71	(1.42-2.07)	
≥4000	150	10.2	250	16.7	2.11	(1.66-2.69)	2.31	(1.78-3.00)	

[1] Each variable in the model is adjusted for all other variables in the model

[2] Excludes primiparous women

3.5.4 Sub-group analysis of low-risk women giving birth in a midwifery unit

Of the 2,976 women included in the main analysis, 2,601 (87%) met the definition of low-risk at the start of labour care. Controls were slightly more likely to be low-risk than cases, 86% and 81%, respectively (Table 3.11). There were 207 controls and 282 cases who did not meet the definition of low-risk. These women were excluded from the sub-group analysis.

Table 3.11 Risk categories among cases and controls

	Controls (n = 1475)		Cases (n = 1501)		p value
	n	%	n	%	
Low risk	1268	86.0	1219	81.2	<0.001
Higher risk	207	14.0	282	18.8	

The results of the univariable analyses of low-risk women are presented in Appendix B.4. Independent risk factors for PPH requiring transfer were broadly similar among women who were considered low risk, compared with the whole study population (Table 3.12). Among low-risk women, smoking status and area deprivation quintile were not significantly associated with PPH requiring transfer, which differs from the findings in the main analysis. The only variable significantly associated with PPH requiring transfer in this sub-group analysis that was not significantly associated in the adjusted analysis of the whole study population was 'maternal complication identified at the start of labour care', which was associated with over twice the odds of PPH requiring transfer (aOR=2.27; 95%CI 1.29-5.95).

Table 3.12 Factors associated with PPH requiring transfer in MUs among low-risk women

	Controls		Cases		Unadjusted analysis		Adjusted analysis		
	n	%	n	%	OR	(95% CI)	aOR	(95% CI)	p value
Parity[1]									<0.001
0	479	37.8	666	54.7	1.83	(1.56-2.14)	1.83	(1.54-2.16)	
1	537	42.4	409	33.6	1		1	.	
2+	252	19.9	144	11.8	0.75	(0.59-0.95)	0.82	(0.65-1.04)	
Gestational age									0.140
36-37	56	4.4	31	2.5	0.55	56	0.70	(0.41-1.21)	
38	147	11.6	114	9.4	0.78	147	0.93	(0.68-1.26)	
39	352	27.8	293	24.0	0.83	352	0.94	(0.78-1.12)	
40	514	40.5	513	42.1	1	514	1	.	
41+	199	15.7	268	22.0	1.35	199	1.25	(0.99-1.59)	
Maternal complications identified at the start of labour care[2]									0.009
None	1254	99.2	1184	97.5	1	.	1		
One or more	10	0.8	31	2.6	3.28	(1.68-6.44)	2.77	(1.29-5.95)	
Birth mode									<0.001
Spontaneous vertex birth or vaginal breech	1255	99.3	1181	97.4	1	.	1	.	
Instrumental birth	9	0.7	30	2.5	3.54	(2.22-5.64)	2.83	(1.62-4.96)	
Duration of third stage of labour									<0.001
< 60 minutes	1201	94.7	1014	83.2	1	.	1	.	
≥ 60 minutes	47	3.7	177	14.5	4.46	(3.10-6.42)	5.02	(3.44-7.33)	
Missing	20	1.6	28	2.3	1.65	(0.91-3.04)	1.58	(0.82-3.06)	
Perineal tear									<0.001
<3rd degree tear or no tear	1223	96.7	1035	85.2	1	.	1	.	
3rd or 4th degree tear	42	3.3	180	14.8	5.06	(3.41-7.53)	4.40	(2.92-6.65)	
Birthweight (gm)									<0.001
<3000	176	13.9	93	7.7	0.68	(0.51-0.91)	0.73	(0.52-1.03)	
3000-3499	548	43.4	426	35.0	1	.	1	.	
3500-3999	417	33.0	511	42.0	1.58	(1.31-1.90)	1.64	(1.35-1.99)	
≥4000	123	9.7	186	15.3	1.95	(1.51-2.52)	2.11	(1.61-2.77)	

[1] Number of previous pregnancies carried to at least 24 completed weeks' gestation.
[2] Maternal tachycardia, hypertension, proteinuria, maternal pyrexia, vaginal blood loss, prolonged rupture of membranes, and reported pain differing from pain normally associated with contractions.

3.5.5 Causes and treatment of postpartum haemorrhage in midwifery units

The most common cause of PPH among cases was uterine atony (37.3%), followed by genital tract trauma (28.9%). Cause of PPH (if any) was not recorded for controls. The most common treatment for PPH was first-line uterotonics, with 84.0% of cases receiving this treatment (Table 3.13). The least common treatment for PPH was an invasive procedure, with 3.9% of cases receiving such treatment. Broadly, the proportion of cases receiving a particular treatment declined as the invasiveness of the procedure increased. Due to the structure of the data collection form, it was not possible to determine

the timing or sequence of the treatments that women received, or to determine whether the treatment was performed under midwifery care or after transfer to obstetric care.

Table 3.13 Cause and treatment of PPH among women who had a PPH requiring transfer

	Cases n=1501	
Cause of PPH	**n**	**%**
Uterine atony	558	37.3
Genital tract trauma	432	28.9
Retained products / morbidly adherent placenta	327	21.8
Other	21	1.4
Not recorded	159	10.6
Management of PPH		
First line treatment		
Bimanual compression	79	5.3
Catheterisation	908	61.1
Cannulation/IV fluids	1,182	79.4
First-line uterotonics[2]	1,262	84.0
Second-line treatment		
Second-line uterotonics[3]	194	12.8
Blood products/ transfusion or iron transfusion	158	10.5
Tranexamic acid	456	30.6
Third-line treatment		
Invasive procedure[4]	58	3.9
Manual removal of placenta	82	5.5
Examination under anesthesia	21	1.4
Sutures	77	5.1
Vaginal pack	6	0.4
PPH treatment not recorded	64	4.3

[2] First line uterotonics comprises: Syntocinon, Syntometrine, misoprostol, ergometrine, prostaglandin

[3] Second-line uterotonics comprises: Hemabate and Carboprost

[4] Invasive procedure includes: intra-abdominal packing, intrauterine balloons or packing, interventional radiology, brace suture and hysterectomy

Transfusion of blood products was more common among women who had a severe PPH (Table 3.14). Most women who had a transfusion of blood products received one (19.2%) or two (66.7%) units of blood products.

Table 3.14 Transfusion of blood products among women who had a PPH requiring transfer to obstetric care care

	Transfusion received		No Transfusion	
	n	%	n	%
Transfusion of blood products by severity of PPH				
Mild-moderate PPH (<1500mL blood loss)	46	4.0	1,087	96.0
Severe PPH (≥ 1500mL blood loss)	112	31.5	251	68.6
Units of blood products received				
1	32	19.2	.	.
2	105	66.7	.	.
3	11	7.1	.	.
4+	10	3.9	.	.

3.5.6 Maternal outcomes among cases and controls

Of women who had a PPH requiring transfer, 10.6% received a blood transfusion and 2.5% had a maternal morbidity reported (Table 3.15). Less than 0.03% of controls and 308 cases (21%) were admitted to higher-level care, which was 'Enhanced maternity care' for the vast majority (98.3%) of cases and for all controls. Five cases were admitted for intensive care. Most cases admitted for higher-level care (74.3%) were reported as being admitted for PPH or for observation following PPH, with a further 14.0% of cases reported as being admitted for observation without PPH being specified. There were no maternal deaths.

Enhanced care or treatment, referred to as 'enhanced care', comprising blood transfusion or admission to higher level-care, was experienced by 24.7% of cases and 0.6% of controls (Table 3.15). The proportion of women who initiated breastfeeding before discharge was similar among controls and cases (79.7% and 81.5%, respectively).

Table 3.15 Maternal outcomes among cases and controls

	Controls n = 1475		Cases n = 1501	
	n	%	n	%
Breastfeeding initiated before discharge				
Yes	1173	79.7	1221	81.5
No	298	20.3	276	18.4
Missing	4	.	4	.
Any 'enhanced treatment or care' [1]	7	0.6	370	24.7
Blood transfusion	na	na	158	10.6
Maternal morbidity reported[2]	<5	<0.3	38	2.5
Admission to higher level of care	<5	<0.3	308	21.0
Type of higher level care[3] **(among women admitted to higher level care)**				
Enhanced maternity care	<5	100.0	303	98.3
Intensive care	0	0	5	1.6
Duration of stay in higher level care[3]				
< 1 day	0	0	<5	<1.6
1 day	<5	na	269	88.8
2 days	<5	na	26	8.6
3 or more days	0	0	<5	<1.6
Missing	0	0	5	.
Primary reason for higher level care†				
PPH and observation following PPH	0	0.0	232	74.3
Observation (without PPH specified)	0	0	42	14.0
Recovery from theatre procedure	<5	<0.3	12	3.6
Sepsis/pyrexia & Other/not clear	<5	<0.3	22	7.1

[1] Any enhanced care or treatment refers to a woman have any of the following: blood transfusion, maternal morbidity reported, admission to higher level-care

[2] Maternal morbidity comprises: readmission for secondary PPH/retained placenta, pyrexia/sepsis, anaemia, urinary

[3] Proportions are among women admitted to higher-level care

3.5.7 Factors associated with enhanced care or treatment after postpartum haemorrhage

Tables 3.16-3.21 present unadjusted analyses comparing women who received enhanced care or treatment with those who did not, among women who had a PPH requiring transfer. For all maternal sociodemographic characteristics, there were no significant differences between women who received enhanced care and those who did not ($p > 0.05$ for all factors) (Table 3.16).

Table 3.16 Maternal sociodemographic characteristics of women who received enhanced care and those who did not, among women transferred for PPH

	No enhanced care (n =1,131)		Enhanced care (n = 370)		Unadjusted ORs		p value
	n	%	n	%	OR	95% CI	
Maternal age							0.364
<20	32	2.8	16	4.3	1.82	(0.97-3.44)	
20-24	150	13.3	55	14.9	1.34	(0.85-2.09)	
25-29	328	29.0	90	24.3	1	.	
30-34	417	37.1	135	36.5	1.18	(0.89-1.56)	
35-40	184	16.2	69	18.7	1.37	(0.93-2.02)	
>40	20	1.8	5	1.4	0.91	(0.30-2.73)	
Missing	0	.	0		.	.	
Smoking status							0.234
Did not smoke during pregnancy	1024	90.5	327	88.4	1	.	
Smoked during pregnancy	88	7.8	33	8.9	1.17	(0.72-1.89)	
Missing	19	1.7	10	2.7	1.64	(0.90-3.02)	
Area deprivation quintile							0.473
1st (least deprived)	285	25.4	95	26.0	1	.	
2nd	217	19.3	84	23.0	1.16	(0.84-1.61)	
3rd	213	19.0	57	15.6	0.80	(0.54-1.17)	
4th	209	18.6	65	17.8	0.93	(0.64-1.35)	
5th (most deprived)	200	17.8	65	17.8	0.98	(0.69-1.37)	
Missing	7	.	4	.	.	.	
Ethnicity							0.217
White (UK and Ireland)	768	67.9	229	61.9	1	.	
White (other)	143	12.7	46	12.4	1.01	(0.68-1.72)	
Asian	122	10.8	49	13.2	1.34	(0.89-2.03)	
Black	43	3.8	21	5.7	1.64	(0.96-2.78)	
Other	55	4.9	25	6.8	1.52	(0.94-2.47)	
Missing	0	.	0	.	.	.	
Socioeconomic status							0.264
Higher managerial	387	34.2	139	37.6	1	.	
Intermediate	201	17.8	63	17.0	0.87	(0.65-1.18)	
Routine and manual	241	21.3	94	25.4	1.09	(0.76-1.56)	
Employed, occupation unknown	81	7.2	22	6.0	0.76	(0.45-1.27)	
Unemployed/ student	64	5.7	16	4.3	0.70	(0.39-1.26)	
Not recorded	157	13.9	36	9.7	0.64	(0.40-1.01)	

Among women who had a PPH requiring transfer, those who received enhanced care had similar pre-existing clinical characteristics to those who did not receive enhanced care (Table 3.17). There were no significant differences between the two groups in terms of BMI, parity, pre-existing medical risk factors or problems in a previous pregnancy (p>0.05 for all factors). For women who had a BMI less than 18.5, the odds of requiring enhanced care were double that of women with a BMI 18.5-24.9 (OR=2.07; 95% CI 1.15-3.70).

Table 3.17 Clinical characteristics arising during pregnancy among women transferred for PPH who received enhanced care and women transferred for PPH who did not receive enhanced care

	No enhanced care (n =1,131)		Enhanced care (n =370)		Unadjusted ORs		p value
	n	%	n	%	OR	95% CI	
BMI at booking							0.052
< 18.5	26	2.3	16	4.3	2.07	(1.15-3.70)	
18.5-24.9	608	53.8	181	48.9	1	.	
25-29.9	326	28.8	106	28.7	1.09	(0.84-1.42)	
30-35	120	10.6	48	13.0	1.34	(0.96-1.89)	
>35	24	2.1	6	1.6	0.83	(0.33-2.09)	
BMI not recorded	27	2.4	13	3.5	1.62	(0.83-3.17)	
Parity[1]							0.726
0	559	49.4	191	51.6	1.10	(0.87-1.39)	
1	418	37.0	130	35.1	1	.	
2 or more	154	13.6	49	13.2	1.02	(0.71-1.48)	
Missing	0	.	0	.	.	.	
Pre-existing medical risk factors[2]							0.431
None	1,109	98.1	365	98.7	1	.	
One or more	22	2.0	5	1.4	0.69	(0.27-1.73)	
Problems in a previous pregnancy, excluding PPH[3]							0.976
No previous complication	495	86.5	155	87.6	1	.	
Previous PPH[4]	56	9.8	18	10.1	1.03	(0.58-1.80)	
Previous complication other than PPH	21	3.7	6	3.4	0.91	(0.34-2.43)	

[1] Parity refers to the number of previous pregnancies carried to at least 24 completed weeks' gestation

[2] Pre-existing medical risk factors includes: Hypertension, Confirmed cardiac disease, Thromboembolic disorder, atypical antibodies, hyperthyroidism, diabetes, renal disease and epilepsy. Includes multiparous women only.

[3] Problems in a previous pregnancy includes: Retained placenta requiring manual removal, Caesarean and uterine surgery excluding Caesarean. Includes multiparous women only.

[4] Includes women with a previous PPH and another previous complication.

Among women who had a PPH requiring transfer, those who received enhanced care had similar clinical characteristics arising during pregnancy to those who did not receive enhanced care (Table 3.18). There were no significant differences between the two groups in terms of current pregnancy problems, sex of the baby or gestational age.

Table 3.18 Clinical characteristics arising during pregnancy among women transferred for PPH who received enhanced care and women transferred for PPH who did not receive enhanced care

	No enhanced care (n =1,131)		Enhanced care (n = 370)		Unadjusted ORs		p value
	n	%	n	%	OR	95% CI	
Current pregnancy problem[1]							0.477
None	1,054	93.2	349	94.3	1	.	
One or more	77	6.8	21	5.7	0.81	(0.48-1.40)	
Sex of baby							0.600
Male	544	48.2	173	46.8	1.06	(0.85-1.32)	
Female	584	51.8	197	53.2	1	.	
Missing	3	.	0	.	.	.	
Gestational age (weeks)							0.429
36-37	28	2.5	10	2.7	1.11	(0.52-2.40)	
38	111	9.8	32	8.7	0.90	(0.60-1.34)	
39	277	24.5	81	21.9	0.91	(0.70-1.19)	
40	446	39.4	143	38.7	1	.	
41-42	269	23.8	104	28.1	1.21	(0.91-1.60)	
Missing	0	.	0	.	.	.	

[1] Current pregnancy problem: BMI at booking >35, post-term (>42 weeks) Anaemia, Group B Streptococcus, Antepartum haemorrhage, pre-eclampsia/pregnancy-induced hypertension, gestational diabetes, and malpresentation (breech or transverse lie).

Among women who had a PPH requiring transfer, those who received enhanced care and those who did not, had similar intrapartum factors (Table 3.19).

Table 3.19 Intrapartum factors of women who received enhanced care and those who did not, among women transferred for PPH

	No enhanced care (n = 1,131)		Enhanced care (n = 370)		Unadjusted ORs		p value
	n	%	n	%	OR	95% CI	
Stage of labour at start of care							0.181
Latent stage	193	17.1	77	20.9	1.22	(0.92-1.63)	
Active 1st stage	809	71.8	263	71.3	1	.	
Passive 2nd stage	37	3.3	9	2.4	0.75	(0.36-1.56)	
Active 2nd stage	88	7.8	20	5.4	0.69	(0.40-1.22)	
Missing	4	.	1	.	.	.	
Induction of labour							0.945
No	1,062	94.2	348	94.3	1	.	
Yes	63	5.6	21	5.6	1.02	(0.63-1.65)	
Missing	6	.	1	.	.	.	
Maternal complications identified at the start of labour care[1]							0.109
None	1,195	97.3	363	98.1	1	.	
One or more	31	2.8	7	1.9	0.68	(0.30-1.54)	
Missing	5	.	1	.	.	.	
Fetal complications identified at the start of labour care[2]							0.749
None	1088	96.6	358	97.0	1	.	
One or more	38	3.4	11	3.0	0.88	(0.40-1.93)	
Missing	5	.	1	.	.	.	
Maternal complications identified during labour (before birth)[3]							0.357
None	1,103	97.5	355	96.0	1	.	
One or more	28	2.5	15	4.1	1.66	(0.89-3.10)	
Missing	0	.	0	.	.	.	
Fetal complications identified during labour (before birth)[4]							0.235
None	1019	90.1	341	92.1	1	.	
One or more	112	9.9	29	7.8	0.77	(0.51-1.18)	
Missing	0	.	0	.	.	.	

[1] Maternal tachycardia, hypertension, proteinuria, maternal pyrexia, vaginal blood loss, prolonged rupture of membranes, and reported pain differing from pain normally associated with contractions.
[2] Significant meconium, abnormal presentation, high or free-floating head, suspected anhydramnios or polyhydramnios, fetal heart rate abnormality, deceleration in fetal heart rate, and reduced fetal movements in the last 24 hours.
[3] Maternal tachycardia, hypertension, maternal prexia, vaginal blood loss, prolonged rupture of membranes.
[4] Significant meconium, confirmed/suspected delay in first stage of labour, confirmed\suspected delay in second stage of labour, obstetric emergency, abnormal presentation, fetal heart rate abnormality, and deceleration in fetal heart rate.

Among women who had a PPH requiring transfer, those who received enhanced care and those who did not had similar birth-related factors (Table 3.20). Women who had a third stage of labour lasting longer than 60 minutes were 80% more likely to receive enhanced care following PPH (OR 1.80, 95% CI 1.36-2.45).

Table 3.20 Birth-related factors of women who received enhanced care and those who did not, among women transferred for PPH

	No enhanced care (n = 1,131)		Enhanced care (n = 370)		Unadjusted ORs		p value
	n	%	n	%	OR	95% CI	
Labour/birth in water							0.113
No immersion in water	307	27.2	118	32.0	1	.	
Immersion in water for labour, land birth	192	17.0	71	19.2	0.96	(0.65-1.41)	
Birth in water	628	55.7	180	48.8	0.75	(0.55-1.01)	
Missing	4	.	1	.			
Birth mode							0.480
Spontaneous vertex birth	1,098	97.8	358	97.3	1	.	
Instrumental	25	2.2	10	2.7	1.22	(0.69-2.16)	
Missing	8	.	2	.	.	.	
Duration of third stage of labour							<0.001
< 60 minutes	956	84.5	284	76.8	1	.	
≥ 60 minutes	148	13.1	79	21.4	1.80	(1.36-2.45)	
Missing	27	2.4	7	1.9	0.87	(0.39-1.92)	
Perineal tear							0.702
<3rd degree tear	969	86.0	321	86.8	1	.	
3rd or 4th degree tear	158	14.0	49	13.2	0.89	(0.67-1.31)	
Missing	4	.	0	.	.	.	
Syntocinon/ Syntometrine for 3rd stage management							0.590
Yes	976	13.5	315	14.6	1	.	
No	151	86.6	54	85.4	0.90	(0.62-1.31)	
Missing	4	.	1	.	.	.	
Birthweight (g)							0.246
<3000	88	7.8	24	6.5	0.92	(0.58-1.46)	
3000-3499	392	34.8	116	31.4	1	.	
3500-3999	468	41.5	160	43.2	1.15	(0.86-1.56)	
≥4000	180	16.0	70	18.9	1.31	(0.96-1.80)	
Missing	3	.	0	.	.	.	

Among women who had a PPH requiring transfer, the odds of requiring enhanced care increased as the amount of postpartum blood loss increased (Table 3.21). In terms of cause of PPH, compared with uterine atony, genital tract trauma was associated with almost a halving of the odds of receiving enhanced care (OR 0.58; 95% CI 0.42-0.80). Women who had a major obstetric haemorrhage call documented were more than five times as likely to receive enhanced care (OR 5.42; 95% CI 4.10-7.24).

Table 3.21 PPH-related factors among women transferred for PPH who received enhanced care and women transferred for PPH who did not receive enhanced care

	No enhanced care (n = 1,131)		Enhanced care (n = 370)		Unadjusted ORs		p value
	n	%	n	%	OR	95% CI	
Blood loss (mL)							<0.001
≤500	60	5.3	<5	<1.2	0.91	(0.24-3.42)	
501-999	525	46.4	29	7.8	1	.	
1000-1499	405	35.8	112	30.3	5.01	(3.06-8.18)	
1500	137	12.1	226	61.1	33.0	(17.1-52.0)	
Missing	4	.	<5	<0.3	.	.	
Major obstetric haemorrhage call documented							<0.001
No	1019	90.4	235	63.5	1	.	
Yes	108	9.6	135	36.5	5.42	(4.10-7.24)	
Missing	4	.	0	.	.	.	
Cause of PPH							<0.001
Uterine atony	406	36.0	152	41.1	1	.	
Genital tract trauma	355	31.5	77	20.8	0.58	(0.42-0.80)	
Retained products / morbidly adherent placenta	221	19.6	106	28.6	1.28	(0.95-1.72)	
Other	15	1.3	6	1.6	1.07	(0.45-2.52)	
Not recorded	130	11.5	29	7.8	0.60	(0.37-0.96)	

First-line uterotonics were the most commonly received treatment for PPH among both women who received enhanced care and those who did not (Table 3.22). All treatment types were more commonly received by women who received enhanced care than women who did not receive enhanced care.

Table 3.22 Treatment of PPH among women who received enhanced treatment or care compared with women who did not

	No enhanced care (n = 1,131)		Enhanced care (n=370)	
	n	%	n	%
Management of PPH				
First line treatment				
Bimanual compression	42	3.8	37	10.0
Catheterisation	602	53.2	306	82.7
Cannulation/IV fluids	834	73.7	348	94.1
First-line uterotonics	921	81.4	341	92.2
Second-line treatment				
Second-line uterotonics	89	7.9	105	28.4
Tranexamic acid	265	23.4	191	51.6
Third-line treatment	18	1.6	40	10.8
Invasive procedure				
PPH treatment not recorded	139	12.3	53	14.3

3.5.8 Neonatal outcomes among cases and controls

Adverse neonatal outcomes were uncommon in this this study population, although slightly higher proportions were observed for all neonatal outcomes among cases compared with controls (Table 3.23). An Apgar score of less than 7 at 5 minutes was reported in 0.8% of controls compared with 1.3% of cases. Twenty-five controls (1.5%) and 41 cases (2.7%) were admitted to neonatal care. Neonatal morbidity was reported for 0.6% of controls and 2.0% of cases. Two neonatal deaths were recorded. There were no stillbirths.

Given the relatively small number of poor neonatal outcomes in this study, there was not sufficient statistical power to perform a multivariable analysis of risk factors for poor neonatal outcomes among cases and controls.

Table 3.23 Neonatal outcomes among cases and controls

	Controls		Cases		
	n	%	n	%	p value
Apgar score <7, at 5 minutes	12	0.8	20	1.3	0.170
Admission to neonatal care[1]	25	1.5	41	2.7	0.097
Neonatal morbidity reported[2]	9	0.6	31	2.0	<0.001

[1]Refers to admission to a neonatal unit or any other paediatric high level care within 48 hours of birth

[2]Neonatal morbidity includes: birth injury, congenital anomaly, jaundice, sepsis/infection, meconium at birth, respiratory distress

3.5.9 Post hoc analysis of case and control characteristics by unit type

The post-hoc analysis of characteristics of women who gave birth in FMUs and women who gave birth in AMUs was conducted to assess whether the difference in incidence of PPH requiring transfer between FMUs and AMUs was due to different characteristics of women giving birth in each type of MU. The results of the analyses are presented in Appendix B.5. Broadly speaking, the cases who gave birth in AMUs were similar to the cases who gave birth in FMUs and the controls who gave birth in AMUs were similar to controls who gave birth in FMUs. For both groups, the only risk factors for PPH requiring transfer that were statistically significantly different between the groups were smoking during pregnancy, which was more common among women giving birth in AMUs, and longer duration of third stage of labour, which was more common among women who gave birth in FMUs ($p < 0.001$). Blood loss was also similar between women giving birth in FMUs and in AMUs for both cases and controls (Table 3.24).

Table 3.24 Blood loss among cases and controls by unit type

	FMU n = 193		AMU n = 2,783		p value
	n	%	n	%	
Blood loss among controls (mL)					0.627
<500	88	96.7	1289	93.5	
500	1	1.1	45	3.3	
501-999	2	2.2	41	3.0	
1000-1499	0	0.0	3	0.2	
Missing	3	.	3	.	
Blood loss among cases (mL)					0.140
<500	1	1.1	1	0.1	
500	3	3.0	58	4.2	
501-999	38	39.4	516	36.9	
1000-1499	31	31.3	486	34.8	
1500	26	26.3	337	24.1	
Missing	0	.	4	.	

3.6 Discussion

3.6.1 Summary

In this national case-control study, the incidence of PPH occurring in UK MUs and requiring transfer to obstetric care was 3.7 per 100 births (95% CI 3.6-3.9). This was higher than expected based on the existing literature. Factors known prior to the unset of labour that were associated with higher odds of PPPH were: primiparity, not smoking in pregnancy, having a previous PPH or problems in a previous pregnancy other than PPH, a gestational age of 41 weeks or more. Of the factors that emerge during labour and the birth, those associated with higher odds of PPH were: instrumental birth, a third stage of labour lasting 60 minutes or more, a 3rd or 4th perineal tear, and birthweight of 3500g or more, were independently associated with a higher odds of PPH requiring transfer. Similar risk factors, with the exception of smoking status, were identified for women who were considered to be at a low-risk of complications at the start of labour care.

Women who had a PPH requiring transfer were more likely to require enhanced care (comprising admission to higher-level care or blood transfusion) after birth, compared with controls (24.7% vs 0.6%). Among cases, women who required enhanced care were not significantly different from women who did not, in terms of sociodemographic, clinical or pregnancy-related factors. The only factors that were significantly associated with increased odds of having enhanced care were a third stage of labour lasting 60 minutes or more and blood loss of 1000mL or more.

3.6.2 Strengths and limitations

The strengths of this study include its robust design, as a national population-based case-control study, including all reported cases of PPH requiring transfer following birth in an MU. The inclusion of all MUs in the UK in the study and 98% participation rate minimised the risk of bias related to regional differences between MUs. Additionally, the high monthly reporting rate, with 95% of monthly requests for data returned, also reduced the likelihood of selection bias. This high monthly reporting rate, coupled with the fact that transfer to obstetric care and the reason for transfer is generally well

documented in a woman's notes, suggest that case ascertainment was high. However, due to the absence of other sources, it is not possible to triangulate the data received with information from other sources to determine what proportion of cases, if any, may have been missed.

The case definition used in this study was based on the decision to transfer a woman to obstetric care, rather than on a specified amount of blood loss. This definition was chosen to capture women whose condition was considered severe enough to warrant transfer to obstetric care, rather than using estimated blood loss, which previous studies have shown to be unreliable. It should be noted, however, that the decision to transfer a woman may have been influenced by the resources and capacity in the MU and the OU at the time of the birth. Free text comments entered by a small number of reporting midwives indicated that, in some cases, the capacity of both MUs and OUs may have influenced the decision to transfer a woman, or not, following a PPH. The study was reliant on anonymised data, entered directly from medical records, which did not include organisational information, so no data were available about several factors that may have been relevant to the decision to transfer or to the management of PPH, including staff levels and capacity in the MU and OU at the time of the birth. As such, it was not possible to adjust for these factors in the analysis.

Despite potential differences in the likelihood of transfer based on resourcing and capacity of MUs and OUs at the time of the birth, it is likely that the results of this study are broadly comparable to studies that use estimated blood loss ≥500mL to define PPH case status. Almost all cases had estimated blood loss ≥500mL and the vast majority of controls had estimated blood loss <500mL. This suggests that the case definition used here is comparable to studies that use the definition of PPH employed in the UK, blood loss ≥500mL, and it is therefore appropriate to compare findings.

It should be noted that the estimated volume of blood loss reported referred to a woman's total blood loss and it was not possible from the way the data were collected to determine what proportion of

the blood loss occurred in midwifery-led care and what proportion occurred after transfer to obstetric-led care. Such information may have provided important context for understanding the management of PPH in midwifery units. Additionally, the data collection form for control women did not include information about the management of blood loss that occurred in midwifery-led care. As managing blood loss is part of midwifery practice and as a small proportion of control women lost 500mL of blood or more, it may have been informative to describe the management that was received where transfer to obstetric care did not occur. Such information would have provided useful context for the development of practices and policies for the management of PPH in MUs.

It is important to note that, by design, this study did not include women who planned birth or began labour care in a MU but were transferred to an OU before the birth. The incidence reported here does not reflect the incidence of PPH among all women who plan birth in a MU and it is possible that some of the risk factors identified are differentially associated with PPH among women who plan birth in a MU but give birth in an OU.

Some of the analyses in this study would have been strengthened, and additional analyses may have been possible, had the size of the study population been larger. Several of the risk factors that may be associated with a higher risk of PPH were relatively uncommon in this study, including pre-existing medical conditions, current pregnancy complications and complications identified during labour. This was as expected, since women who give birth in MUs are more likely to be healthy with straightforward pregnancies. Consequently, there was insufficient power to exclude the role of chance in the association between these variables and PPH requiring transfer. The relatively small number of women requiring enhanced treatment or care also limited the power of this analysis to detect associations between some risk factors and the need for enhanced treatment or care. Furthermore, the low proportions of poor neonatal outcomes was anticipated based on the study population. In a larger study, it might have been possible to explore associations between maternal and care factors

and neonatal outcomes following a transfer for PPH. This study was planned to run for 12 months but was terminated early due to the COVID-19 pandemic. Had data collection been able to proceed as planned, the study would have had greater power to detect associations between PPH and risk factors or outcomes that were uncommon in this population.

3.6.3 Conclusions

This study has estimated the incidence of PPH requiring transfer to obstetric care following birth in an MU in the UK to be 3.7%. This was higher than expected, however, it aligns with recent trends observed in hospital episode statics in England and evidence from international research that suggests an increase in the incidence of PPH in high-income countries. The risk factors most strongly associated with increased odds of a PPH requiring transfer to obstetric care were related to labour and birth, most notably third stage of labour lasting 60 minutes or more, and perineal trauma. Generally, the risk factors identified in this study broadly align with those reported in previous studies and with current midwifery practice in the UK, suggesting midwives should continue to follow national guidance in the management of risk factors for PPH.

The results about outcomes for women who have a PPH in an MU are broadly reassuring for midwives and women who plan birth in an MU, in that current management of PPH appears to be appropriate and leads to generally good outcomes for women and babies overall. However, it is important that MUs have robust guidelines about the management of PPH, access to the necessary resources, and ready access to transfer when required.

While this study provided important evidence about the incidence and risk factors for PPH requiring transfer in a low-risk population across the UK, the results are not generalisable to the wider birthing population, including both higher risk women and low-risk women who give birth in an OU.

The incidence of PPH observed in this study compared with previous data suggest an increasing in the incidence of PPH in the UK even among low-risk women, however, the study design meant it was not possible to explore trends over time or examine the ways in which the incidence and risk factors for PPH have changed over time in the UK. A large population-based study conducted over a longer time period would be needed to address these research objectives. The next chapter presents the methods and results of such a study.

Chapter 4: Incidence and risk factors for postpartum haemorrhage in a Scottish population over 31 years: a case-control study

4.1 Introduction

Recent evidence from studies in high-income countries suggests that the incidence of PPH is increasing (8, 14, 33). Posited explanations for this trend include the increasing prevalence of potential risk factors for PPH, including giving birth via caesarean, increasing maternal age, and increasing obesity (7, 10). However, even after accounting for the potential influence of rising prevalence of risk factors, previous research has shown that an unexplained increase in incidence remains. There is limited research investigating risk factors among women who might be considered at low-risk of PPH though. To date, there has been no published research investigating long-term trends in PPH in a UK population. This study aims to address these gaps.

4.2 Aims and objectives

The aims of this study were to identify risk factors for PPH in a UK population and investigate potential changes in the prevalence of risk factors over time. The objectives were to:

1. Estimate the incidence of PPH and SPPH over time;
2. Investigate and identify maternal, intrapartum and birth-related factors associated with (a) PPH and (b) SPPH;
3. Investigate and identify maternal, intrapartum and birth-related factors associated with (a) PPH and (b) SPPH in women who are healthy with straightforward pregnancies;
4. Explore the relationship between changes in incidence of PPH and the prevalence of risk factors over time.

4.3 Methods

4.3.1 Study design

This was a population-based case-control study of all cases of PPH and SPPH recorded in the NHS Grampian region of Scotland between 1986 and 2006.

4.3.2 Setting and database description

Data from the Aberdeen Maternal and Neonatal Databank (AMND) were analysed. This is a population-based database containing information about all pregnancies and obstetric events for women presenting to the University of Aberdeen Maternity Hospital, a tertiary maternity hospital for the NHS Grampian region. It is the only maternity hospital in the region and has an AMU for women at low risk of complications. With around 5,000 births per year, the AMND holds information about more than 270,000 pregnancies since 1950 (149). Data for all fertility-related events are recorded in the database and each woman is assigned a unique study number such that multiple fertility events can be linked to the same woman Data are validated by comparing records on the database with the original hard copy patient records (149). The population in the region is relatively stable, with limited migration (149), enabling trends over time to be analysed with a relatively low risk of bias associated with underlying population changes.

4.3.3 Inclusion and exclusion criteria

The study population comprised all women who gave birth at Aberdeen Maternity Hospital from 1986-2016. The analysis population were women who gave birth following a pregnancy of at least 24 completed weeks, for whom postpartum blood loss was recorded, irrespective of mode of birth or outcome of birth.

4.3.3.1 Exclusion criteria:

Records were excluded if:

- blood loss information was missing or was recorded as <30mL (as this was considered implausible and therefore a potential data entry error),
- mode of birth was missing, or
- mode of birth was stated to be ‘destructive’.

4.3.4 Data and definitions

4.3.4.1 Case definitions

Risk factors for PPH and SPPH were analysed separately. For analyses relating to PPH, 'cases' were women with a recorded blood loss of ≥500mL in the 24hrs following the birth. 'Cases' of SPPH were women with a recorded blood loss of ≥1500mL.

For births that occurred in the delivery room, blood loss was estimated visually, unless a major bleed (≥1500mL) was recorded, in which case blood loss was typically measured by the volume of blood in a jug and by weighing swabs. For all births occurring in theatre, blood loss was weighed, including weighing swabs.

4.3.4.2 Control definition

Controls for both groups were all women who had a recorded blood loss of <500mL in the 24hrs following the birth.

4.3.4.3 Definition of 'low-risk' women

Analyses relating to women at a low risk of complications were carried out in the sub-group of all cases and controls who were healthy, with straightforward pregnancies at the start of care in labour. For each birth, women were classified as 'low-risk', if they:

- had a singleton pregnancy,
- gave birth between 37 and 42 completed weeks' gestation,
- did not have a planned caesarean, and
- did not have pre-existing medical or obstetric conditions or current pregnancy complications, as listed in Tables 6 and 7 of the NICE intrapartum care guidelines for healthy women and their babies (146).

These tables set out the conditions or situations that indicate there may be increased risk for the woman or the baby during labour and birth, for which planned birth in an obstetric unit would be expected to reduce that risk. The pre-existing medical and obstetric conditions included in Tables 6 and 7 in the NICE intrapartum care guidelines were mapped, were possible, to data from the AMNDB. For some conditions, an appropriate specific category or indicator variable was available in the

dataset, in which case this information was used, while other conditions were identified using ICD 9 codes. For some conditions, there was no equivalent information available or data were of insufficient quality to be used for these analyses. Details about how each of the medical and obstetric conditions in the NICE tables were operationalised in this dataset are provided in Appendix C.

4.3.4.4 Risk factors

A wide range of maternal, perinatal and intrapartum variables were analysed to identify factors associated with an increased risk of PPH, including those that have been identified as potential risk factors for PPH in previous research, identified in Chapter 2. Risk factors were categorised into one of six groups:

1. Maternal socio-demographic factors
3. Pre-existing clinical and obstetric history factors
4. Clinical characteristics arising during pregnancy
5. Intrapartum factors
5. Birth-related factors
6. Baby characteristics.

Table 4.1 describes how each of these was categorised/defined in the dataset.

Table 4.1 Risk factor variables and definitions

Variable	*Description and additional information*
Mode of birth	Analyses was carried out on sub-populations based on mode of birth, classified into two categories: • Vaginal birth • Caesarean (for multiple births, if any of the babies were born by caesarean, the birth was classified as a caesarean)
Year of birth	Provided as individual year of the birth and classified into the following categories for the regression analyses: • 1986-1990 • 1991-1995 • 1996-2000 • 2001-2005 • 2006-2010 • 2011-2016
Maternal sociodemographic characteristics	
Maternal age	Maternal age at the birth, provided as an integer and categorised for analysis as: • <20 • 20-24 • 25-29 • 30-34 • 35-49 • 40+
Smoker status	Derived using two self-reported variables: 1. Smoking status during pregnancy. Reported as: • Non-smoker • Ex-smoker • Smoker 2. Number of cigarettes smoked per day, provided as an integer and categorised for analysis as: • 1-5 cigarettes per day • 6-10 cigarettes per day • 11+ cigarettes per day
Area deprivation quintile	The Scottish Index of Multiple Deprivation (SIMD) is an area-based measure of relative deprivation across 6,976 small areas identified by postcode, which are ranked according to deprivation, measured across seven domains: income, employment, health, education, crime, access to services and housing (Government of Scotland, 2020). This information is provided in the AMND for each record in the form of deciles, ranked from 1 (least deprived) to 10 (most deprived) and these were converted into quintiles for the purposes of analyses.

Ethnicity	Ethnicity was provided in the following sub-categories and grouped into the broader categories for the purposes of analysis:
	• White
	  ○ North America
	  ○ Britain
	  ○ Ireland
	  ○ Northern Europe
	  ○ Western Europe

Variable	*Description and additional information*
	○ Eastern Europe ○ Southern Europe ○ Europe Other ○ Australasia ○ Historic White • Black ○ Sub-Sahara ○ Africa Other ○ Caribbean ○ Historic Negro ○ Historic African • Asian ○ India ○ Pakistan ○ Bangladesh ○ China ○ Far East Asia - Other ○ South East Asia ○ Asia Other ○ Historic Asian ○ Historic Indian • Other ethnicity ○ North Africa ○ South America ○ Middle East ○ Middle East Other ○ Historic Arabic
Marital status	Marital status was provided as the following sub-categories and grouped into the broader categories for the purpose of analysis: • Married/co-habituating ○ Married ○ Cohabitating • Single/separated ○ Single ○ Separated ○ Widowed ○ Divorced
Pre-existing clinical and obstetric history characteristics	
BMI	BMI was calculated using a woman's height and weight recorded at booking, using the formula weight (kg)/height (m)^2
Parity	Parity was provided as the number of previous births and categorised for the purposes of analysis into the following: • 0 • 1 • 2-4 • 5+
Diabetes	Diabetes status was provided as any current diabetes (gestational or chronic): • Yes • No

Variable	Description and additional information
Hypertension	Hypertension was provided in the following categories: • None • Gestational hypertension • Pre-eclampsia • Eclampsia • Chronic hypertension
Previous PPH	• Yes • No
Previous caesarean	• Yes • No
Pregnancy-related factors	
Multiple pregnancy	Plurality of pregnancy was provided as the number of gestations and grouped into two categories: • Singleton • Multiple
Gestational age	Gestational age at the birth was provided as the number of weeks and grouped into the following categories: • 24-31 • 32-36 • 37 • 38 • 39 • 40 • 41 • 42-44
Intrapartum factors	
Caesarean after labour	Derived using two variables: Method of birth = caesarean Onset of labour = spontaneous or induced This was categorised as caesarean after the onset of labour: • Yes • No
Number of methods of induction	The number of methods of induction was calculated by summing a count of each reported method of induction and categorised into the following: • 0 • 1 • 2+
Augmentation of labour	• Yes • No
Prolonged first stage of labour	In accordance with the NICE intrapartum care guideline CG190 (146), first stage of labour was classified as possibly prolonged if it lasted more than 12 hours. A first stage of labour lasting longer than 30 hours was considered to be implausible and therefore records with a duration >30 were classified as missing for this variable.
Prolonged second stage of labour	In accordance with the NICE intrapartum care guideline CG190(146), prolonged second stage of labour was defined as:

Variable	*Description and additional information*
	Nulliparous women: second stage lasting longer than 2 hours Multiparous women: second stage lasting longer than 1 hour A second stage of labour longer than 6 hours was considered implausible and therefore records with a duration > 6 were categorised as missing for this variable.
	Birth-related factors

Instrumental birth	Instrumental birth was provided in the following sub-categories and grouped into the broader categories below:
	• Instrumental birth
	  ○ Forceps
	  ○ Kiellands Forceps
	  ○ Vacuum Extraction
	  ○ Assisted breech
	• Non-instrumental birth
	  ○ Spontaneous vaginal birth
	  ○ Breech extraction

Presentation	Presentation of baby was categorised based on the presentation of the first baby and categorised as:
	• Vertex
	  ○ Occiput anterior
	• Non-vertex
	  ○ Occiput posterior
	  ○ Occiput transverse
	  ○ Breech
	  ○ Face, brow
	  ○ Shoulder
	  ○ Cord
	  ○ Compound
	  ○ Other

Duration of 3rd stage of labour	Provided in minutes and categorised as • <30 minutes • ≥30 minutes

Perineal tear	Perineal tear was provided as the following sub-categories and categorised into the broader groups below:
	• No tear or laceration
	• <3rd degree tear
	  ○ Laceration
	  ○ Episiotomy
	  ○ Episiotomy and laceration
	  ○ Labial tear
	• 3rd or 4th degree tear
	  ○ 3rd degree tear
	  ○ 3rd degree tear and episiotomy
	  ○ 4th degree tear
	  ○ 4th degree tear and episiotomy

Retained placenta	• Yes • No
	Baby characteristics
Birth status	Birth status was classified as:

Variable	*Description and additional information*
	• Live birth • Stillbirth (For multiple births, if one of the babies was stillborn, the record was classified as a stillbirth
Head circumference	Provided in centimetres and classified as: • <35cm • ≥35 cm
Birthweight	Birthweight was provided in grams and was classified into the following groups: • <3000g • 3000-3499g • 3500-3999g • ≥4000g For multiple births, the weight of the first baby was used.

4.3.5 Statistical analysis

4.3.5.1 Incidence and temporal trends

The overall incidence of PPH and SPPH, and the incidence for each year from 1986 to 2016, were estimated with 95% CIs by mode of birth (vaginal birth and caesarean), for all women and for low-risk women. There were therefore eight separate analyses of incidence:

All women:

- PPH among all women who had a vaginal birth (Model 1)
- PPH among all women who had a caesarean birth (Model 2)
- SPPH among all women who had a vaginal birth (Model 3)
- SPPH among all women who had a caesarean birth (Model 4)

Low-risk women:

- PPH among low-risk women who had a vaginal birth (Model 5)
- PPH among low-risk women who had a caesarean birth (Model 6)
- SPPH among low-risk women who had a vaginal birth (Model 7)
- SPPH among low-risk women who had a caesarean birth (Model 8).

Estimates of incidence were calculated using the number of cases in each group as the numerator and the total number of births in that population as the denominator.

The annual incidence of vaginal birth and caesarean birth from 1986 to 2016 was estimated with 95% CIs by dividing the number of births in each birth mode category per year by the total number of births in each year.

Temporal trends for incidence of PPH and SPPH and for the incidence of vaginal births and caesarean were assessed graphically. The Cochran-Armitage test for linear trend, with year of birth as the independent variable, was used to assess the association between year of birth and the occurrence of PPH and SPPH for all women, and for low-risk women. For all analyses $p<0.05$ was considered statistically significant.

4.3.5.2 Risk factors

Frequencies and proportions of each potential risk factor were tabulated for PPH and SPPH separately within each population for cases and controls, and compared using two-sided chi square tests. Unconditional logistic regression was used to investigate univariable associations between explanatory variables and each outcome (PPH and SPPH) in each analysis population, generating OR with 95% CI.

Risk factors for PPH and SPPH were assessed using multivariable unconditional logistic regression models. Eight multivariable logistic regression models were constructed (Models 1-8, as described above). For each model, controls were women within the sub-population who did not experience a PPH (blood loss <500mL).

The eight models were created separately using a stepwise forward logistic regression, entering explanatory variables into the regression equation in sequential order based on the categories listed above, from distal (e.g., ethnicity) to proximal (e.g., induction of labour). The impact of the inclusion of each individual variable was examined using a Wald test, and any non-significant variables removed, before the next group of variables was added. The output of the models was generated by removing

variables, until only those significantly improving the fit of the data remained. To account for the non-independence of women with more than one birth in the study period, robust standard errors were used to deal with this clustering (150).

4.3.5.2.1 Risk associated with multiple factors

To investigate the impact of multiple risk factors on the odds of PPH, using the methods described by Kayem and colleages (151) , a score of one was assigned to each risk factor identified as significantly associated with PPH in the multivariable analysis. This scorewas summed for each woman's record and the total number of risk factors, was used to estimate the incremental odds of PPH for increasing numbers of risk factors. This analysis was conducted for PPH among all women who had a vaginal birth and for all women who had a caesarean as, together, these groups comprise the whole population and these models had the greatest power in the study.

Potential temporal variations in the risk factor scores, were examined using stacked bar charts which displayed the proportion of women in each risk factor score group (0-2, 3-4, 5-6, 7-8, 9+ risk factors) for each of the year groups. This analysis was conducted and presented separately by mode of birth (vaginal and caesarean).

4.3.6 Prevalence of risk factors over time

The contribution of risk factors to the changing incidence of PPH over time was assessed in two ways, (1) by calculating population attributable fractions and (2) by calculating the prevalence of risk factors over time, among women with vaginal births and among women who gave birth by caesarean. These two populations were chosen for this analysis because, as explained above, these two groups comprise the whole analysis population and they had the greatest power to detect statistically significant associations.

4.3.6.1 Population attributable fractions

Population attributable fractions (PAFs) were used to estimate the fraction of cases attributable to each risk factor. For this analysis, a multivariable logistic regression model was built, using the method described above, but excluding year of the birth from the model so that analyses could show how risk factors changed over time. For each risk factor identified as significantly associated with PPH in this model, indicator variables were created to identify whether a woman had that risk factor or not. For example, if being 30 years or over was identified as a risk factor, an indicator variable that classified women as being <30 or ≥ 30 was created. These indicator variables were then included in a multivariable logistic regression model and the PAF for each risk factor estimated using the method described by (102), considered the standard method for calculating PAF for case-control studies.

The proportion of the population that had each risk factor was calculated and presented along with the OR and 95% CIs from the multivariable logistic regression. Risk factors were grouped into categories based on when, in relation to pregnancy, the risk factor occurs and whether, or not, it may be modifiable after conception. This resulted in three categories of risk factors:

1. Pre-pregnancy non-modifiable
2. Pregnancy-related; non-modifiable
3. Potentially modifiable.

For example, while the age at which a woman conceives may be modifiable within the woman's lifetime, once conception has occurred age is no longer modifiable. Maternal age was therefore classified as a 'pre-pregnancy, non-modifiable' risk factor. Induction of labour is a care-related choice and thus modifiable after conception and therefore was classified as a 'potentially modifiable' risk factor.

4.3.6.2 Prevalence of risk factors over time

The proportions of women with each risk factor identified in Model 1 and Model 2, as described above were estimated, for each 5-year interval from 1986-2016. These proportions were presented in line

graphs, grouped by whether the risk factor was considered pre-pregnancy, pregnancy-, or birth-related and either unmodifiable or potentially modifiable.

4.3.7 Sample size calculation

The sample size was determined by the number of records in the AMND database over the 31-year study period. For each of the eight analyses, a power calculation was conducted to identify the minimum detectable odds ratio for risk factors with a prevalence of 5% (e.g. maternal age ≥35), and 30% (e.g. birthweight 3500-3999g) in the control group (Table 4.2, below). For example, among all women who had vaginal births, for the outcome of PPH, the study had 80% power at the 5% level of significance to detect ORs of 1.12 and 1.06 or greater, assuming putative risk factors with a prevalence of 5% and 30%, respectively (Table 4.2). The minimum detectable ORs were higher for the smaller analysis groups. For example, among low-risk women who had a caesarean birth, for the outcome of SPPH, there were 132 cases and 867 controls and the study had 80% power at the 5% level of significance to detect ORs of 2.78 and 1.74 or greater, assuming putative risk factors with a prevalence of 5% and 30%, respectively.

Table 4.2 Sample size and selected minimum detectable odds ratios for each cohort

Population	***Cases***	***Controls***	***Prevalence of risk factor among controls***	***Minimum detectable OR***
All women	13,795	104,329	.05	1.12
PPH - vaginal birth			.3	1.06
All women	1,298	104,329	.05	1.40
SPPH - vaginal birth			.3	1.18
All women	21,114	12,953	.05	1.15
PPH - caesarean birth			.3	1.07
All women	2,014	12,959	.05	1.34
SPPH - caesarean birth			.3	1.15
Low risk	4,587	53,470	.05	1.21
PPH - vaginal birth			.3	1.10
Low risk	344	53,470	.05	1.89
SPPH - vaginal birth			.3	1.38
Low risk	1,557	867	.05	1.63
PPH - caesarean birth			.3	1.29
Low risk	132	867	.05	2.78
SPPH - caesarean birth			.3	1.74

4.3.8 Data analysis software

All statistical analysis was conducted using STATA statistical software 15(147).

4.3.1 Research ethics

Research ethics approval was not required because this study involved the analysis of anonymised administrative data only. The data access request was approved by the AMND Steering Committee, following the provision of a study-specific data request application, outlining the study's purpose and variables required. Data were extracted by the Data Management Team at the University of Aberdeen.

4.4 Results

4.4.1 Population, incidence and temporal trends

Following exclusions, the total analysis population over the 31-year period from 1986 to 2016 consisted of 152,191 women (Figure 4.1). In this period, there were 13,795 women who had a PPH among a total of 118,124 women having vaginal births, representing an overall incidence of 11.7% (95% CI 11.5-11.9) (Table 4.3). There were 21,114 women who had a PPH among a total of 34,097 women who gave birth by caesarean, representing an incidence of 62.0% (95% CI 61.5-62.5). The incidence of SPPH among vaginal births was 1.1% (95% CI 1.0-1.2) and among caesarean births was 5.9% (95% CI 5.7-6.2).

A total of 60,481 women were classified as 'low-risk' at the start of labour care, most of whom (58,057, 84%) had a vaginal birth. Among low-risk women who had a vaginal birth, the incidence of PPH was 7.9% (95% CI 7.7-8.1) and the incidence of SPPH was 0.6% (95% CI 0.5-0.7). Of the 2,424 low-risk women who had a caesarean birth, 64.2% (95% CI 62.3-66.1) had a PPH, and 5.5% (95% CI 4.6-6.4) had a SPPH.

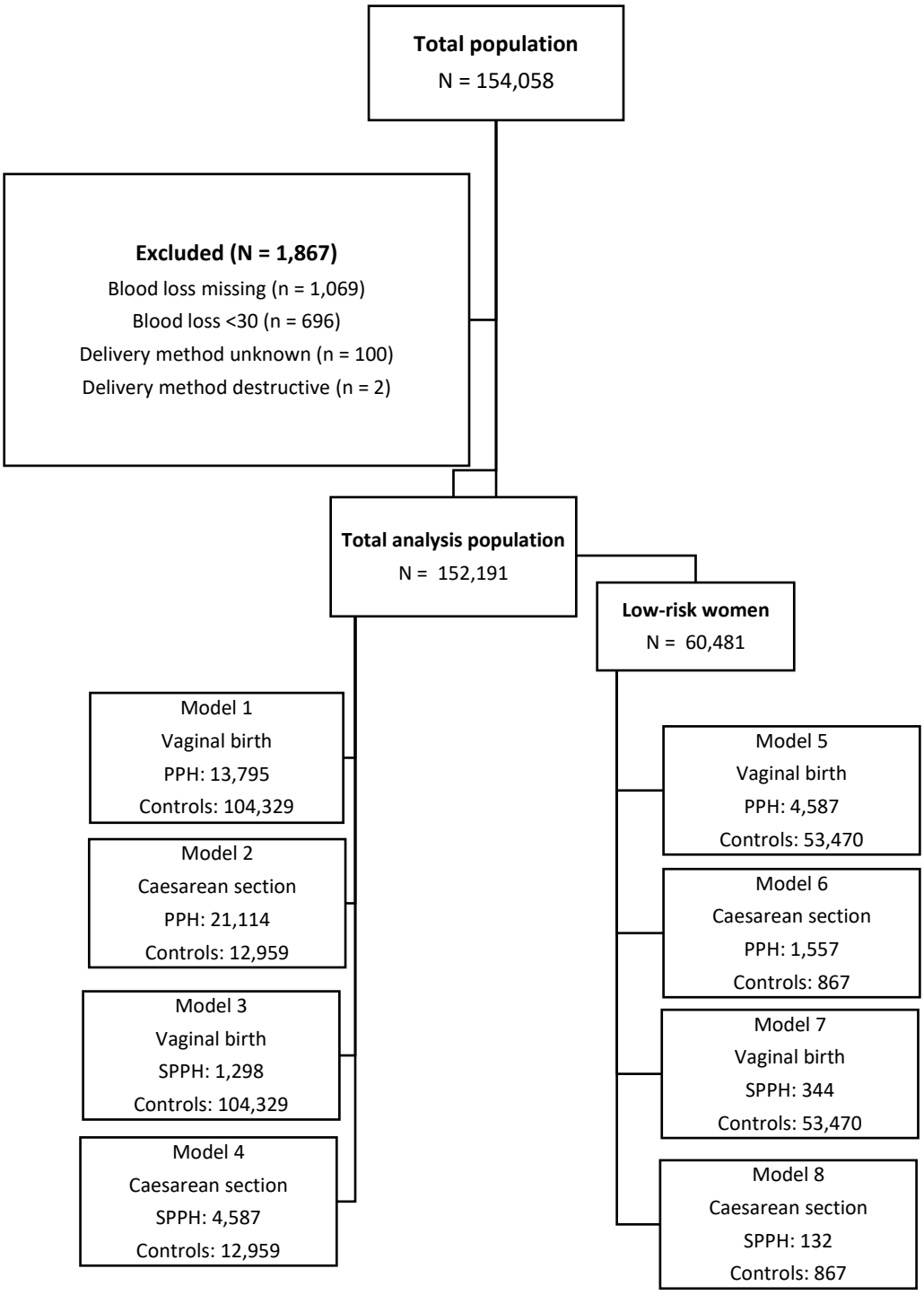


Figure 4.1 Population and participant flow chart

Table 4.3 Incidence ofPPH and SPPH in Aberdeen Maternity Hospital 1986-2016 by mode of birth among all women and 'low-risk' women

			Outcome					
			PPH			SPPH		
Population	*Mode of birth*	*Total births (n)*	*n*	*%*	*CI*	*n*	*%*	*CI*
All women	Vaginal birth	118,124	13,795	11.7	(11.5-11.9)	1,298	1.1	(1.0-1.2)
	Caesarean birth	34,067	21,114	62.0	(61.5-62.5)	2,014	5.9	(5.7-6.2)
Low risk	Vaginal birth	58,057	4,587	7.9	(7.7-8.1)	344	0.6	(0.5-0.7)
	Caesarean birth	2,424	1,557	64.2	(62.3-66.1)	132	5.5	(4.6-6.4)

4.4.1.1 Temporal trends in postpartum haemorrhage

Over the 31-year period, the incidence of PPH among all women who had a vaginal birth increased, from 5.0% in 1986 to 23.7% in 2016 (test for linear trend p<0.001) (Figure 4.2). The incidence of PPH among women who had a caesarean birth increased from 38.4% to 74.2% (p<0.001) (Figure 4.2). Among low-risk women the incidence of PPH over time showed a similar trend, increasing for women who had a vaginal birth from 3.4% to 20.0% (p<0.001), and from 35.1% to 84.4% among low-risk women who gave birth by caesarean (p<0.001) (Figure 4.3).

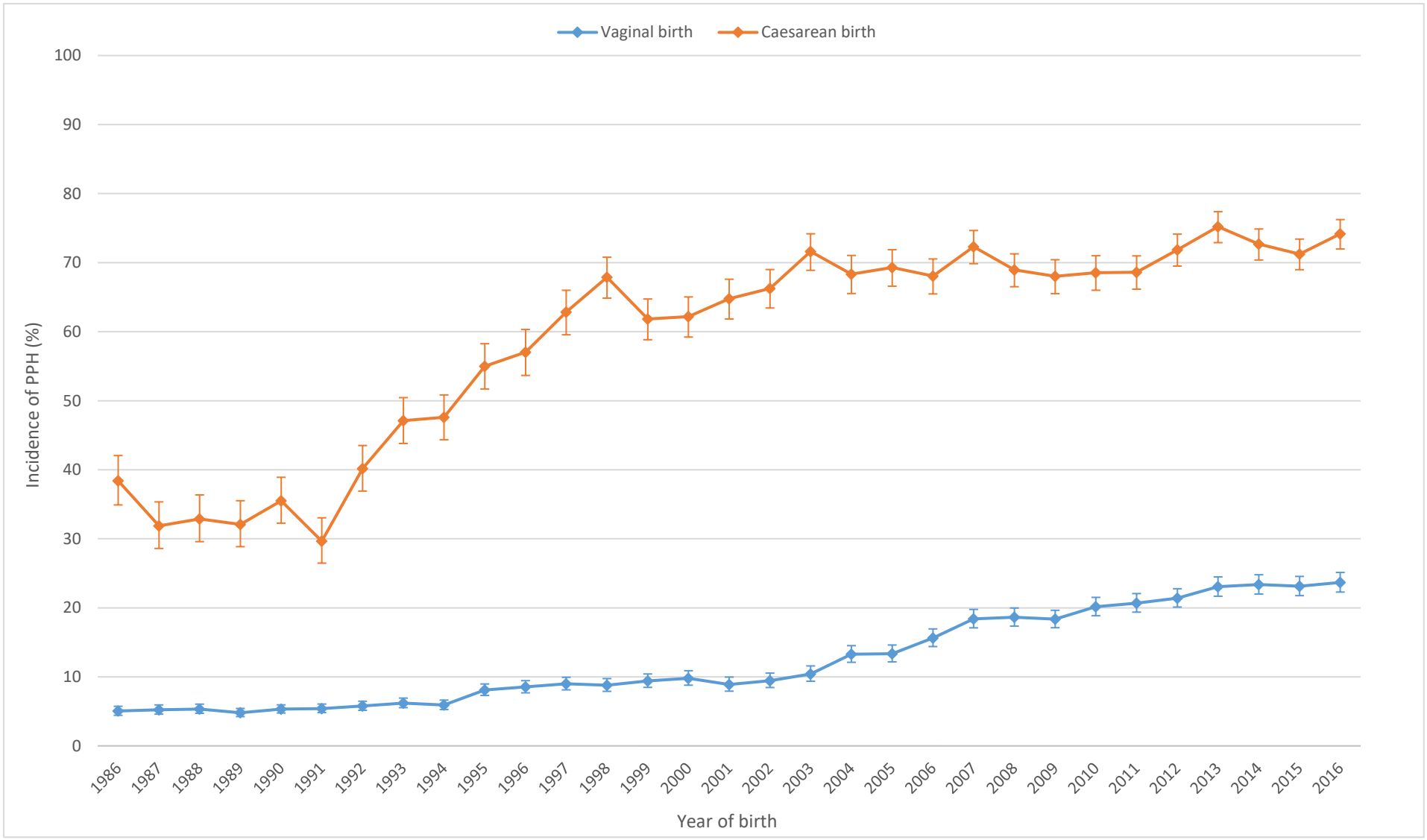


Figure 4.2 Incidence of PPH among all women, by mode of birth, Aberdeen 1986-2016

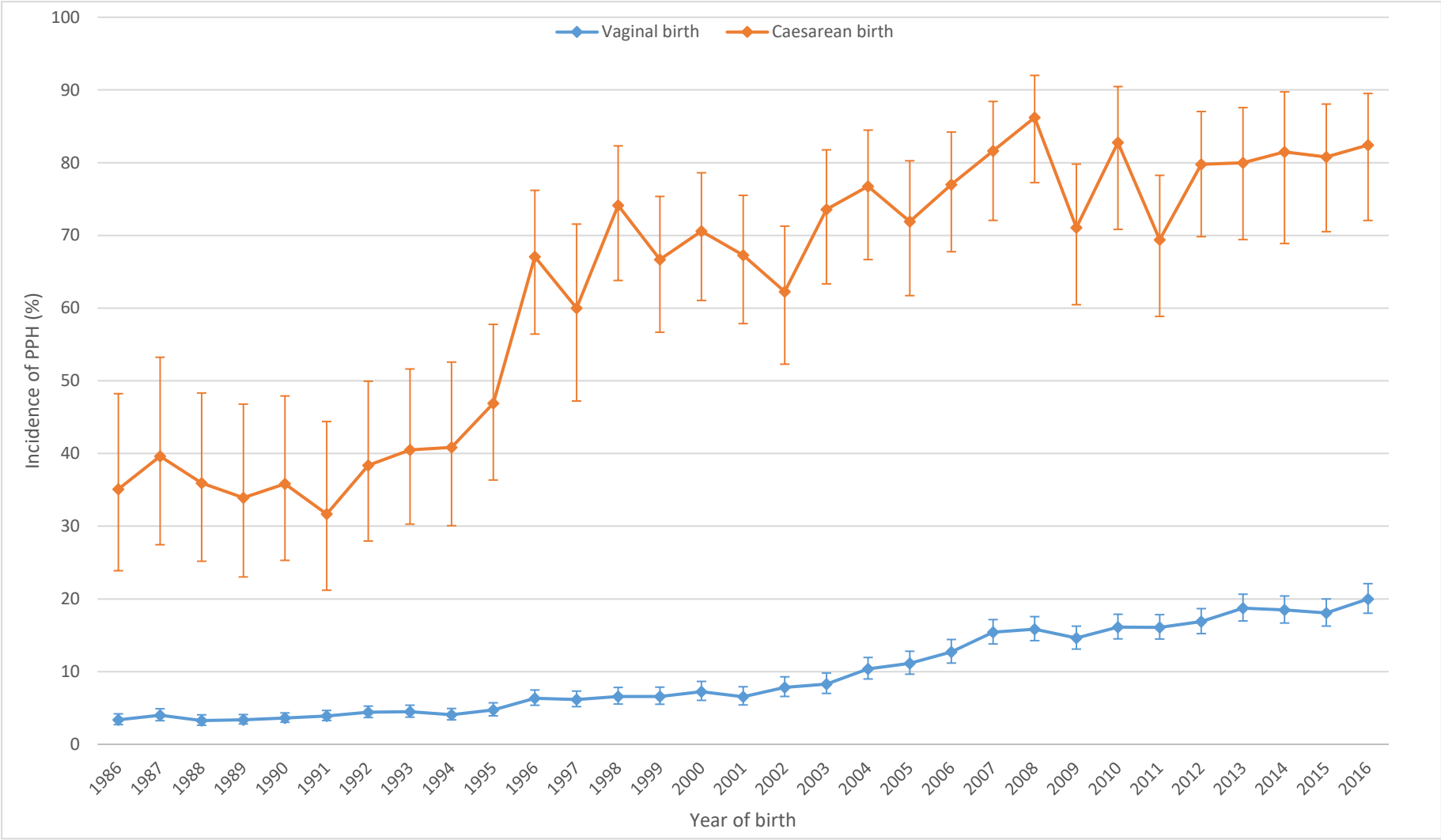


Figure 4.3 Incidence of PPH among low-risk women, by mode of birth, Aberdeen 1986-2016

4.4.1.2 Temporal trends in severe postpartum haemorrhage

The incidence of SPPH among vaginal births increased, from 0.2% in 1986 to 1.8% in 2016 (p<0.001) (Figure 4.4). The incidence of SPPH among caesarean births also increased, from 1.2% in 1986 to 7.2% in 2016 (p<0.001). Among low-risk women who had vaginal births, the incidence of SPPH increased from 0.1% in 1986 to 1.5% in 2016 (p<0.001) (Figure 4.5). The incidence of SPPH among low-risk women who had a caesarean also increased, from 0% in 1986 to 4.1% in 2016 (p<0.001).

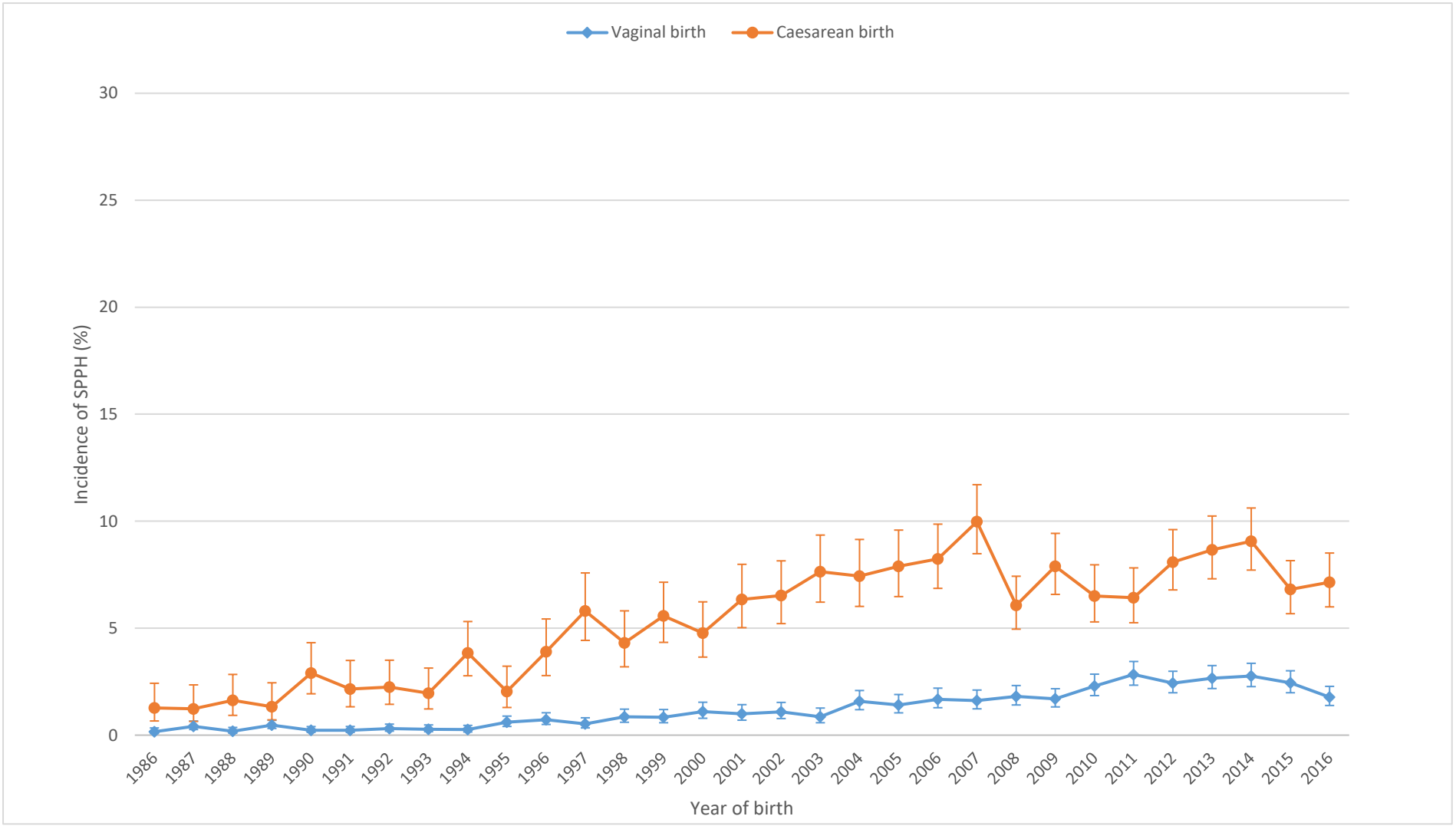


Figure 4.4 Incidence of SPPH among all women, by mode of birth, Aberdeen 1986-2016

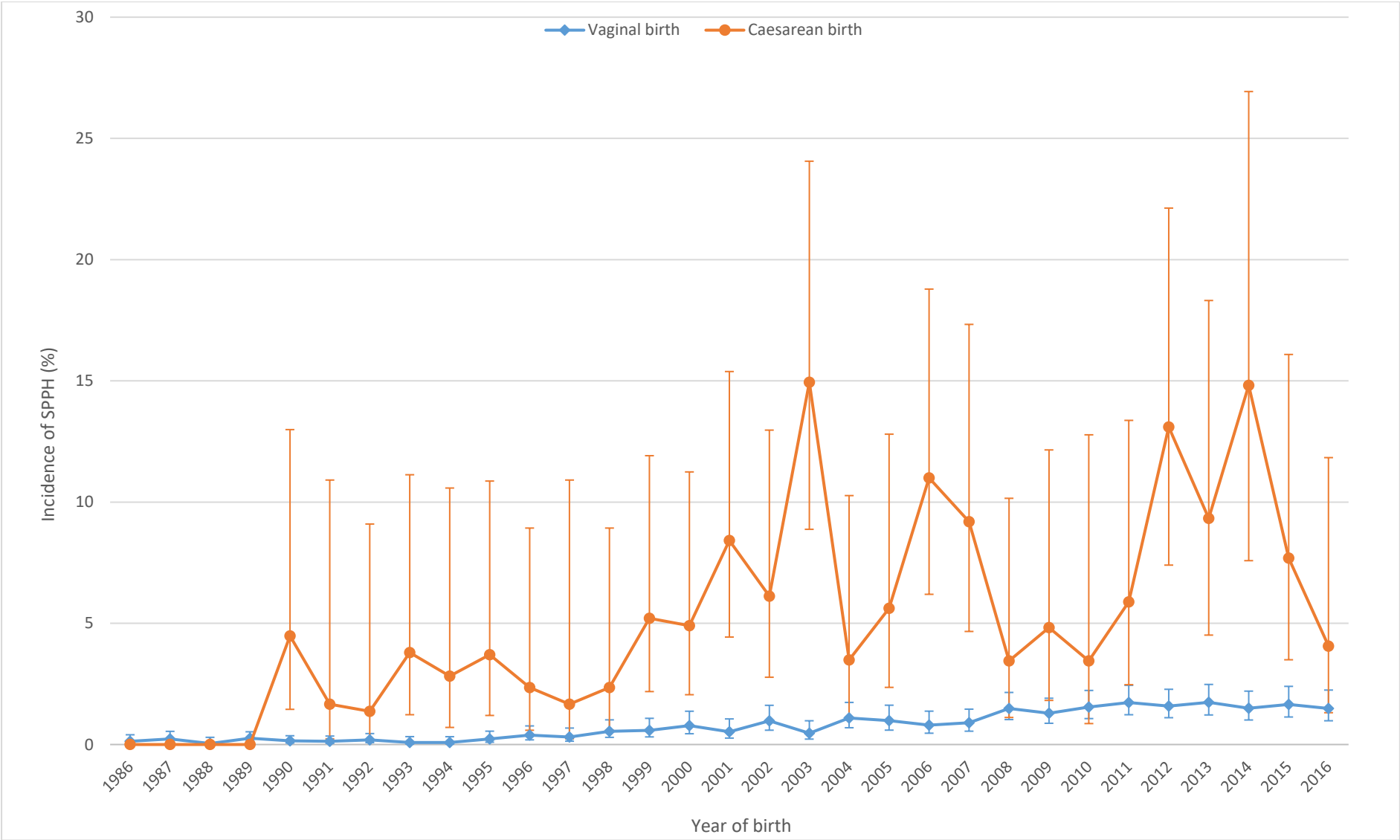


Figure 4.5 Incidence of SPPH among low-risk women, by mode of birth, Aberdeen 1986-2016

4.4.1.3 *Temporal trends in rates of vaginal births and caesarean births*

Over the study period, there was a statistically significant decline in the proportion of births that took place vaginally, from 86% in 1986 to 68% in 2016 ($p < 0.001$), while the rate of caesarean birth increased from 14% to 32% ($p < 0.001$) (Figure 4.6).

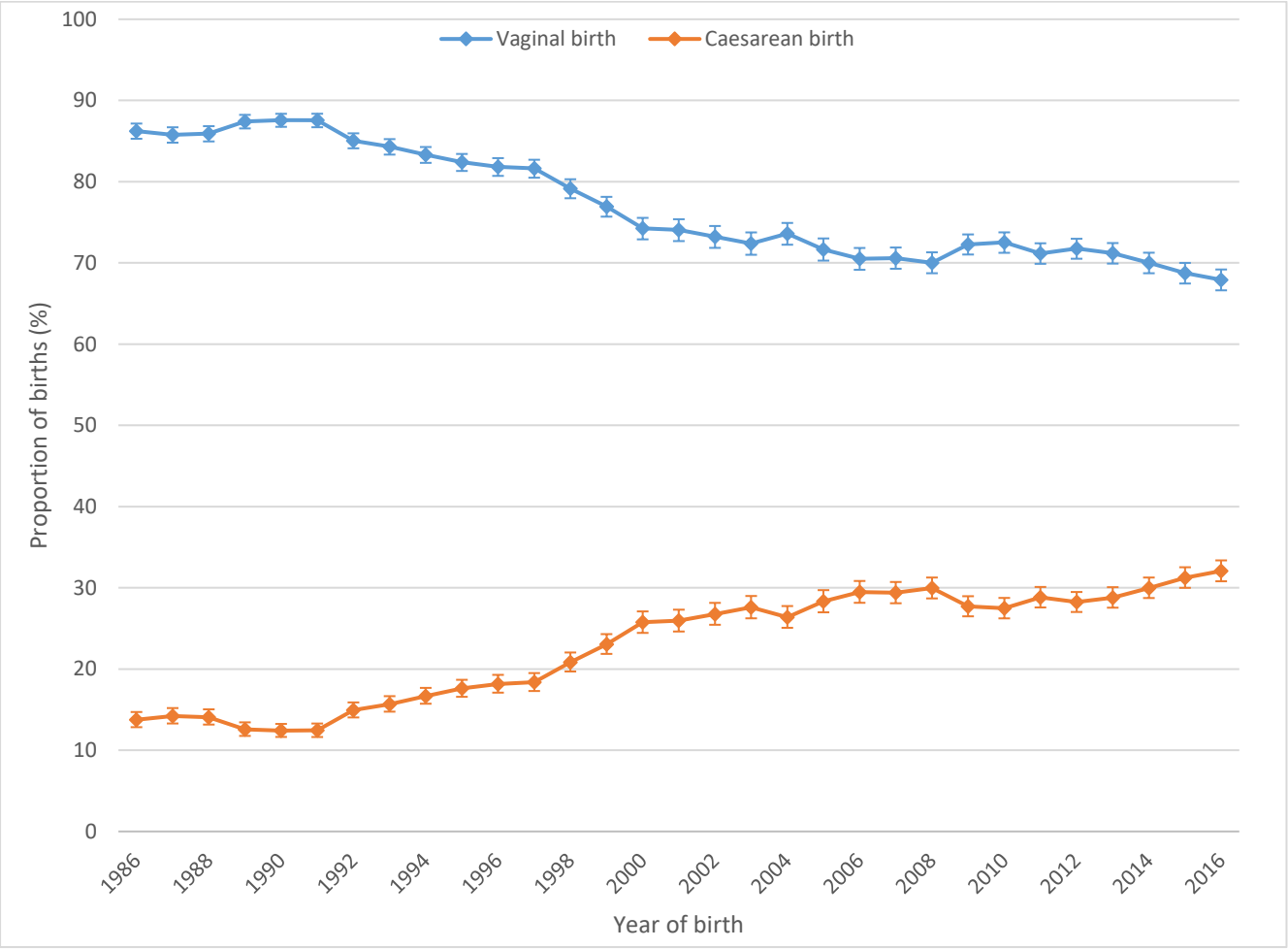


Figure 4.6 Rates of vaginal birth and caesarean birth, Aberdeen 1986-2016

4.4.2 Risk factors for postpartum haemorrhage and severe postpartum haemorrhage

Risk factors for PPH and SPPH among each of the study populations are presented in Tables 4.3-4.6. The risk factors for PPH among all women who had vaginal births and all women who had caesareans are described in detail in sections 4.4.2.1 and 4.4.2.2. In subsequent sections, results of other analyses (SPPH in all women, and PPH and SPPH in low-risk women) are presented in detail in tables, but to avoid undue repetition are described only briefly in text, with reference to the results for PPH in all women.

4.4.2.1 Postpartum haemorrhage after vaginal birth (Model 1)

The results of the univariable and multivariable analyses for women who had a PPH after a vaginal birth are presented in Table 4.3. Among women who had a vaginal birth, after adjustment for all other variables in the model, the odds of PPH increased four-fold over the study period, with women who gave birth in 2011-2016 having the highest odds of PPH compared with the baseline years of 1986-1990 (aOR=4.23; 95% CI 3.89-4.6) (Table 4.4).

Most women, among both cases and controls, reported not smoking in pregnancy (79.3% and 69.9%, respectively). In the adjusted analysis, having smoked before pregnancy was associated with nearly 20% lower odds of PPH (aOR=0.82; 95% CI 0.75-0.89), while smoking 1-5 cigarettes per day and 5-10 cigarettes per day during pregnancy were both associated with 10% lower odds of PPH (aOR=0.90; 95% CI 0.80-1.00 and aOR=0.88; 95% CI 0.80-0.96, respectively). Most women in the analysis population were of White ethnicity (92.3% of cases and 96.1% of controls). Compared with White women, Black women had 71% higher odds of PPH (aOR=1.71; 95% CI 1.46-1.99), as did Asian women (aOR=1.72; 95% CI 1.54-1.93).

Higher BMI was associated with higher odds of PPH. Compared with the reference group of women with a BMI of 18.5-24.9, the odds of PPH were 10% higher for women with a BMI of 25-29.9 (aOR=1.11; 95% CI 1.05-1.16), 15% higher for those with a BMI of 30-34.9 (aOR=1.15 95% CI 1.05-1.22), and 24% higher for those with a BMI ≥35 (aOR=1.24; 95% CI 1.14-1.38). Nulliparous women had over twice the odds of PPH compared with women who had given birth 2-4 times previously (aOR=2.06; 95% CI 1.89-2.4). Women who had one previous birth were 16% more likely to have a PPH compared with the reference group (aOR=1.16; 95% CI 1.06-1.25).

Compared with women with no hypertension, gestational hypertension was associated with 35% higher odds of PPH, and pre-eclampsia/eclampsia with nearly 50% higher odds of PPH, (aOR=1.35;

95% CI 1.26-1.44 and aOR=1.48; 95% CI 1.32-1.66, respectively). Among women who had given birth previously, previous PPH was associated with almost twice the odds of subsequent PPH (aOR=1.90; 95% CI 1.75-2.09), and previous caesarean was associated with 50% higher odds of PPH (aOR=1.58; 95% CI 4.40-1.80).

Among the small group of women who had a vaginal birth and gave birth to multiples, the odds of PPH were more than two and a half times higher than those who gave birth to singletons (aOR=2.59; 95% CI 2.15-3.11). Pre-term birth (32-36 weeks gestation) was associated with higher odds of PPH compared with birth at 40 weeks (aOR=1.24; 95% CI 1.09-1.39). Giving birth after 40 weeks was also associated with higher odds of PPH, with women giving birth at 41 weeks having an aOR=of 1.08 (95% CI 1.02-1.15) and those at 42-44 weeks having an aOR of 1.16 (95% CI 1.04-1.29).

Induced labour was associated with higher odds of PPH compared with spontaneous onset. Women who had only one method of induction had 30% higher odds of PPH (aOR=1.31; 95% CI 1.24-1.39) and those who had two or more methods of induction had more than 50% higher odds of PPH (aOR=1.53; 95% CI 1.39-1.69), compared with women with no induction of labour. Any augmentation of labour was associated with 35% higher odds of PPH (aOR=1.35; 95% CI 1.27-1.42). Prolonged first stage of labour was associated with 9% higher odds of PPH and prolonged second stage of labour was associated with 30% higher odds of PPH, compared with labour within national guidance (aOR=1.09; 95% CI 1.03-1.16 and aOR=1.30; 95%CI 1.23-1.36, respectively).

In terms of birth-related factors, women who had an instrumental birth were 2.56 times as likely to have a PPH compared with women who did not have an instrumental birth (95% CI 2.42-2.70). Non-vertex presentation was associated with 20% higher odds of PPH (aOR=1.21; 95% CI 1.13-1.30). Women who had a third stage of labour that was 30 minutes or longer were more than four times as likely to have a PPH, compared with women who had a third stage <30 minutes (aOR=4.30; 95% CI

3.95-4.68). Compared with women who had no laceration or tearing, those who had a <3rd degree tear were 1.56 times as likely to have a PPH (95% CI 1.46-1.67) and those who had a 3rd or 4th degree tear were 4.50 times as likely (95% CI 3.98-5.09). Women who had a retained placenta were nearly six times as likely to have a PPH (aOR=5.91; 95% CI 5.00-6.98). Larger baby head circumference (≥35cm) was associated with a 12% increase in the odds of PPH (aOR=1.12; 95% CI 1.06-1.18).

Birthweight was significantly associated with the odds of PPH, with women giving birth to babies weighing <3000g being 26% less likely to have a PPH compared with the reference group of women giving birth to babies weighing 3000-3499g (aOR=0.74 95% CI 0.69-0.80). Women who gave birth to a baby weighing 3500-3999g were 1.36 times more likely to have a PPH (aOR=1.36; 95% CI 1.29-1.44) and those giving birth to a baby weighing ≥4000g were twice as likely to have a PPH (aOR=2.00; 95% CI 1.85-2.15).

4.4.2.2 Postpartum haemorrhage after caesarean birth (Model 2)

While the incidence of PPH was markedly higher among women who had a caesarean compared with those who had a vaginal birth, many of the risk factors for PPH were similar for both groups. Over the 31-year study period, the odds of PPH increased significantly, having adjusted for all other variables in the model, with women giving birth by caesarean in 2011-2016 being four and a half times more likely to experience a PPH, compared with those who gave birth in 1986-1990 (aOR=4.47; 95% CI 4.06-4.94). In the adjusted analysis, there was a small but significant association between maternal age and odds of PPH among women who had a caesarean. Women who gave birth at <20 were almost 20% less likely to have a PPH and those aged 20-24 were nearly 10% less likely compared with women who gave birth at 25-29 (aOR=0.83; 95% CI 0.732-0.97 and aOR=0.91; 05% CI 0.84-0.99). Women who gave birth at 35-39 were just over 10% more likely to have a PPH, and those giving birth at 40+ were almost 25% more likely to have a PPH, compared with the reference group (aOR=1.11; 95% CI 1.03-1.20 and aOR=1.23 ; 95% CI 1.07-1.42, respectively).

Smoking status was significantly and inversely associated with odds of PPH, with those who smoked 1-5 cigarettes per day being 17% less likely to have a PPH and those who smoked 11 or more cigarettes per day being 16% less likely to have a PPH, compared with non-smokers (aOR=0.83; 95% CI 0.72-0.94 and aOR=0.84; 95% CI 0.76-0.93). Black women were 30% more likely to have a PPH compared with White women (aOR=1.30; 95% CI 1.08-1.55).

Higher BMI was associated with increased odds of PPH. For women who had a BMI at booking of 25-29, the odds of PPH were increased by 7%, while women with a BMI of 30-34.9 had 22% higher odds and those with a BMI ≥35 had 43% higher odds, compared with women with a BMI of 18.5-24.9 (aOR=1.07; 95% CI 1.01-1.14, aOR=1.11; 95% CI 1.12-1.32, aOR=1.43; 95% CI 1.29-1.58, respectively). Compared with women who had given birth 2-4 times previously, women who had given birth just once before had 11% higher odds of PPH (aOR=1.11; 95% CI 1.02-1.20), with no significant association found for nulliparous women or those who had given birth five or more times previously.

In contrast to women who had a vaginal birth, among women who had caesarean births pre-eclampsia/eclampsia was associated with 16% lower odds of PPH (aOR=0.86; 95% CI 0.77-0.95). Gestational diabetes was also associated with lower odds of PPH, although this association was not statistically significant (aOR=0.93; 95% CI 0.85-1.01). Previous PPH was associated with 50% higher odds of subsequent PPH (aOR=1.51; 95% CI 1.39-1.65). Previous caesarean birth was associated with more than 50% lower odds off PPH (aOR=0.45; 95% CI 0.41-0.49). Women who had a multiple pregnancy were more than twice as likely to have a PPH compared with those having a singleton (aOR=2.32; 95% CI 1.98-2.70).

Women who gave birth at 32-36 weeks' gestation had 26% higher odds of PPH, and those giving birth at 37 weeks had 19% higher odds of PPH, compared with the reference group of women giving birth

at 40 weeks' (aOR=1.26; 95% CI 1.11-1.43 and aOR=1.19; 95% CI 1.05-1.35), while women who gave birth at 39 weeks had 15% lower odds of PPH (aOR=0.85; 95% CI 0.78-0.92).

Women who had a caesarean after the onset of labour had 31% higher odds of PPH, compared with those who had a caesarean without labour (aOR=1.31; 95% CI 1.23-1.40). Among women who laboured, those who had induced labour were at higher odds of PPH. One method of induction increased the odds of PPH by 10% and two or more methods of induction increased the odds of PPH by 30% (aOR=1.10; 95% CI 1.02-1.19 and aOR=1.31; 95% CI 1.16-1.47, respectively).

Birthweight was significantly associated with PPH. Women who gave birth to babies weighing <3000g had 28% lower odds of PPH, compared with those giving birth to a 3000-3499g baby. Women who gave birth to heavier babies had increased odds of PPH, with babies weighing 3500-3999g increasing the odds by 30% and those weighing 4000g or more increasing the odds by more than 80% (aOR=1.31; 94% CI 1.23-1.40 and aOR=1.83; 95% CI 1.69-2.00, respectively).

Table 4.4 Risk factors for PPH among all women who had vaginal births and caesarean births (Model 1 and 2)

	Vaginal births (Model 1)								Caesarean births (Model 2)							
	Controls (n = 104,329)		Cases (n =13,795)		Unadjusted ORs		Adjusted ORs* n = 101,380		Controls (n = 12,953)		Cases (n =21,114)		Unadjusted ORs		Adjusted ORs* (n = 29,817)	
	n	%	n	%	OR	95% CI	OR	p-value (95% CI)	n	%	n	%	OR	95% CI	OR	p-value (95%CI)
Year						<0.001		<0.001						<0.001		<0.001
1986-1990	22,639	21.7	1,228	8.9	1	ref	1	ref	2,454	18.9	1,272	6.0	1	ref	1	ref
1991-1995	22,057	21.1	1,462	10.6	1.22	(1.13-1.32)	1.19	(1.09-1.31)	2,358	18.2	8,884	8.9	1.54	(1.41-1.69)	1.51	(1.36-1.69)
1996-2000	16,253	15.6	1,620	11.7	1.84	(1.7-1.99)	1.67	(1.52-1.83)	1,790	13.8	2,976	14.9	3.21	(2.93-3.51)	2.88	(2.59-3.2)
2001-2005	13,315	12.8	1,659	12.0	2.30	(2.13-2.48)	2.07	(1.88-2.27)	1,763	13.6	3,765	17.8	4.12	(3.77-4.51)	3.66	(3.29-4.06)
2006-2010	13,717	13.2	3,069	22.3	4.12	(3.84-4.43)	3.63	(3.33-3.96)	2,092	16.2	4,694	22.2	4.33	(3.97-4.72)	3.86	(3.49-4.27)
2011-2016	16,348	15.7	4,757	34.5	5.36	(5.02-5.74)	4.23	(3.89-4.6)	2,496	19.3	6,523	30.9	5.04	(4.64-5.48)	4.47	(4.05-4.94)
Maternal age						<0.001								<0.001		<0.001
<20	6,831	6.6	760	5.5	0.86	(0.80-0.94)	.	.	472	3.6	554	2.6	0.78	(0.69-0.89)	0.83	(0.72-0.97)
20-24	32,050	20.2	2,378	17.2	0.88	(0.83-0.92)	.	.	1,969	15.2	2,425	11.5	0.82	(0.76-0.88)	0.91	(0.84-0.99)
25-29	34,021	32.6	4,384	31.8	1	ref	.	.	3,858	29.8	5,785	27.4	1	ref	1	ref
30-34	29,178	28.0	4,245	30.8	1.13	(1.08-1.18)	.	.	4,075	31.5	7,223	34.2	1.18	(1.12-1.25)	1.07	(1-1.14)
35-49	11,339	10.9	1,744	12.6	1.19	(1.12-1.27)	.	.	2,141	16.5	4,144	19.6	1.29	(1.21-1.38)	1.11	(1.03-1.2)
40+	1,903	1.8	282	2.0	1.15	(1.01-1.31)	.	.	436	3.4	982	4.6	1.50	(1.33-1.70)	1.23	(1.07-1.42)
Missing	7	.	2	.	.	.	.	.	2	.	1	.	.	.	.	.
Smoking status						<0.001		<0.001						<0.001		0.001
Non-smoker	71031	69.9	10728	79.3	1	ref	1	ref	8989	71.3	16092	77.9	1	ref	1	ref
Ex-smoker	6564	6.5	923	6.8	0.93	(0.87-1.00)	0.82	(0.75-0.89)	801	6.4	1470	7.1	1.03	(0.94-1.12)	0.97	(0.88-1.08)
Smoker (1-5 per day)	5098	5.0	527	3.9	0.68	(0.62-0.75)	0.90	(0.8-1.00)	576	4.6	746	3.6	0.72	(0.65-0.81)	0.83	(0.72-0.94)
Smoker (5-10 per day)	8491	8.4	713	5.3	0.56	(0.51-0.60)	0.88	(0.8-0.96)	976	7.7	1124	5.4	0.64	(0.59-0.70)	0.93	(0.84-1.04)
Smoker (11+ per day)	10369	10.2	641	4.7	0.41	(0.38-0.45)	0.80	(0.73-0.89)	1268	10.1	1224	5.9	0.54	(0.50-0.59)	0.84	(0.76-0.93)
Missing	2776	.	263	.	.	.	.	.	343	.	458	.	.	.	.	.
Area deprivation quintile						<0.001								0.007		
1st (most deprived)	11834	12.1	1299	10.0	0.79	(0.74-0.85)	.	.	1217	10.3	1797	9.2	0.87	(0.8-0.95)	.	.
2nd	13633	14.0	1732	13.3	0.92	(0.86-0.97)	.	.	1598	13.5	2539	13.0	0.94	(0.87-1.01)	.	.
3rd	15169	15.5	2042	15.7	0.97	(0.92-1.03)	.	.	1983	16.8	3202	16.4	0.95	(0.89-1.02)	.	.
4th	21930	22.4	3083	23.7	1.01	(0.97-1.07)	.	.	2753	23.3	4700	24.1	1.01	(0.94-1.07)	.	.

	Vaginal births (Model 1)								Caesarean births (Model 2)							
	Controls (n = 104,329)		Cases (n =13,795)		Unadjusted ORs		Adjusted ORs* n = 101,380		Controls (n = 12,953)		Cases (n =21,114)		Unadjusted ORs		Adjusted ORs* (n = 29,817)	
	n	%	n	%	OR	95% CI	OR	p-value (95% CI)	n	%	n	%	OR	95% CI	OR	p-value (95%CI)
5th (least deprived)	35190	36.0	4879	37.4	1	ref	.	.	4261	36.1	7238	37.2	1	ref	.	.
Missing	6573	.	760	.	.	.	.	.	1141	.	1638	.	.	.	.	.
Ethnicity						<0.001		<0.001						<0.001		0.024
White	98454	96.1	12605	92.3	1	ref	1	ref	12013	94.5	19247	92.1	1.00	ref	1	ref
Black	1120	1.1	330	2.4	2.30	(2.01-2.63)	1.71	(1.46-1.99)	192	1.5	639	3.0	2.08	(1.76-2.46)	1.30	(1.08-1.55)
Asian	2381	2.3	609	4.5	2.00	(1.81-2.20)	1.72	(1.54-1.93)	404	3.2	810	3.9	1.25	(1.10-1.43)	0.98	(0.85-1.12)
Other	542	0.5	112	0.8	1.61	(1.31-1.99)	1.14	(0.89-1.46)	103	0.8	210	1.0	1.27	(0.99-1.63)	0.86	(0.67-1.12)
Missing	1832	.	139	.	.	.	.	.	241	.	208	.	.	.	.	.
Marital status						<0.001								0.004		
Married or co-habiting	88370	85.8	11982	87.5	1	ref	.	.	11318	88.5	18709	89.5	1.00	ref	.	.
Single or separated	14616	14.2	1719	12.6	0.87	(0.82-0.92)	.	.	1475	11.5	2196	10.6	0.90	(0.84-0.97)	.	.
Missing	1343	.	94	.	.	.	.	.	160	.	209	.	.	.	.	.
Pre-existing clinical factors																
BMI at booking						<0.001		<0.001						<0.001		<0.001
< 18.5	2574	2.6	285	2.2	0.91	(0.80-1.03)	0.91	(0.78-1.05)	258	2.1	250	1.3	0.67	(0.56-0.80)	0.73	(0.6-0.88)
18.5-24.9	56758	58.2	6917	52.6	1	ref	1	ref	5950	49.3	8606	43.0	1	ref	1	ref
25-29.9	25730	26.4	3802	28.9	1.21	(1.16-1.27)	1.11	(1.05-1.16)	3574	29.6	6056	30.2	1.17	(1.11-1.24)	1.07	(1.01-1.14)
30-34.9	8516	8.7	1383	10.5	1.33	(1.25-1.42)	1.13	(1.05-1.22)	1458	12.1	3008	15.0	1.43	(1.33-1.53)	1.22	(1.12-1.32)
>35	4003	4.1	760	5.8	1.56	(1.43-1.70)	1.25	(1.14-1.38)	827	6.9	2112	10.5	1.77	(1.61-1.93)	1.43	(1.29-1.58)
BMI not recorded	6748	.	648	.	.	.	.	.	886	.	1082	.	.	.	.	.
Parity						<0.001		<0.001						<0.001		<0.001
0	46512	44.6	9042	65.6	3.07	(2.89-3.27)	2.06	(1.89-2.24)	6151	47.5	11016	52.2	1.28	(1.20-1.36)	0.93	(0.84-1.02)
1	37994	36.4	3499	25.4	1.45	(1.36-1.56)	1.16	(1.06-1.25)	4553	35.2	6918	32.8	1.08	(1.01-1.16)	1.11	(1.02-1.2)
2-4	19180	18.4	1214	8.8	1	ref	1	ref	2185	16.9	3068	14.5	1	ref	1	ref
5+	639	0.6	39	0.3	0.96	(0.68-1.36)	0.96	(0.61-1.49)	63	0.5	108	0.5	1.22	(0.89-1.68)	0.91	(0.62-1.34)
Missing	4	.	1	.	.	.	.	.	1	.	4	.	.	.	.	.
Diabetes						<0.001								<0.001		
No diabetes	102980	98.7	13560	98.3	1	ref	.	.	12603	97.3	20310	96.2	1	ref	.	.
Diabetes	1349	1.3	235	1.7	1.32	(1.15-1.52)	.	.	350	2.7	804	3.8	1.43	(1.25-1.62)	.	.
Hypertension						<0.001		<0.001						0.004		0.013
None	90016	86.3	10875	78.8	1	ref	1	ref	10206	78.8	16979	80.4	1	ref		
Gestational	10917	10.5	2115	15.3	1.60	(1.52-1.69)	1.35	(1.26-1.44)	1583	12.2	2366	11.2	0.90	(0.84-0.96)	0.93	(0.85-1.01)

	Vaginal births (Model 1)								Caesarean births (Model 2)							
	Controls (n = 104,329)		Cases (n =13,795)		Unadjusted ORs		Adjusted ORs* n = 101,380		Controls (n = 12,953)		Cases (n =21,114)		Unadjusted ORs		Adjusted ORs* (n = 29,817)	
	n	%	n	%	OR	95% CI	OR	p-value (95% CI)	n	%	n	%	OR	95% CI	OR	p-value (95%CI)
Pre-eclampsia /eclampsia	2540	2.4	700	5.1	2.28	(2.09-2.49)	1.48	(1.32-1.66)	1007	7.8	1516	7.8	0.90	(0.83-0.98)	0.86	(0.77-0.95)
Pre-existing	856	0.8	105	0.8	1.02	(0.83-1.25)	1.15	(0.9-1.48)	157	1.2	253	1.2	0.97	(0.79-1.18)	1.00	(0.79-1.26)
Previous PPH						<0.001		<0.001						<0.001		<0.001
No	51220	88.6	3363	70.8	1	ref	1	ref	4227	62.2	5722	56.7	1.00	ref	1	ref
Yes	6593	11.4	1389	29.2	3.21	(2.99-3.44)	1.91	(1.75-2.09)	2574	37.9	4372	43.3	1.25	(1.18-1.34)	1.51	(1.39-1.65)
Previous CS						<0.001		<0.001						<0.001		<0.001
No	55305	95.7	4175	87.9	1	ref	1	ref	2557	37.6	5134	50.9	1.00	ref	1	ref
Yes	2508	4.3	577	12.1	3.05	(2.77-3.35)	1.58	(1.4-1.8)	4244	62.4	4960	49.1	0.58	(0.55-0.62)	0.45	(0.41-0.49)
Current pregnancy factors																
Multiple pregnancy						<0.001		<0.001						<0.001		<0.001
Singleton	103434	99.1	13517	98.0	1	ref	1	ref	12631	97.5	20114	95.3	1	ref	1	ref
Multiple	895	0.9	278	2.0	2.38	(2.07-2.72)	2.59	(2.15-3.11)	322	2.5	1000	4.7	1.95	(1.72-2.22)	2.32	(1.98-2.7)
Gestation age						<0.001		<0.001						<0.001		<0.001
24-31	957	0.9	103	0.8	0.83	(0.67-1.02)	1.10	(0.79-1.54)	409	3.2	535	2.5	0.69	(0.60-0.80)	1.20	(0.99-1.45)
32-36	5232	5.0	644	4.7	0.95	(0.87-1.03)	1.23	(1.09-1.39)	1341	10.4	2110	10.0	0.83	(0.76-0.91)	1.26	(1.11-1.43)
37	4857	4.7	527	3.8	0.83	(0.76-0.92)	1.03	(0.92-1.17)	847	6.5	1354	6.4	0.84	(0.76-0.94)	1.19	(1.05-1.35)
38	11330	10.9	1161	8.4	0.79	(0.74-0.84)	0.96	(0.88-1.04)	2439	18.8	3071	14.5	0.66	(0.61-0.72)	0.99	(0.9-1.09)
39	22886	21.9	2486	18.0	0.84	(0.79-0.88)	0.98	(0.92-1.05)	3915	30.2	5743	27.2	0.77	(0.72-0.83)	0.85	(0.78-0.92)
40	31949	30.6	4153	30.1	1	ref	1	ref	1830	14.1	3468	16.4	1	ref	1	ref
41	22899	22.0	3900	28.3	1.31	(1.25-1.37)	1.08	(1.02-1.15)	1658	12.8	3723	17.6	1.18	(1.09-1.28)	1.04	(0.95-1.13)
42-44	4219	4.0	821	6.0	1.50	(1.38-1.63)	1.16	(1.04-1.29)	514	4.0	1110	5.3	1.14	(1.01-1.28)	0.97	(0.85-1.11)
Intrapartum factors																
Labour and CS														<0.001		<0.001
CS without onset of labour	.	.	.	.	.	.	.	.	6168	47.6	7727	36.6	1	ref	.	.
CS with labour	.	.	.	.	.	.	.	.	6785	52.4	13387	62.4	1.57	(1.51-1.65)	1.31	(1.23-1.4)
Number of methods of induction						<0.001		<0.001						<0.001		<0.001
No induction	82680	79.3	9321	67.6	1	ref	1	ref	10489	81.0	15332	72.6	1.00	ref	1	ref
1	18524	17.8	3486	25.3	1.67	(1.60-1.74)	1.31	(1.24-1.39)	1939	15.0	4090	19.4	1.44	(1.36-1.53)	1.10	(1.02-1.19)
2+	3125	3.0	988	7.2	2.8	(2.60-3.02)	1.53	(1.39-1.69)	525	4.0	1692	8.0	2.20	(1.99-2.44)	1.31	(1.16-1.47)

	Vaginal births (Model 1)								Caesarean births (Model 2)							
	Controls (n = 104,329)		Cases (n =13,795)		Unadjusted ORs		Adjusted ORs* n = 101,380		Controls (n = 12,953)		Cases (n =21,114)		Unadjusted ORs		Adjusted ORs* (n = 29,817)	
	n	%	n	%	OR	95% CI	OR	p-value (95% CI)	n	%	n	%	OR	95% CI	OR	p-value (95%CI)
Augmentation of labour						<0.001		<0.001								
No	89323	85.7	9804	71.1	1	ref	1	ref	.	.	.	.	.	.	.	.
Yes	14926	14.3	3980	28.9	2.43	(2.33-2.53)	1.35	(1.27-1.42)	.	.	.	.	.	.	.	.
Missing	80	.	11	.	.	.	.	.	.	.	.	.	.	.	.	.
Prolonged first stage of labour						<0.001		0.004								
Within guidance	87182	85.3	10581	78.8	1	ref	1	ref	.	.	.	.	.	.	.	.
Possibly prolonged	15081	14.8	2840	21.2	1.55	(1.48-1.62)	1.09	(1.03-1.16)	.	.	.	.	.	.	.	.
Missing	2066		374	.	.	.	.	.	.	.	.	.	.	.	.	.
Prolonged second stage of labour						<0.001		<0.001								
Within guidance	84514	82.1	7704	57.5	1	ref	1	ref	.	.	.	.	.	.	.	.
Possibly prolonged	18492	18.0	5701	42.5	3.38	(3.26-3.51)	1.30	(1.23-1.36)	.	.	.	.	.	.	.	.
Missing	1323	.	390	.	.	.	.	.	.	.	.	.	.	.	.	.
Birth related factors																
Instrumental birth						<0.001		<0.001								
Non-instrumental	85832	82.3	7156	51.9	1	ref	1	ref	.	.	.	.	.	.	.	.
Instrumental	18497	17.7	6639	48.1	4.31	(4.15-4.47)	2.56	(2.42-2.7)	.	.	.	.	.	.	.	.
Presentation						<0.001		<0.001						0.605		
Vertex	97279	93.4	11529	83.6	1	ref	1	ref	8728	67.7	14187	67.4	1	ref	.	.
Non-vertex	6906	6.6	2255	16.4	2.76	(2.62-2.90)	1.21	(1.13-1.30)	4172	32.3	6866	32.6	1.01	(0.97-1.06)	.	.
Missing	144	.	11	.	.	.	.	.	53	.	61	.	.	.	.	.
Duration of third stage						<0.001		<0.001								
<30 mins	100024	96.4	12119	89.2	1	ref	1	ref	.	.	.	.	.	.	.	.
≥30 mins	3760	3.6	1470	10.8	3.23	(3.03-3.44)	4.30	(3.95-4.68)	.	.	.	.	.	.	.	.
Missing	545	.	206	.	.	.	.	.	.	.	.	.	.	.	.	.
Perineal tear						<0.001		<0.001								
No laceration or tearing	28762	27.6	1819	13.2	1	ref	1	ref	.	.	.	.	.	.	.	.
< 3rd degree tear	74475	71.4	11003	76.8	2.34	(2.22-2.46)	1.56	(1.46-1.67)	.	.	.	.	.	.	.	.
3rd or 4th degree perineal tear	1092	1.1	973	7.1	14.09	(12.75-15.57)	4.50	(3.98-5.09)	.	.	.	.	.	.	.	.
Retained placenta						<0.001		<0.001								

	Vaginal births (Model 1)								Caesarean births (Model 2)							
	Controls (n = 104,329)		Cases (n =13,795)		Unadjusted ORs		Adjusted ORs* n = 101,380		Controls (n = 12,953)		Cases (n =21,114)		Unadjusted ORs		Adjusted ORs* (n = 29,817)	
	n	%	n	%	OR	95% CI	OR	p-value (95% CI)	n	%	n	%	OR	95% CI	OR	p-value (95%CI)
No	103629	99.3	13261	96.1	1	ref	1	ref	.	.	.	.	.	.	.	.
Yes	700	0.7	534	3.9	5.96	(5.32-6.68)	5.91	(5.00-6.98)	.	.	.	.	.	.	.	.
Baby characteristics																
Birth status						0.001								0.941		
Live born	103688	99.4	13678	99.2	1	ref	.	.	12915	99.7	21053	99.7	1	ref	.	.
Stillbirth	641	0.6	117	0.9	1.38	(1.14-1.69)	.	.	38	0.3	61	0.3	0.98	(0.66-1.48)	.	.
Head circumference						<0.001		<0.001						<0.001		
<35cm	56867	54.9	6158	45.0	1	ref	1	ref	6844	53.2	9288	44.3	1	ref	.	.
≥35cm	46753	45.1	7538	55.0	1.49	(1.44-1.54)	1.12	(1.06-1.18)	6020	46.8	11702	55.8	1.43	(1.37-1.50)	.	.
Missing	709	.	99	.	.	.	.	.	89	.	124	.	.	.	.	.
Birthweight						<0.001		<0.001						<0.001		<0.001
<3000g	20581	20.1	1826	13.6	0.81	(0.76-0.86)	0.74	(0.69-0.8)	3717	30.0	4532	22.5	0.87	(0.82-0.92)	0.72	(0.67-0.79)
3000-3499g	38685	37.9	4243	31.6	1	ref	1	ref	4225	34.1	5920	29.4	1	ref	1	ref
3500-3999g	32332	31.7	4978	37.1	1.40	(1.34-1.47)	1.36	(1.29-1.44)	3332	26.9	6427	31.9	1.38	(1.30-1.46)	1.31	(1.23-1.4)
≥4000g	10567	10.3	2380	17.7	2.05	(1.94-2.17)	2.00	(1.86-2.15)	1117	9.0	3279	16.3	2.10	(1.94-2.27)	1.83	(1.68-2)
Missing	2164	.	368	.	.	.	.	.	562	.	956	.	.	.	.	.

* Adjusted for all variables included in the multivariable analysis

4.4.2.3 Severe postpartum haemorrhage after vaginal birth (Model 3)

The results of the univariable analyses and multivariable analysis for women who had an SPPH after a vaginal birth are presented in Table 4.5. Because of the broadly similar nature of the results for SPPH after vaginal birth and PPH after vaginal birth, the description of results is brief. The same approach has been taken for section 4.4.2.4 summarising results for SPPH after caesarean birth.

Unless stated otherwise, the direction and magnitude of effect was similar between SPPH and PPH after vaginal births, with a tendency for slightly higher ORs in the SPPH analysis. The following risk factors were independently associated with SPPH after a vaginal birth: year of birth, Black and Asian ethnicity, nulliparity, gestational hypertension, pre-eclampsia/eclampsia, previous PPH, previous caesarean, multiple birth, increasing gestational age, induction of labour, prolonged second stage of labour, instrumental birth, non-vertex presentation, third stage of labour lasting 30 minutes or longer, larger baby head circumference (≥35cm) and increasing birthweight.

Compared with the PPH analysis, the odds of SPPH were markedly higher for women who had a retained placenta. Women who had a retained placenta were twenty times more likely to have a SPPH (aOR=20.0; 95% CI 15.7-25.5) while in the PPH analysis retained placenta was associated with six-fold higher odds (aOR=5.91; 95% CI 5.00-6.98). In contrast to the PPH analysis, stillbirth was significantly associated with SPPH, with women who had a stillborn baby being nearly four times more likely to have a SPPH, compared with those who had a liveborn baby (aOR=3.93; 95% CI 1.88-8.22).

4.4.2.4 Severe postpartum haemorrhage after caesarean birth (Model 4)

The results of univariable and multivariable analysis of women who had an SPPH after a caesarean birth are presented in Table 4.5. The risk factors associated with higher odds of SPPH after a caesarean that were comparable to the findings of the PPH after caesarean analyses were: maternal age of 35 or greater, not smoking in pregnancy, Black ethnicity, BMI 30+, gestational age less than 38 weeks, caesarean after labour onset, induction of labour, non-vertex presentation, birthweight of 3500g or more.

In the analysis of PPH after caesarean there was no statistically significant association between parity and PPH, but in this analysis nulliparity was found to be associated with almost 50% lower odds of SPPH, compared with women who had 2-4 previous births (aOR=0.55; 95% CI 0.45-0.66). As observed in the PPH analysis, pre-eclampsia/eclampsia was associated with lower odds of SPPH, as was previous caesarean. In contrast to other analyses, previous PPH was not significantly associated with SPPH among women who had a caesarean.

Table 4.5 Risk factors for SPPH among all women who had vaginal births and caesarean births (Models 3 and 4)

	Vaginal births (Model 3)								Caesarean births (Model 4)							
	Controls (n = 104,329)		Cases (n = 1,298)		Unadjusted ORs		Adjusted ORs* n = 99,199		Controls (n = 12,953)		Cases (n =2,014)		Unadjusted ORs		Adjusted ORs* n = 12,833	
		%	n	%	OR	(95% CI)	OR	(95% CI)	n	%	n	%	OR	(95% CI)	OR	(95% CI)
Year						<0.001		<0.001						<0.001		<0.001
1986-1990	22,639	21.7	70	5.4	1	ref	1	ref	2,454	18.9	63	3.1	1	ref	1	ref
1991-1995	22,057	21.1	77	5.9	1.13	(0.82-1.56)	0.89	(0.62-1.28)	2,358	18.2	105	5.2	1.73	(1.26-2.38)	1.69	(1.16-2.46)
1996-2000	16,253	15.6	142	10.9	2.83	(2.12-3.76)	2.33	(1.71-3.19)	1,790	13.8	233	11.6	5.07	(3.81-11.53)	4.79	(3.4-6.75)
2001-2005	13,315	12.8	178	13.7	4.32	(3.28-5.7)	3.49	(2.58-4.73)	1,763	13.6	297	19.7	8.77	(6.67-11.54)	8.52	(6.11-11.88)
2006-2010	13,717	13.2	306	23.6	7.21	(5.56-9.36)	5.53	(4.15-7.39)	2,092	16.2	523	26.0	9.74	(7.44-12.74)	9.51	(6.84-13.23)
2011-2016	16,348	15.7	525	40.5	10.4	(8.08-13.34)	7.09	(5.35-9.39)	2,496	19.3	693	34.4	10.8	(8.30-14.09)	10.1	(7.27-14.08)
Maternal age						<0.001								<0.001		<0.001
<20	6,831	6.6	69	5.3	0.89	(0.69-1.16)	.	.	472	3.6	37	1.8	0.56	(0.4-0.79)	0.60	(0.39-0.91)
20-24	32,050	20.2	207	16.0	0.87	(0.73-1.03)	.	.	1,969	15.2	178	8.8	0.65	(0.54-0.77)	0.77	(0.63-0.95)
25-29	34,021	32.6	384	29.6	1	ref	.	.	3,858	29.8	539	26.8	1	ref	1	ref
30-34	29,178	28.0	410	31.6	1.24	(1.08-1.43)	.	.	4,075	31.5	699	34.7	1.23	(1.09-1.39)	1.12	(0.97-1.29)
35-49	11,339	10.9	187	14.4	1.46	(1.22-1.74)	.	.	2,141	16.5	445	22.1	1.49	(1.3-1.71)	1.26	(1.06-1.48)
40+	1,903	1.8	40	3.1	1.86	(1.34-2.59)	.	.	436	3.4	116	5.8	1.90	(1.52-2.39)	1.50	(1.15-1.96)
Missing	7	.	1	.	.	.	.	.	2	.	0	.	.	.	.	.
Smoking status						<0.001								<0.001		0.001
Non-smoker	71031	69.9	1015	79.9	1	ref			8989	71.3	1597	81.3	1	ref	1	ref
Ex-smoker	6564	6.5	89	7.0	0.95	(0.76-1.19)	.	.	801	6.4	136	6.9	0.96	(0.79-1.16)	0.95	(0.76-1.18)
Smoker (1-5 per day)	5098	5.0	46	3.6	0.63	(0.47-0.85)	.	.	576	4.6	54	2.8	0.53	(0.40-0.70)	0.61	(0.44-0.85)
Smoker (5-10 per day)	8491	8.4	62	4.9	0.51	(0.39-0.67)	.	.	976	7.7	90	4.6	0.53	(0.42-0.65)	0.77	(0.59-1)
Smoker (11+ per day)	10369	10.2	59	4.6	0.40	(0.31-0.52)	.	.	1268	10.1	88	4.5	0.39	(0.31-0.49)	0.67	(0.51-0.87)
Missing	2776	.	27	.	.	.	.	.	343	.	49	.	.	.	.	.
Area deprivation quintile						0.047								0.199		
1st (most deprived)	11834	12.1	118	9.5	0.80	(0.65-0.98)	.	.	1217	10.3	175	9.4	0.88	(0.73-1.05)	.	.
2nd	13633	14.0	187	15.1	1.10	(0.93-1.31)	.	.	1598	13.5	221	11.9	0.84	(0.71-0.99)	.	.
3rd	15169	15.5	210	17.0	1.11	(0.94-1.31)	.	.	1983	16.8	308	16.6	0.95	(0.82-1.1)	.	.
4th	21930	22.4	286	23.1	1.05	(0.9-1.22)	.	.	2753	23.3	452	24.4	1.00	(0.88-1.14)	.	.
5th (least deprived)	35190	36.0	438	35.4	1	ref	.	.	4261	23.3	699	37.7	0.88	(0.73-1.05)	.	.

	Vaginal births (Model 3)								Caesarean births (Model 4)							
	Controls (n = 104,329)		Cases (n = 1,298)		Unadjusted ORs		Adjusted ORs* n = 99,199		Controls (n = 12,953)		Cases (n =2,014)		Unadjusted ORs		Adjusted ORs* n = 12,833	
		%	n	%	OR	(95% CI)	OR	(95% CI)	n	%	n	%	OR	(95% CI)	OR	(95% CI)
Missing	6573	.	59	.	.	.	.	.	1141	36.1	159		1	ref	.	.
Ethnicity						<0.001		<0.001						<0.001		<0.001
White	98454	96.1	1172	90.7	1.00	ref	1	ref	12013	94.5	1804	90.7	1	ref		
Black	1120	1.1	50	3.9	3.75	(2.81-5.01)	2.35	(1.65-3.35)	192	1.5	103	5.2	3.57	(2.76-4.62)	2.10	(1.55-2.85)
Asian	2381	2.3	61	4.7	2.15	(1.66-2.80)	2.09	(1.56-2.81)	404	3.2	59	3.0	0.97	(0.74-1.28)	0.68	(0.5-0.93)
Other	542	0.5	9	0.7	1.39	(0.72-2.71)	0.86	(0.40-1.88)	103	0.8	24	1.2	1.55	(0.98-2.46)	0.82	(0.5-1.35)
Missing	1832	.	6	.	.	.	.	.	241	.	24	.	.	.	.	.
Marital status						0.750								0.012		
Married or co-habiting	88370	85.8	1102	85.5	1	ref	.	.	11318	88.5	1795	90.4	1	ref	.	.
Single or separated	14616	14.2	187	14.5	1.03	(0.88-1.20)	.	.	1475	11.5	191	9.6	0.82	(0.70-0.96)	.	.
Missing	1343	.	9	.	.	.	.	.	.160	.	28	.	.	.	.	.
Pre-existing clinical factors																
BMI at booking						<0.001								<0.001		<0.001
< 18.5	2574	2.6	31	2.5	1.10	(0.77-1.58)	.	.	258	2.1	18	1.0	0.53	(0.33-0.87)	0.57	(0.34-0.96)
18.5-24.9	56758	58.2	621	50.3	1	ref	.	.	5950	49.3	779	41.0	1	ref	1	ref
25-29.9	25730	26.4	356	28.8	1.26	(1.11-1.44)	.	.	3574	29.6	575	30.2	1.23	(1.09-1.38)	1.04	(0.91-1.19)
30-34.9	8516	8.7	139	11.3	1.49	(1.24-1.80)	.	.	1458	12.1	300	15.8	1.57	(1.36-1.82)	1.28	(1.09-1.52)
>35	4003	4.1	88	7.1	2.01	(1.60-2.53)	.	.	827	6.9	230	12.1	2.12	(1.79-2.51)	1.47	(1.2-1.8)
BMI not recorded	6748	.	63	.	.	.	.	.	886	.	112	.	.	.	.	.
Parity						<0.001		<0.001						<0.001		<0.001
0	46512	44.6	827	63.7	2.87	(2.36-3.47)	2.24	(1.73-2.89)	6151	47.5	1002	49.8	1.01	(0.89-1.15)	0.55	(0.45-0.66)
1	37994	36.4	344	26.5	1.46	(1.18-1.80)	1.18	(0.93-1.51)	4553	35.2	648	32.2	0.88	(0.77-1.02)	0.92	(0.78-1.09)
2-4	19180	18.4	119	9.2	1	ref	1	ref	2185	16.9	352	17.5	1	ref	1	ref
5+	639	0.61	8	0.6	2.02	(0.98-4.16)	1.14	(0.41-3.16)	63	0.5	12	0.6	1.18	(0.63-2.21)	0.79	(0.36-1.71)
Missing	4	.	0	.	.	.	.	.	1	.	0	.	.	.	.	.
Diabetes						0.007								<0.001		
No diabetes	102980	98.7	1270	97.8	1	ref	.	.	12603	97.3	1931	95.9	1	ref	.	.
Diabetes	1349	1.3	28	2.2	1.68	(1.15-2.46)	.	.	350	2.7	83	4.1	1.55	(1.21-1.98)	.	.
Hypertension						<0.001		<0.001						0.267		0.011
None	90016	86.3	978	75.4	1	ref	1	ref	10206	78.8	1621	80.5	1	ref	1	ref
Gestational	10917	10.5	212	16.3	1.79	(1.54-2.08)	1.58	(1.32-1.89)	1583	12.2	225	11.2	0.89	(0.77-1.04)	0.94	(0.79-1.13)

	Vaginal births (Model 3)								Caesarean births (Model 4)							
	Controls (n = 104,329)		Cases (n = 1,298)		Unadjusted ORs		Adjusted ORs* n = 99,199		Controls (n = 12,953)		Cases (n =2,014)		Unadjusted ORs		Adjusted ORs* n = 12,833	
		%	n	%	OR	(95% CI)	OR	(95% CI)	n	%	n	%	OR	(95% CI)	OR	(95% CI)
Pre-eclampsia/eclampsia	2540	2.4	101	7.8	3.66	(3.97-4.52)	2.43	(1.88-3.14)	1007	7.8	150	7.5	0.94	(0.78-1.12)	0.68	(0.54-0.86)
Pre-existing hypertension	856	0.8	7	0.5	0.75	(0.36-1.59)	0.80	(0.32-2.01)	157	1.2	18	0.9	0.72	(0.44-1.18)	0.75	(0.43-1.33)
Previous PPH						<0.001		<0.001						0.153		
No	51220	88.6	302	64.1	1	ref	1	ref	4227	62.2	605	59.8	1	ref	.	.
Yes	6593	11.4	169	35.9	4.35	(3.59-5.26)	2.30	(1.82-2.90)	2574	37.9	407	40.2	1.10	(0.96-1.27)	.	.
Previous CS						<0.001		0.022						<0.001		
No	55305	95.7	410	87.1	1	ref	1	ref	2557	37.6	669	66.1	1	ref	.	.
Yes	2508	4.3	61	13.0	3.28	(2.50-4.30)	1.52	(1.06-2.16)	4244	62.4	343	33.9	0.31	(0.27-0.36)	0.32	(0.27-0.38)
Current pregnancy factors																
Multiple pregnancy						<0.001		<0.001						<0.001		<0.001
Singleton	103434	99.1	1264	97.4	1	ref	1	ref	12631	97.5	1848	91.8	1	ref	1	ref
Multiple pregnancy	895	0.9	34	2.6	3.11	(2.20-4.40)	3.19	(2.10-4.86)	322	2.5	166	8.2	3.52	(2.90-4.28)	3.29	(2.53-4.26)
Gestation age						<0.001		0.007						<0.001		<0.001
24-31	957	0.9	10	0.8	0.92	(0.49-1.73)	0.59	(0.19-1.8)	409	3.2	78	3.9	1.06	(0.81-1.40)	1.66	(1.1-2.5)
32-36	5232	5.0	77	5.9	1.30	(1.01-1.66)	1.67	(1.19-2.35)	1341	10.4	304	15.1	1.26	(1.06-1.50)	1.83	(1.4-2.39)
37	4857	4.7	51	3.9	0.92	(0.69-1.24)	1.22	(0.86-1.75)	847	6.5	143	7.1	0.94	(0.76-1.17)	1.41	(1.08-1.84)
38	11330	10.9	107	8.2	0.83	(0.67-1.03)	1.08	(0.83-1.39)	2439	18.8	241	12.0	0.55	(0.46-0.66)	0.89	(0.72-1.11)
39	22886	21.9	224	17.3	0.86	(0.73-1.02)	1.13	(0.93-1.36)	3915	30.2	417	20.7	0.59	(0.51-0.69)	0.66	(0.55-0.81)
40	31949	30.6	363	28.0	1	ref	1	ref	1830	14.1	328	16.3	1	ref	1	ref
41	22899	22.0	380	29.3	1.46	(1.26-1.69)	1.11	(0.94-1.32)	1658	12.8	379	18.8	1.28	(1.08-1.50)	1.07	(0.89-1.29)
42-44	4219	4.0	86	6.6	1.79	(1.43-2.27)	1.47	(1.1-1.96)	514	4.0	124	6.2	1.35	(1.07-1.69)	1.03	(0.78-1.36)
Intrapartum factors																
Labour and CS														<0.001		<0.001
CS without onset of labour	.	.	.	.	.	.	.	.	6168	47.6	636	31.6	1	ref	1	ref
CS with labour	.	.	.	.	.	.	.	.	6785	52.4	1378	68.4	1.97	(1.78-2.18)	1.56	(1.34-1.80)
Number of methods of induction						<0.001								<0.001		
No induction	82680	79.3	808	62.3	1	ref	1	ref	10489	81.0	1403	69.7	1	ref	1	ref

	Vaginal births (Model 3)								Caesarean births (Model 4)							
	Controls (n = 104,329)		Cases (n = 1,298)		Unadjusted ORs		Adjusted ORs* n = 99,199		Controls (n = 12,953)		Cases (n =2,014)		Unadjusted ORs		Adjusted ORs* n = 12,833	
		%	n	%	OR	(95% CI)	OR	(95% CI)	n	%	n	%	OR	(95% CI)	OR	(95% CI)
1	18524	17.8	367	28.3	2.03	(1.79-2.30)	1.43	(1.23-1.67)	1939	15.0	406	20.2	1.57	(1.39-1.77)	1.12	(0.95-1.32)
2+	3125	3.0	123	9.5	4.03	(3.32-4.89)	1.61	(1.23-2.09)	525	4.1	205	10.2	2.92	(2.46-3.46)	1.50	(1.20-1.88)
Augmentation of labour						<0.001		0.004								
No	89323	85.7	944	72.7	1	ref	1	ref	.	.	.	.	.	.	.	.
Yes	14926	14.3	354	27.3	2.24	(1.98-2.54)	1.25	(1.07-1.46)	.	.	.	.	.	.	.	.
Missing	80	.	0	.	.	.	.	.	.	.	.	.	.	.	.	.
Prolonged first stage of labour						<0.001										
Within guidance	87182	85.3	1006	80.2	1	ref	.	.	.	.	.	.	.	.	.	.
Possible prolonged	15081	14.8	249	19.8	1.43	(1.24-1.65)	.	.	.	.	.	.	.	.	.	.
Missing	2066	.	43	.	.	.	.	.	.	.	.	.	.	.	.	.
Prolonged second stage of labour						<0.001		<0.001								
Within guidance	84514	82.1	682	54.9	1	ref	1	ref	.	.	.	.	.	.	.	.
Possibly prolonged	18492	18.0	560	45.1	3.8	(3.35-4.20)	1.36	(1.18-1.57)	.	.	.	.	.	.	.	.
Missing	1323	.	56	.	.	.	.	.	.	.	.	.	.	.	.	.
Birth related factors																
Instrumental birth						<0.001		<0.001								
Non-instrumental	85832	82.3	655	50.5	1	ref	1	ref	.	.	.	.	.	.	.	.
Instrumental	18497	17.7	643	49.5	4.56	(4.08-5.09)	3.02	(2.56-3.57)	.	.	.	.	.	.	.	.
Presentation						<0.001		0.007						0.002		0.035
Vertex	97279	93.4	1075	83.0	1.00	ref	1	ref	8728	67.7	1289	64.1	1.00	ref	1	ref
Non-vertex	6906	6.6	221	17.1	2.90	(2.50-3.36)	1.30	(1.07-1.57)	4172	32.3	721	35.9	1.17	(1.06-1.29)	1.14	(1.01-1.29)
Missing	144	.	2	.	.	.	.	.	53	.	4	.	.	.	.	.
Duration of third stage						<0.001		<0.001								
<30 mins	100024	96.4	1033	81.5	1	ref	1	ref	.	.	.	.	.	.	.	.
≥30 mins	3760	3.6	235	18.5	6.05	(5.23-7.01)	6.79	(5.65-8.16)	.	.	.	.	.	.	.	.
Missing	545	.	30	.	.	.	.	.	.	.	.	.	.	.	.	.
Perineal tear						<0.001		<0.001								
No laceration or tearing	28762	27.6	223	17.2	1	ref	1	ref	.	.	.	.	.	.	.	.
< 3rd degree tear	74475	71.4	969	74.7	1.68	(1.45-1.94)	1.11	(0.93-1.34)	.	.	.	.	.	.	.	.

	Vaginal births (Model 3)								Caesarean births (Model 4)							
	Controls (n = 104,329)		Cases (n = 1,298)		Unadjusted ORs		Adjusted ORs* n = 99,199		Controls (n = 12,953)		Cases (n =2,014)		Unadjusted ORs		Adjusted ORs* n = 12,833	
		%	n	%	OR	(95% CI)	OR	(95% CI)	n	%	n	%	OR	(95% CI)	OR	(95% CI)
3rd or 4th degree perineal tear	1092	1.1	106	8.2	12.5	(9.85-15.91)	3.17	(2.35-4.27)	.	.	.	.	.	.	.	.
Retained placenta								<0.001								
No	103629	99.3	1118	86.1	1	ref	1	ref	.	.	.	.	.	.	.	.
Yes	700	0.7	180	13.9	23.8	(20.5-28.3)	20.02	(15.7-25.4)	.	.	.	.	.	.	.	.
Baby characteristics																
Birth status						<0.001		<0.001						0.001		
Live born	103688	99.4	1268	97.7	1	ref	1	ref	12915	99.7	1995	99.1	1	ref	.	.
Stillbirth	641	0.6	30	2.3	3.83	(2.64-5.54)	3.93	(1.88-8.22)	38	0.3	19	0.9	3.80	(1.81-7.97)	.	.
Head circumference						<0.001		0.009						<0.001		
<35cm	56867	54.9	547	42.5	1	ref	1	ref	6844	53.2	921	46.0	1	ref	.	.
≥35cm	46753	45.1	741	57.5	1.65	(1.47-1.84)	1.24	(1.06-1.45)	6020	46.8	1083	54.0	1.34	(1.22-1.47)	.	.
Missing	709	.	10	.	.	.	.	.	89	.	10	.	.	.	.	.
Birthweight						<0.001		<0.001						<0.001		<0.001
<3000g	20581	20.1	177	14.3	0.97	(0.81-1.16)	0.67	(0.52-0.85)	3717	30.0	504	26.7	1.27	(1.11-1.45)	0.75	(0.62-0.91)
3000-3499g	38685	37.9	343	27.7	1	ref	1	ref	4225	34.1	452	23.9	1	ref	1	ref
3500-3999g	32332	31.7	437	35.2	1.52	(1.32-1.76)	1.54	(1.30-1.82)	3332	26.9	567	30.0	1.59	(1.39-1.82)	1.57	(1.35-1.82)
≥4000g	10567	10.3	283	22.8	3.02	(2.57-3.55)	2.96	(2.41-3.64)	1117	9.0	368	19.5	3.08	(2.64-3.59)	2.85	(2.39-3.39)
Missing	2164	.	58	.	.	.	.	.	562	.	123	.	.	.	.	.

* Adjusted for all variables included in the multivariable analysis

4.4.2.5 Postpartum haemorrhage after vaginal birth among low-risk women (Model 5)

The results of univariable and multivariable analyses of low-risk women who had a PPH after a vaginal birth are presented in Table 4.6. These results are presented below in comparison to the results of PPH after vaginal birth among all women. Unless stated otherwise, the direction and magnitude of effect was similar between PPH and SPPH after vaginal births, with a tendency for slightly higher ORs in the SPPH analysis.

As observed in the main analysis, the following factors were associated with higher odds of PPH among low-risk women: giving birth in later years of the study compared with earlier, not smoking during pregnancy, Black or Asian ethnicity, BMI of 25 or more, nulliparity and primiparity, previous PPH, augmentation of labour, prolonged second stage of labour, instrumental birth, third stage of labour lasting 30 minutes or longer, perineal laceration and tearing, retained placenta, and birthweight of 3500g or more.

In contrast to the analysis of PPH among all women, stillbirth was significantly associated with PPH among low-risk women (aOR=1.21; 95% CI 1.11-1.31).

4.4.2.6 Postpartum haemorrhage after caesarean birth among low-risk women (Model 6)

The analysis to identify risk factors for PPH after caesarean birth among low-risk women was underpowered to detect statistically significant associations between many of the potential risk factors and PPH. However, the results of the univariable analysis were broadly similar to those of the analysis of PPH and SPPH after caesarean in the 'all-women' group (Table 4.6). The factors that were significantly associated with PPH after caesarean in the multivariable analysis were later year of birth, maternal age 30-34, and birthweight ≥3500g.

Table 4.6 Risk factors for PPH among low-risk women who had vaginal births and caesarean births (Models 5 and 6)

	Vaginal births (Model 5)								Caesarean births (Model 6)							
	Controls (n = 53,470)		**Cases (n =4,587)**		**Unadjusted ORs**		**Adjusted ORs* (n = 51,125)**		**Controls (n =867)**		**Cases (n =1,557)**		**Unadjusted ORs**		**Adjusted ORs***	
	n	**%**	**n**	**%**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**n**	**%**	**n**	**%**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Year								<0.001						<0.001		<0.001
1986-1990	11999	22.4	400	8.72	1.00	ref	1	ref	192	22.2	108	6.9	1.00	ref	1	ref
1991-1995	11589	21.7	500	10.9	1.29	(1.33-1.48)	1.23	(1.06-1.44)	218	25.1	146	9.4	1.19	(0.87-1.63)	1.22	(0.87-1.71)
1996-2000	8032	15.0	498	10.9	1.86	(1.63-2.13)	1.61	(1.38-1.88)	136	15.7	292	18.8	3.82	(2.79-5.21)	3.79	(2.72-5.27)
2001-2005	6669	12.5	575	12.5	2.59	(2.27-2.95)	2.08	(1.79-2.42)	140	16.2	327	21.0	4.15	(3.05-5.65)	4.18	(3-5.84)
2006-2010	7265	136	1102	24.0	4.55	(4.04-5.12)	3.60	(3.14-4.13)	85	9.8	330	21.2	6.90	(4.94-9.65)	6.98	(4.9-9.93)
2011-2016	7916	14.8	1512	33.0	5.73	(5.11-6.42)	4.00	(3.49-4.58)	96	11.1	354	22.7	6.56	(4.73-9.09)	6.59	(4.66-9.33)
Maternal age														<0.001		0.03
<20	3232	6.0	244	6.0	0.9	(0.78-1.03)	.	.	47	5.4	76	4.9	1.08	(0.73-1.59)	1.35	(0.87-2.11)
20-24	10518	19.7	757	19.2	0.86	(0.78-0.94)	.	.	155	17.9	185	11.9	0.79	(0.61-1.03)	0.87	(0.65-1.16)
25-29	17560	32.8	1477	32.8	1	ref	.	.	290	33.5	436	28.0	1	ref	1	ref
30-34	15613	29.2	1485	29.5	1.13	(1.05-1.22)	.	.	244	28.1	539	34.6	1.47	(1.19-1.82)	1.34	(1.06-1.69)
35-49	5717	10.6	536	10.8	1.11	(1.00-1.24)	.	.	112	12.9	268	17.2	1.59	(1.22-2.08)	1.24	(0.93-1.67)
40+	826	1.5	88	1.6	1.27	(1.01-1.59)	.	.	19	2.2	53	3.4	1.86	(1.08-3.20)	1.34	(0.72-2.51)
Missing	4	.	0	.	.	.	.	.	.	.	.	.	.	.	.	.
Smoking status								<0.001						<0.001		
Non-smoker	36613	70.4	3641	80.5	1	ref	1	ref	571	67.4	1149	75.8	1	ref	.	.
Ex-smoker	3141	6.0	272	6.0	0.87	(0.77-0.99)	0.77	(0.67-0.89)	54	6.4	103	6.8	0.95	(0.67-1.34)	.	.
Smoker (1-5 per day)	2673	5.1	178	3.9	0.67	(0.57-0.78)	0.92	(0.77-1.09)	55	6.5	65	4.3	0.59	(0.40-0.85)	.	.
Smoker (5-10 per day)	4421	8.5	224	45.0	0.51	(0.44-0.59)	0.78	(0.67-0.92)	77	9.1	108	7.1	0.70	(0.51-0.95)	.	.
Smoker (11+ per day)	5193	10.0	211	4.7	0.41	(0.35-0.47)	0.87	(0.74-1.02)	90	10.6	90	5.9	0.50	(0.36-0.68)	.	.
Missing	1429	.	61	.	.	.	.	.	20	.	42	.	.	.	.	.
Area deprivation quintile						0.001								0.379		
1st (most deprived)	6051	11.9	443	10.0	0.81	(0.73-0.91)	.	.	77	9.5	126	8.6	0.85	(0.62-1.17)	.	.
2nd	6701	13.1	556	12.5	0.92	(0.83-1.02)	.	.	121	15.0	191	13.0	0.82	(0.63-1.07)	.	.
3rd	7446	14.6	633	14.3	0.94	(0.86-1.04)	.	.	132	16.4	221	15.1	0.87	(0.67-1.12)	.	.
4th	11523	22.6	1064	24.0	1.02	(0.95-1.11)	.	.	166	20.6	332	22.6	1.04	(0.83-1.31)	.	.
5th (least deprived)	19336	37.9	1743	39.3	1	ref	.	.	311	38.5	598	40.7	1	ref	.	.

	Vaginal births (Model 5)								Caesarean births (Model 6)							
	Controls (n = 53,470)		**Cases (n =4,587)**		**Unadjusted ORs**		**Adjusted ORs* (n = 51,125)**		**Controls (n =867)**		**Cases (n =1,557)**		**Unadjusted ORs**		**Adjusted ORs***	
	n	**%**	**n**	**%**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**n**	**%**	**n**	**%**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Missing	2413	.	148	.	.	.	.	.	60	.	89	.	.	.	.	.
Ethnicity								<0.001						0.062		
White	50263	95.6	4127	90.9	1	ref	.	.	784	92.2	1369	89.1	1	ref	.	.
Black	637	1.2	141	3.1	2.70	(2.21-3.28)	1.94	(1.55-2.43)	16	1.9	48	3.1	1.72	(0.97-3.05)	.	.
Asian	1363	2.6	226	5.0	2.02	(1.74-2.34)	1.73	(1.45-2.06)	44	5.2	98	6.4	1.28	(0.88-1.84)	.	.
Other	304	0.6	47	1.0	1.88	(1.39-2.56)	1.28	(0.9-1.83)	6	0.7	22	1.4	2.10	(0.85-5.20)	.	.
Missing	903	.	46	.	.	.	.	.	17	.	20	.	.	.	.	.
Marital status						0.009								0.550		
Married or co-habiting	45880	68.9	4024	88.2	1	ref	.	.	746	87.2	1327	86.3	1	ref	.	.
Single or separated	6936	13.1	537	11.8	0.88	(0.80-0.97)	.	.	110	12.9	211	13.7	1.08	(0.84-1.38)	.	.
Missing	654	.	26	.	.	.	.	.	11	.	19	.	.	.	.	.
Pre-existing clinical factors																
BMI at booking						<0.001		0.002						<0.001		
< 18.5	1474	2.9	103	2.3	0.84	(0.68-1.03)	0.77	(0.61-0.97)	20	2.5	20	1.4	0.62	(0.33-1.16)	.	.
18.5-24.9	32185	63.9	2684	60.9	1	ref	1	ref	494	60.6	800	54.6	1	ref	.	.
25-29.9	13053	25.9	1224	27.8	1.12	(1.05-1.21)	1.10	(1.01-1.19)	236	29.0	468	32.0	1.22	(1.01-1.48)	.	.
30-34.9	3649	7.3	395	9.0	1.30	(1.16-1.45)	1.17	(1.02-1.33)	65	8.0	177	12.1	1.68	(1.24-2.28)	.	.
BMI not recorded	3109	.	181	.	.	.	.	.	52	.	92	.	.	.	.	.
Parity						<0.001		<0.001						0.790		
0	21362	40.0	2812	61.3	3.12	(2.8-3.46)	2.10	(1.84-2.39)	650	75.0	1139	73.2	0.94	(0.68-1.30)	.	.
1	21729	40.6	1337	29.2	1.46	(1.30-1.63)	1.21	(1.07-1.37)	154	17.8	301	19.3	1.05	(0.72-1.51)	.	.
2-4	10113	18.9	427	9.3	1	ref	1	ref	60	6.9	112	7.2	1	ref	.	.
5+	263	0.5	10	0.2	0.90	(0.451.81)	0.92	(0.40-2.13)	3	0.4	5	0.3	0.89	(0.21-3.87)	.	.
Missing	3	.	1	.	.	.	.	.	.	.	.	.	.	.	.	.
Previous PPH						<0.001		<0.001						0.004		
No	29452	91.7	1380	77.8	1	ref	1	ref	207	95.4	368	88.0	1	ref	.	.
Yes	2653	8.3	394	22.2	3.17	(2.81-3.58)	2.04	(1.77-2.35)	10	4.6	50	12.0	2.81	(1.40-5.67)	.	.
Current pregnancy factors																
Gestational age						<0.001								0.101		
37	2067	3.9	121	2.6	0.65	(0.54-0.79)	.	.	40	4.6	71	4.6	1.07	(0.71-1.62)	.	.
38	5647	10.6	356	7.8	0.70	(0.63-0.79)	.	.	86	9.9	145	9.3	1.02	(0.75-1.38)	.	.
39	13740	25.7	978	21.3	0.80	(0.73-0.86)	.	.	181	20.9	294	18.9	0.98	(0.78-1.24)	.	.
40	19740	36.9	1767	38.5	1	ref	.	.	311	35.9	515	33.1	1	ref	.	.

	Vaginal births (Model 5)								Caesarean births (Model 6)							
	Controls (n = 53,470)		**Cases (n =4,587)**		**Unadjusted ORs**		**Adjusted ORs* (n = 51,125)**		**Controls (n =867)**		**Cases (n =1,557)**		**Unadjusted ORs**		**Adjusted ORs***	
	n	**%**	**n**	**%**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**n**	**%**	**n**	**%**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
41	12276	23.0	1365	29.8	1.24	(1.15-1.34)	.	.	249	28.7	532	34.2	1.29	(1.05-1.59)	.	.
Intrapartum factors																
Augmentation of labour						<0.001		<0.001	.	.	.	.	.	.	.	.
No	48025	89.9	3388	73.94	1	ref	1	ref	.	.	.	.	.	.	.	.
Yes	5406	10.1	1194	26.06	3.13	(2.91-3.36)	1.52	(1.39-1.67)	.	.	.	.	.	.	.	.
Missing	39	.	5	.	.	.	.	.	.	.	.	.	.	.	.	.
Prolonged first stage of labour						<0.001										
Within guidance	44509	85.0	3438	77.2	1	ref	.	.	.	.	.	.	.	.	.	.
Possible prolonged	7885	15.0	1015	22.8	1.67	(1.55-1.79)	.	.	.	.	.	.	.	.	.	.
Missing	1076	.	134	.	.	.	.	.	.	.	.	.	.	.	.	.
Prolonged second stage of labour						<0.001		<0.001								
Within guidance	45340	85.9	2884	64.4	1	ref	1	ref	.	.	.	.	.	.	.	.
Possibly prolonged	7470	14.2	1592	35.6	3.35	(3.14-3.58)	1.31	(1.21-1.43)	.	.	.	.	.	.	.	.
Missing	660	.	111	.	.	.	.	.	.	.	.	.	.	.	.	.
Birth related factors																
Instrumental birth						<0.001		<0.001								
Non-instrumental	47981	89.7	2990	65.2	1	ref	1	ref	.	.	.	.	.	.	.	.
Instrumental	5489	10.3	1597	34.8	4.67	(4.37-4.99)	2.83	(2.58-3.11)	.	.	.	.	.	.	.	.
Duration of third stage						<0.001		<0.001								
<30 mins	51135	96.1	3922	36.6	1	ref	1	ref	.	.	.	.	.	.	.	.
≥30 mins	2083	3.9	607	13.4	3.80	(3.45-4.19)	4.26	(3.76-4.82)	.	.	.	.	.	.	.	.
Missing	252	.	58	.	.	.	.	.	.	.	.	.	.	.	.	.
Perineal tear						<0.001		<0.001								
No tear	15433	28.9	625	13.6	1	ref	1	ref	.	.	.	.	.	.	.	.
< 3rd degree tear	37502	70.1	3641	79.4	2.40	(2.20-2.62)	1.66	(1.49-1.84)	.	.	.	.	.	.	.	.
3rd or 4th degree perineal tear	535	1.0	321	7.0	14.82	(12.6-17.4)	4.85	(3.99-5.88)	.	.	.	.	.	.	.	.
Retained placenta								<0.001								
No	53171	99.4	4424	96.5	1	ref	1	ref	.	.	.	.	.	.	.	.
Yes	299	0.6	163	3.6	6.55	(5.40-7.95)	5.77	(4.33-7.7)	.	.	.	.	.	.	.	.

	Vaginal births (Model 5)								Caesarean births (Model 6)							
	Controls (n = 53,470)		**Cases (n =4,587)**		**Unadjusted ORs**		**Adjusted ORs* (n = 51,125)**		**Controls (n =867)**		**Cases (n =1,557)**		**Unadjusted ORs**		**Adjusted ORs***	
	n	**%**	**n**	**%**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**n**	**%**	**n**	**%**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Baby characteristics																
Birth status						0.114										
Live born	53443	100.0	4582	99.9	1	ref	.	.	866	99.9	1557	100	1	ref	.	.
*Stillbirth**	27	0.1	5	0.1	2.16	(0.83-5.61)	.	.	1	0.1	0	0.0	.	.	.	.
Head circumference						<0.001		<0.001						0.001		
<35cm	28861	54.3	1979	43.3	1	ref	1	ref	419	48.4	646	41.7	1	ref	.	.
≥35cm	24329	45.7	2588	56.7	1.55	(1.46-1.65)	1.21	(1.11-1.31)	446	51.6	904	58.3	1.31	(1.11-1.55)	.	.
Missing	280	.	20	.	.	.	.	.	2	.	7	.	.	.	.	.
Birthweight						<0.001		<0.001						<0.001		<0.001
<3000g	7595	14.5	348	7.8	0.65	(0.58-0.74)	0.69	(0.6-0.79)	142	17.4	163	10.9	0.81	(0.62-1.06)	0.84	(0.62-1.12)
3000-3499g	21416	40.7	1505	33.6	1	ref	1	ref	326	39.9	460	30.8	1	ref	1	ref
3500-3999g	18010	34.3	1810	40.4	1.43	(1.33-1.54)	1.34	(1.23-1.46)	263	32.2	560	37.5	1.51	(1.23-3.37)	1.57	(1.26-1.95)
≥4000g	5552	10.6	820	18.3	2.10	(1.92-2.30)	2.00	(1.78-2.25)	86	10.5	310	20.8	2.55	(1.93-3.37)	2.80	(2.09-3.74)
Missing	897	.	104	.	.	.	.	.	50	.	64	.	.	.	.	.

* Adjusted for all variables included in the multivariable analysis

4.4.2.7 *Severe postpartum haemorrhage after vaginal birth among low-risk women (Model 7)*

Factors significantly associated with SPPH after vaginal birth among low-risk women were broadly similar to those identified for all women who had vaginal births (Table 4.7). Year of birth was associated with higher odds of SPPH following vaginal birth among low-risk women, as was Black and Asian ethnicity, nulliparity and previous PPH. Augmentation of labour, instrumental birth, third stage of labour lasting 30 minutes or longer, ≥3rd degree perineal tear, retained placenta and higher birthweight were all associated with higher odds of SPPH among low-risk women who had a vaginal birth.

4.4.2.8 *Severe postpartum haemorrhage after caesarean birth among low-risk women (Model 8)*

As with the analysis of PPH after caesarean among low-risk women, the analysis of SPPH after caesarean in low-risk women was also underpowered to detect statistically significant associations between many of the potential risk factors. The factors that were significantly associated with SPPH after caesarean among low-risk women in the multivariable analysis were later years of birth, giving birth at 41 weeks' gestation, and birthweight ≥4000g (Table 4.7).

Table 4.7 Risk factors for SPPH among low-risk women who had vaginal births and caesarean births (Models 7 and 8)

	Vaginal births (Model 7)								*Caesarean births (Model 8)*							
	Controls (n =53,470)		*Cases (n =344)*		*Unadjusted ORs*		*Adjusted ORs* (n= 51,778)*		*Controls (n =867)*		*Cases (n =132)*		*Unadjusted ORs*		*Adjusted ORs* (n=942)*	
	n	*%*	*n*	*%*	*OR*	*(95% CI)*	*OR*	*(95% CI)*	*n*	*%*	*n*	*%*	*OR*	*(95% CI)*	*OR*	*(95% CI)*
Year						<0.001								<0.001		<0.001
1986-1990	11999	22.4	20	5.8	1	ref	1	ref	192	22.2	3	2.3	1	ref		
1991-1995	11589	21.7	17	4.9	0.88	(0.46-1.68)	0.70	(0.36-1.38)	218	25.1	10	7.6	2.94	(0.80-10.8)		
1996-2000	8032	15.0	36	10.5	2.69	(1.56-4.65)	2.10	(1.2-3.66)	136	15.7	15	11.4	7.06	(2.00-24.8)	4.10	(1.84-9.13)
2001-2005	6669	12.5	49	14.2	4.41	(2.62-7.42)	3.07	(1.81-5.21)	140	16.2	36	27.3	16.6	(4.6-54.6)	7.75	(3.82-15.7)
2006-2010	7265	13.6	89	25.9	7.35	(4.52-11.9)	4.51	(2.75-7.42)	85	9.8	28	21.2	21.1	(6.23-71.3)	12.2	(5.69-25.9)
2011-2016	7916	14.8	133	38.7	10.1	(6.30-16.1)	5.19	(3.17-8.5)	96	11.1	40	30.3	26.7	(8.04-88.5)	16.3	(7.86-33.9)
Maternal age						<0.001								0.012		
<20	3232	6.0	12	3.5	0.60	(0.33-1.09)	.	.	47	5.4	3	2.3	0.51	(0.15-1.74)	.	.
20-24	10518	19.7	40	11.6	0.61	(0.43-0.88)	.	.	155	17.9	14	10.6	0.73	(0.38-1.39)	.	.
25-29	17560	32.8	109	31.7	1	ref	.	.	290	33.5	36	27.3	1	ref	.	.
30-34	15613	29.2	132	38.4	1.36	(1.06-1.76)	.	.	244	28.1	47	35.6	1.55	(0.97-2.47)	.	.
35-49	5717	10.7	42	12.2	1.18	(0.83-1.69)	.	.	112	12.9	28	21.2	2.01	(1.17-3.46)	.	.
40+	826	1.5	9	2.6	1.76	(0.89-3.48)	.	.	19	2.2	4	3.0	1.70	(0.09-0.18)	.	.
Missing	4	.	0	.	.	.	.	.	.	.	.	.	.	.	.	.
Smoking status						<0.001								0.028		
Non-smoker	36613	70.4	287	84.9	1	ref	.	.	571	67.4	104	80.6	1	ref	.	.
Ex-smoker	3141	6.0	14	4.1	0.57	(0.33-0.97)	.	.	54	6.4	8	6.2	0.81	(0.38-1.76)	.	.
Smoker (1-5 per day)	2673	5.1	7	2.1	0.33	(0.16-0.71)	.	.	55	6.5	5	3.9	0.50	(0.20-1.28)	.	.
Smoker (5-10 per day)	4421	8.5	16	4.7	0.46	(0.28-0.76)	.	.	77	9.1	9	7.0	0.64	(0.31-1.32)	.	.
Smoker (11+ per day)	5193	10.0	14	4.1	0.34	(0.20-0.59)	.	.	90	10.6	3	2.3	0.18	(0.06-0.59)	.	.
Missing	1429	.	6	.	.	.	.	.	20	.	3	.	.	.	.	.
Area deprivation quintile						0.577								0.593		
1st (most deprived)	6051	11.9	30	9.0	0.81	(0.73-0.91)	.	.	77	9.5	11	9.43	0.81	(0.4-1.62)	.	.
2nd	6701	13.1	48	14.4	0.92	(0.83-1.02)	.	.	121	15.0	15	14.6	0.70	(0.38-1.29)	.	.
3rd	7446	14.6	50	15.0	0.94	(0.86-1.04)	.	.	132	16.4	24	16.7	1.03	(0.61-1.73)	.	.
4th	11523	22.6	79	23.7	1.02	(0.95-1.11)	.	.	166	20.6	21	20.0	0.72	(0.42-1.22)	.	.
5th (least deprived)	19336	37.9	127	38.0	1	ref	.	.	311	38.5	55	39.2	1	ref	.	.

	Vaginal births (Model 7)								Caesarean births (Model 8)							
	Controls (n =53,470)		Cases (n =344)		Unadjusted ORs		Adjusted ORs* (n= 51,778)		Controls (n =867)		Cases (n =132)		Unadjusted ORs		Adjusted ORs* (n=942)	
	n	%	n	%	OR	(95% CI)	OR	(95% CI)	n	%	n	%	OR	(95% CI)	OR	(95% CI)
Missing	2413	.	10	.	.	.	.	.	60	.	6	.	.	.	.	.
Ethnicity						<0.001		<0.001						0.012		
White	50263	95.6	298	87.1	1	ref	.	.	784	92.2	111	85.4	1	ref	.	.
Black	637	1.2	20	5.9	5.30	(3.35-8.38)	3.46	(2.06-5.81)	16	1.9	8	6.2	3.53	(1.48-8.45)	.	.
Asian	1363	2.6	22	6.4	2.72	(1.76-4.22)	2.62	(1.61-4.25)	44	5.2	8	6.2	1.28	(0.59-2.80)	.	.
Other	304	0.6	2	0.6	1.11	(0.27-4.48)	0.61	(0.13-2.82)	6	0.7	3	2.3	3.53	(0.87-14.3)	.	.
Missing	903	.	2	.	.	.	.	.	17	.	2	.	.	.	.	.
Marital status						0.792								0.427		
Married or co-habiting	45880	86.9	297	87.4	1	ref	.	.	746	87.2	110	84.6	1	ref	.	.
Single or separated	6936	13.1	43	12.7	0.96	(0.69-1.32)	.	.	110	12.9	20	15.4	1.23	(0.74-2.07)	.	.
Missing	654	.	4	.	.	.	.	.	11	.	2	.	.	.	.	.
Pre-existing clinical factors																
BMI at booking						0.007								0.006		
< 18.5	1474	2.9	5	1.5	0.57	(0.23-1.38)	.	.	20	2.5	2	1.6	0.87	(0.20-3.81)	.	.
18.5-24.9	32185	63.9	192	58.0	1	ref	.	.	494	60.6	57	46.3	1	ref	.	.
25-29.9	13053	25.9	97	29.3	1.25	(0.98-1.59)	.	.	236	29.0	45	36.6	1.65	(1.09-2.52)	.	.
30-34.9	3649	7.3	37	11.2	1.70	(1.19-2.42)	.	.	65	8.0	19	15.5	2.53	(1.42-4.53)	.	.
BMI not recorded	3109	.	13	.	.	.	.	.	52	.	9	.	.	.	.	.
Parity						<0.001		<0.001						0.037		
0	21362	40.0	203	59.0	2.91	(2.01-4.21)	2.04	(1.29-3.25)	650	75.0	88	66.7	0.48	(0.27-0.86)	.	.
1	21729	40.6	106	30.8	1.49	(1.01-2.21)	1.18	(0.77-1.8)	154	17.8	27	20.5	0.62	(0.31-1.22)	.	.
2-4	10113	19.9	33	9.6	1	ref	1.00	(0-0)	60	6.9	17	12.9	1	ref	.	.
5+	263	0.5	2	0.6	2.33	(0.56-9.78)	2.95	(0.67-13.04)	3	0.4	0	0	1.00	N/A	.	.
Missing	3	.	0	.	.	.	.	.	.	.	.	.	.	.	.	.
Previous PPH						<0.001		<0.001						<0.001		
No	29452	91.7	96	68.1	1	ref	.	.	207	95.4	35	79.6	1	ref	.	.
Yes	2653	8.3	45	31.9	5.20	(3.64-7.43)	2.71	(1.80-4.08)	10	4.6	9	20.5	5.32	(2.02-14.06)	.	.
Current pregnancy factors																
Gestation age						<0.001								0.005		0.036
37	2067	3.9	8	2.3	0.55	(0.27-1.13)	.	.	40	4.6	6	4.6	1.20	(0.48-3.00)	1.49	(0.52-4.29)
38	5647	10.6	28	8.1	0.71	(0.47-1.07)	.	.	86	9.9	6	4.6	0.56	(0.23-1.36)	0.56	(0.21-1.5)
39	13740	25.7	55	16.0	0.57	(0.42-0.78)	.	.	181	20.9	22	16.7	0.97	(0.56-1.69	0.86	(0.45-1.64)
40	19740	36.9	138	40.1	1	ref	.	.	311	35.9	39	29.6	1	ref	1	ref
41	12276	23.0	115	33.4	1.34	(1.05-1.72)	.	.	249	28.7	59	44.7	0.13	(0.09-0.17)	1.78	(1.09-2.9)

	Vaginal births (Model 7)								Caesarean births (Model 8)							
	Controls (n =53,470)		Cases (n =344)		Unadjusted ORs		Adjusted ORs* (n= 51,778)		Controls (n =867)		Cases (n =132)		Unadjusted ORs		Adjusted ORs* (n=942)	
	n	%	n	%	OR	(95% CI)	OR	(95% CI)	n	%	n	%	OR	(95% CI)	OR	(95% CI)
Intrapartum factors																
Augmentation of labour						<0.001										
No	48025	89.9	253	73.6	1	ref	1	ref	.	.	.	.	.	.	.	.
Yes	5406	10.1	91	26.5	3.20	(2.51-4.07)	1.48	(1.09-2.00)	.	.	.	.	.	.	.	.
Missing	39	.	0	.	.	.	.	.	.	.	.	.	.	.	.	.
Prolonged first stage of labour						<0.001										
Within guidance	44509	85.0	253	76.4	1	ref	.	.	.	.	.	.	.	.	.	.
Possible prolonged	7885	15.1	78	15.1	1.74	(1.35-2.25)	.	.	.	.	.	.	.	.	.	.
Missing	1076	.	13	.	.	.	.	.	.	.	.	.	.	.	.	.
Prolonged second stage of labour						<0.001										
Within guidance	45340	85.9	206	61.9	1	ref	.	.	.	.	.	.	.	.	.	.
Possibly prolonged	7470	14.2	127	38.1	3.74	(3.00-4.67)	.	.	.	.	.	.	.	.	.	.
Missing	660	.	11	.	.	.	.	.	.	.	.	.	.	.	.	.
Birth related factors																
Instrumental birth						<0.001		<0.001								
Non-instrumental	47981	89.7	209	60.8	1	ref			.	.	.	.	.	.	.	.
Instrumental	5489	10.3	135	39.2	5.65	(4.54-7.02)	4.69	(3.51-6.27)	.	.	.	.	.	.	.	.
Duration of third stage						<0.001		<0.001								
<30 mins	51135	96.09	271	80.42	1	ref	.	.	.	.	.	.	.	.	.	.
≥30 mins	2083	3.91	66	19.58	5.98	(4.55-7.85)	5.29	(3.8-7.35)	.	.	.	.	.	.	.	.
Missing	252	.	7	.	.	.	.	.	.	.	.	.	.	.	.	.
Perineal tear						<0.001		<0.001								
No tear	15433	28.9	51	14.8	1	ref	.	.	.	.	.	.	.	.	.	.
< 3rd degree tear	37502	70.1	265	77.0	2.14	(1.58-2.89)	1.33	(0.93-1.88)	.	.	.	.	.	.	.	.
3rd or 4th degree perineal tear	535	1.0	28	8.1	15.84	(9.90-25.33)	3.44	(1.91-6.19)	.	.	.	.	.	.	.	.
Retained placenta						<0.001		<0.001								
No	53171	99.4	298	86.6	1	ref	.	.	.	.	.	.	.	.	.	.
Yes	299	0.6	46	13.4	27.45	(19.7-38.21)	18.3	(11.6-28.89)	.	.	.	.	.	.	.	.
Baby characteristics																
Birth status						0.086										

	Vaginal births (Model 7)								Caesarean births (Model 8)							
	Controls (n =53,470)		Cases (n =344)		Unadjusted ORs		Adjusted ORs* (n= 51,778)		Controls (n =867)		Cases (n =132)		Unadjusted ORs		Adjusted ORs* (n=942)	
	n	%	n	%	OR	(95% CI)	OR	(95% CI)	n	%	n	%	OR	(95% CI)	OR	(95% CI)
Live born	53443	100.0	343	99.7	1	ref	.	.	866	99.9	132	100	1	ref	.	.
*Stillbirth**	27	0.1	1	0.3	5.77	(0.78-42.59)	.	.	1	0.1	0	0.0	1.00	N/A	.	.
Head circumference						<0.001								0.124		
<35cm	28861	54.3	134	39.0	1	ref	.	.	419	48.4	54	41.2	1	ref	.	.
≥35cm	24329	45.7	210	61.1	1.86	(1.50-2.31)	.	.	446	51.6	77	58.8	1.34	(0.92-1.94)	.	.
Missing	280	.	0	.	.	.	.	.	2	.	1	.	.	.	.	.
Birthweight						<0.001		<0.001						<0.001		<0.001
<3000g	7595	14.5	22	6.6	0.59	(0.37-0.94)	0.49	(0.3-0.81)	142	17.4	14	11.2	1.00	(0.52-1.94)	0.98	(0.48-2.01)
3000-3499g	21416	40.7	105	31.5	1	ref	1	(0-0)	326	39.9	32	25.6	1	ref	1	(0-0)
3500-3999g	18010	34.3	126	37.8	1.43	(1.10-1.85)	1.51	(1.14-2)	263	32.2	35	28.0	1.36	(0.82-2.25)	1.45	(0.84-2.51)
≥4000g	5552	10.6	80	24.0	2.94	(2.19-3.94)	3.12	(2.25-4.35)	86	10.5	44	35.2	5.21	(3.12-8.71)	5.54	(3.09-9.91)
Missing	897	.	11	.	.	.	.	.	50	.	7	.	.	.	.	.

* Adjusted for all variables included in the multivariable analysis

4.4.3 Number of risk factors and risk of postpartum haemorrhage

4.4.3.1 Number of risk factors among women who had vaginal births

The number of risk factors each woman had, among all women who had a vaginal birth, are presented in Table 4.8. There were 10 cases of PPH and 666 controls who had no risk factors identified in the multivariable analysis. The odds of having a PPH among women who had a vaginal birth increased with an increase in the number of risk factors a woman had. Compared with women who had just one risk factor, those with five risk factors had more than five times the odds of having a PPH (OR=5.20; 95% CI 4.00-6.76) and for women with ten or more risk factors the odds of having a PPH were almost 35 times higher (OR=34.83; 95% CI 26.8-45.3).

Table 4.8 Incremental odds of PPH associated with increasing numbers of independent risk factors among all women who had a vaginal birth

Number of risk factors	*Controls (n = 104,329)*		*Cases (n = 13,795)*		*Unadjusted ORs*		*p value*
	n	*%*	*n*	*%*	*OR*	*95% CI*	
							<0.001
0	666	0.6	10	0.1	0.83	(0.42-1.63)	
1	3,366	3.2	61	0.4	1	ref	
2	8,489	8.1	258	1.9	1.68	(1.26-2.23)	
3	15,019	14.4	616	4.5	2.26	(1.73-2.96)	
4	18,679	17.9	1,109	8.0	3.28	(2.52-4.27)	
5	18,628	17.9	1,756	12.7	5.20	(4.00-6.76)	
6	15,524	14.9	2,211	16.0	7.86	(6.05-10.2)	
7	10,750	10.3	2,202	16.0	11.30	(8.70-14.7)	
8	6,620	6.4	2,090	15.2	17.42	(13.4-22.6)	
9	3,616	3.5	1,606	11.6	24.51	(18.8-31.9)	
10+	2,972	2.9	1,876	13.6	34.83	(26.8-45.3)	

The number of risk factors each woman had increased over the study period. Among women who gave birth in 1986-1990, 45% had less than five risk factors for PPH, whereas in 2011-2016 the proportion of women with less than five risk factors was 35% (Figure 4.7).

In 1986-1990, 45% of women giving birth vaginally had between zero and four risk factors, compared with 35% in 2011-2016.

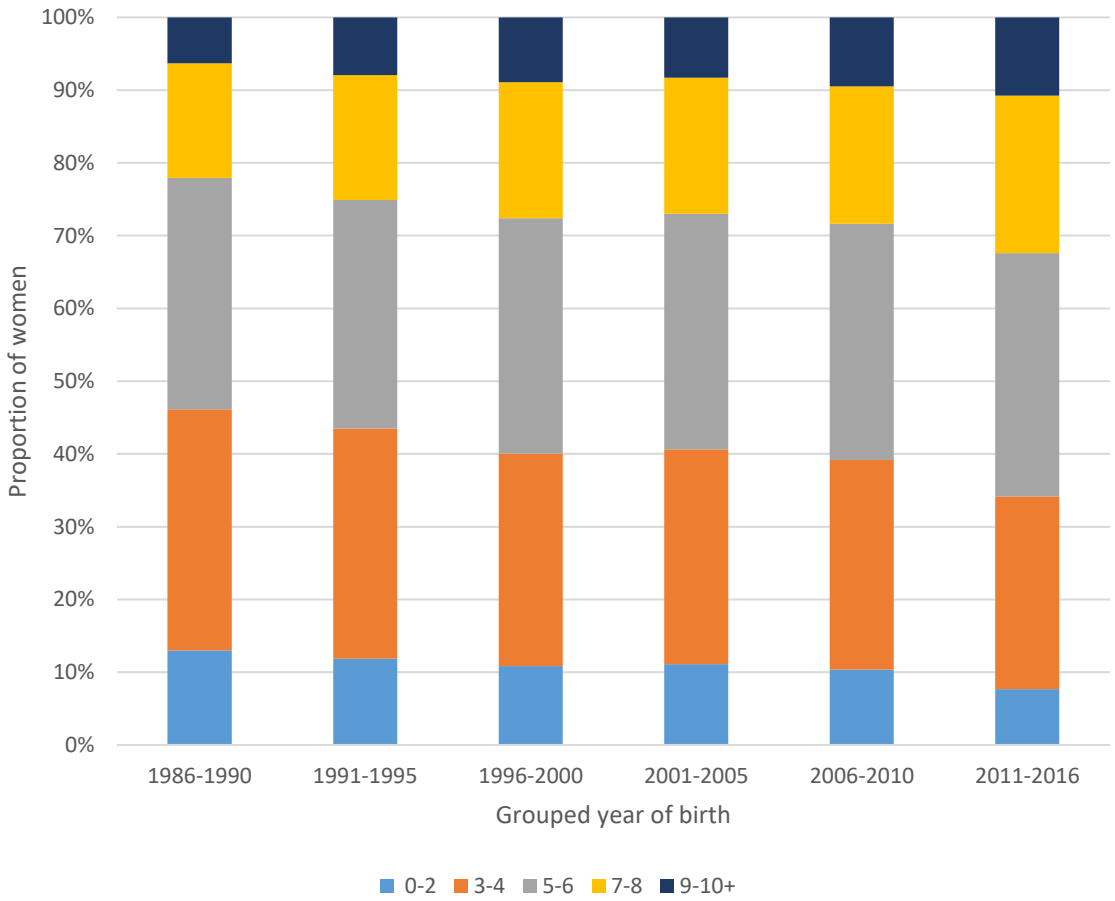


Figure 4.7 Number of risk factors among women who had a vaginal birth, by grouped year of birth

4.4.3.2 Number of risk factors among women who had caesarean births

The number of risk factors each women had, among all women who had a caesarean birth, are presented in Table 4.9. As seen among vaginal births, there was a very small number of cases and controls who had no risk factors identified in the multivariable analysis. The odds of PPH among women who had a caesarean birth increased as the number of risk factors a woman had increased, as was observed among women who had a vaginal birth. Compared with women who had just one risk factor, those with five risk factors had an OR of 2.33 (95% CI 1.53-3.56) and those with ten or more risk factors had an OR of 9.77 (95% CI 3.75-25.5).

Table 4.9 Incremental odds of PPH associated with an increase in the number of independent risk factors among all women who had a caesarean birth

Number of risk factors	*Controls (n =12,953)*		*Cases (n =21,114)*		*Unadjusted ORs*		*p value*
	n	*%*	*n*	*%*	*OR*	*95% CI*	
							<0.001
0	3	0.0	1	0.0	0.51	(0.05-5.25)	
1	54	0.4	35	0.2	1	ref	
2	519	4.0	268	1.3	0.80	(0.51-1.24)	
3	1,578	12/2	1,206	5.7	1.18	(0.77-1.81)	
4	2,771	21.4	3,163	15.0	1.76	(1.15-2.69)	
5	3,466	26.8	5,236	24.8	2.33	(1.53-3.56)	
6	2,737	21.1	5,639	26.7	3.18	(2.08-4.86)	
7	1,387	10.7	3,757	17.8	4.18	(2.73-6.40)	
8	374	2.9	1,457	6.9	6.01	(3.88-9.30)	
9	58	0.5	314	1.5	8.35	(5.03-13.9)	
10+	6	0.1	38	0.2	9.77	(3.75-25.5)	

Among women who had a caesarean, the number of risk factors each woman had increased over time (Figure 4.8), as was seen among women who had a vaginal birth. At the start of the study period, almost 50% of women had less than five risk factors, but by the end of the study period this had decreased to 20%. The number of women who had nine or more risk factors increased ten-fold, from 0.2% in 1986-1990 to 2.1% in 2011-2016.

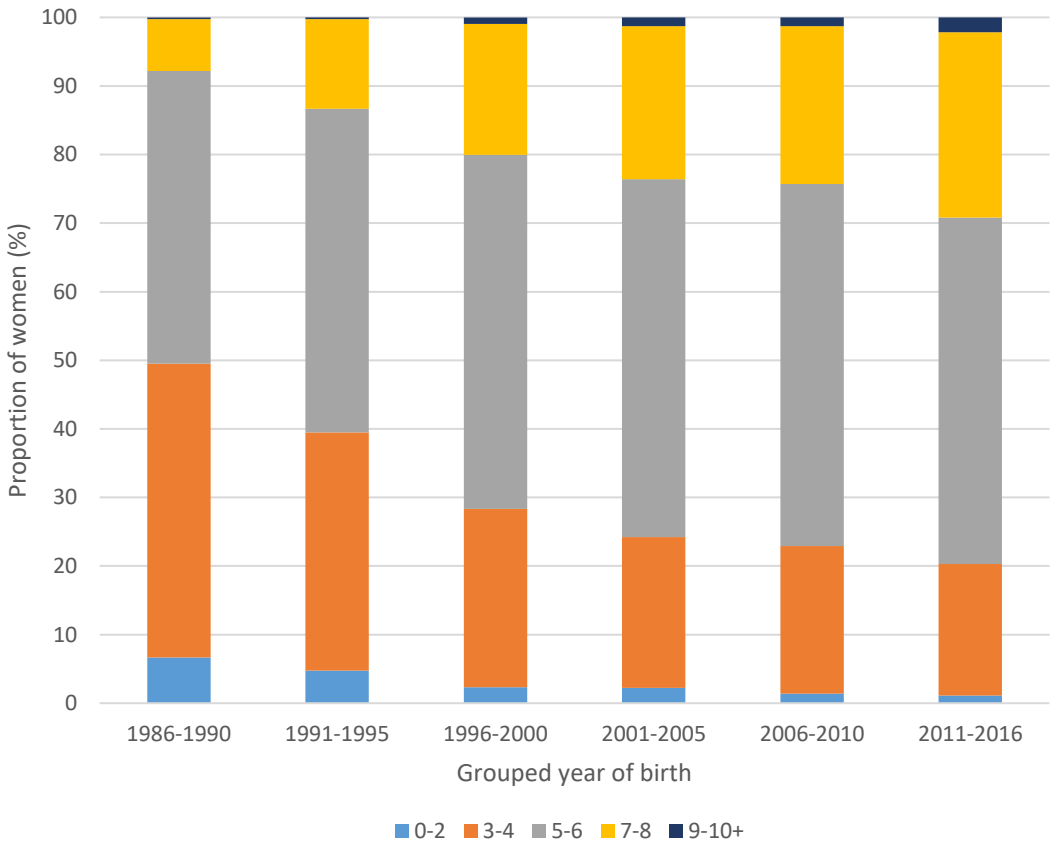


Figure 4.8 Number of risk factors among women who had a caesarean birth, by grouped year of birth

4.4.4 Prevalence of risk factors over time

4.4.4.1 Prevalence of risk factors among women who had vaginal births

The population attributable fractions for individual risk factors for PPH among women who had a vaginal birth are presented in Table 4.10. Of the pre-pregnancy, non-modifiable risk factors, nulliparity was the most important factor contributing to the PAF, contributing 18.6% of the increased odds (95%CI 17.6-19.5%) (Table 4.10). Of the pregnancy-related non-modifiable risk factors, perineal tear contributed most to the PAF (18.9%; 95%CI 16.2-21.6) and among the potentially modifiable risk factors, 17.1% of the increased odds could be attributed to not smoking in pregnancy (95% CI 14.8-19.3).

Table 4.10 Population attributable fractions (PAF) for independent risk factors for PPH, among all women who had a vaginal birth

Risk factor	*Prevalence (%)*	*Adjusted analysis*		*PAF*	
		OR	*(95 % CI)*	*(%)*[1]	*95% CI (%)*
Non-modifiable; pre-pregnancy					
Age ≥30 vs <30	41.2	1.19	(1.14-1.24)	6.21	(4.83-7.57)
Black or Asian ethnicity	3.8	2.34	(2.16-2.55)	1.39	(1.30-1.47)
Socioeconomic quintile 2,3,4[2]	38.7	1.10	(1.05-1.14)	3.54	(2.04-5.01)
BMI > 25	43.7	1.20	(1.15-1.24)	6.80	(5.44-8.15)
Nulliparity	47.0	1.99	(1.89-2.09)	18.59	(17.6-19.5)
Previous PPH	6.8	2.40	(2.22-2.60)	2.92	(2.75-3.08)
Previous CS	2.6	1.36	(1.21-1.52)	0.50	(0.34-0.67)
Non-modifiable; pregnancy and birth					
Hypertension[3]	3.6	1.30	(1.19-1.42)	0.58	(0.4-0.75)
Multiple pregnancy	1.0	2.03	(1.75-2.36)	0.29	(0.25-0.34)
Non-vertex presentation	7.8	1.22	(1.15-1.30)	0.78	(0.57-0.99)
Perineal tear[4]	74.1	1.39	(1.32-1.48)	18.90	(16.2-21.6)
Retained placenta	1.0	5.94	(5.14-6.87)	0.11	(0.11-0.12)
Birthweight ≥3500g	42.6	1.68	(1.61-1.75)	14.88	(14.0-15.8)
Potentially modifiable					
Non-smoker vs Smoker	69.2	1.36	(1.30-1.43)	17.07	(14.8-19.3)
Gestational age > 40 weeks	27.0	1.11	(1.06-1.16)	2.35	(1.42-3.27)
Induction	22.1	1.50	(1.44-1.57)	5.79	(5.28-6.29)
Augmentation	16.0	1.36	(1.30-1.42)	2.76	(2.4-3.12)
Prolonged second stage	20.5	1.55	(1.48-1.62)	4.13	(3.8-4.47)
Third stage ≥ 60 mins	4.4	4.33	(4.03-4.66)	1.53	(1.5-1.57)
Instrumental birth	21.3	2.45	(2.33-2.57)	5.89	(5.69-6.1)

[1] The proportions add up to more than 100% because many women had more than one risk factor

[2] Socioeconomic quintiles are derived from the Scottish Indices of Multiple Deprivation, with quintile 1 being the most deprived and quintile 5 the least deprived.

[3] Gestational hypertension, pre-eclampsia or eclampsia

[4] Perineal laceration, episiotomy, labial tear, third degree tear, fourth degree tear, and any combination of these

Figure 4.9 presents the prevalence of non-modifiable pre-pregnancy risk factors for PPH among women who had a vaginal birth over time. Over the 31-year study period, the prevalence of nulliparity, previous caesarean birth and socio-economic status quintile 2, 3 and 4 remained relatively stable. The prevalence of BMI >25 increased from 30.1% in 1986-1990 to 43.7% in 2011-2016, maternal age ≥30 increased from 26.7% to 50.9%, Black or Asian ethnicity increased from 2.1% to 9.1%, and previous PPH increased from 3.5% to 11.6%.

The prevalence of pregnancy and birth-related, non-modifiable risk factors for PPH among women who had a vaginal birth are presented in Figure 4.10. The prevalence of multiple pregnancy, gestational hypertension or preeclampsia, and non-vertex presentation remained relatively stable over the 31-year study period. The prevalence of birthweight ≥3500g increased from 40.1% to 45% and while the prevalence of retained placenta remained low throughout the study period, the proportional increase over time was notable at 0.5% and 2%.

Figure 4.11 presents the prevalence of potentially modifiable risk factors among women who had a vaginal birth over time. The prevalence of instrumental birth and augmentation of labour increased moderately over the study period, while the prevalence of gestational age 41+ weeks remained relatively steady. The prevalence of perineal tear was relatively stable, decreasing in prevalence in 2006-2010, before returning to the previous proportions in 2011-2016. The proportion of non-smokers increased markedly over the study period, as did induction of labour, prolonged second stage of labour and delayed third stage of labour.

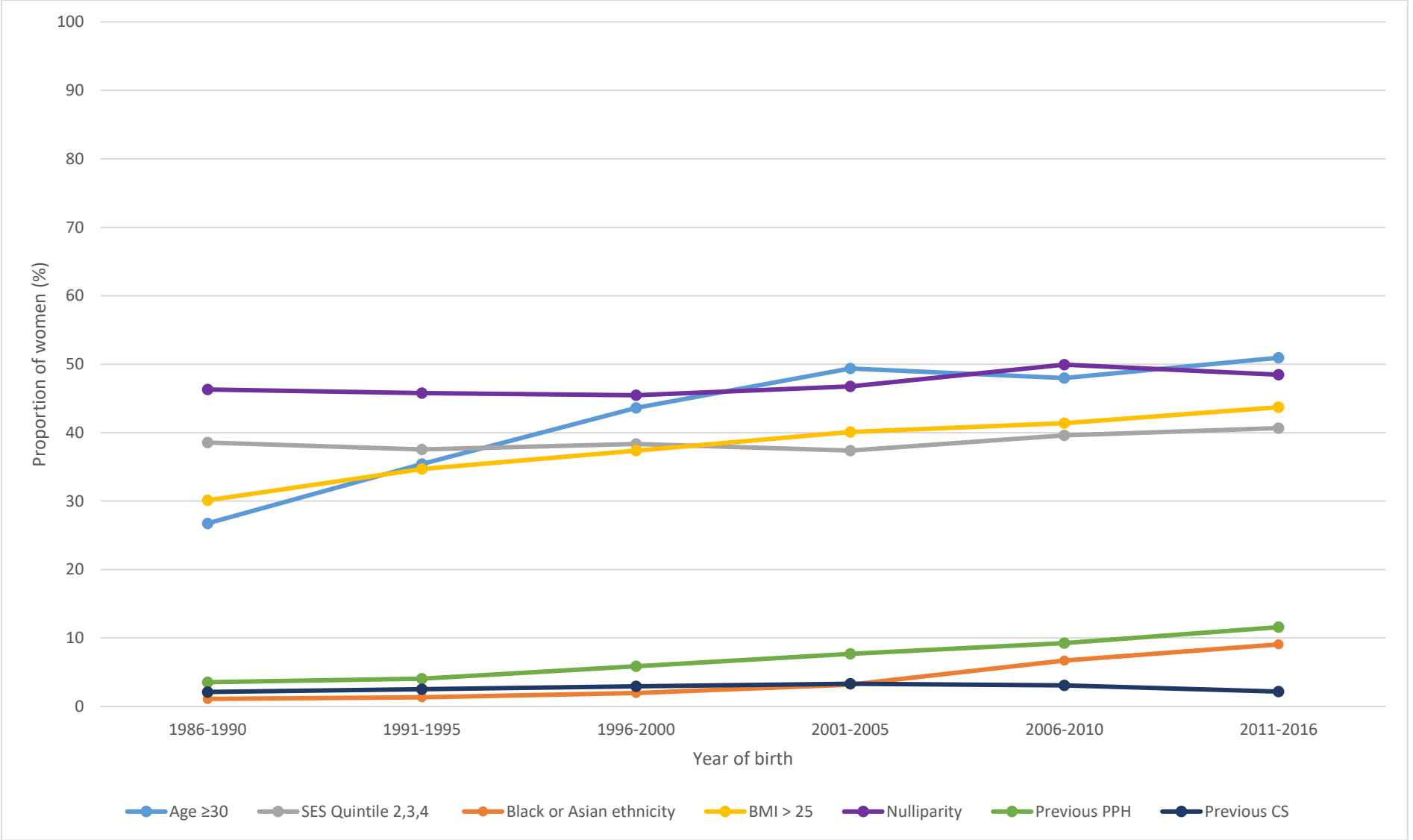


Figure 4.9 Prevalence of non-modifiable, pre-pregnancy risk factors among women who had a vaginal birth, Aberdeen 1986-2016

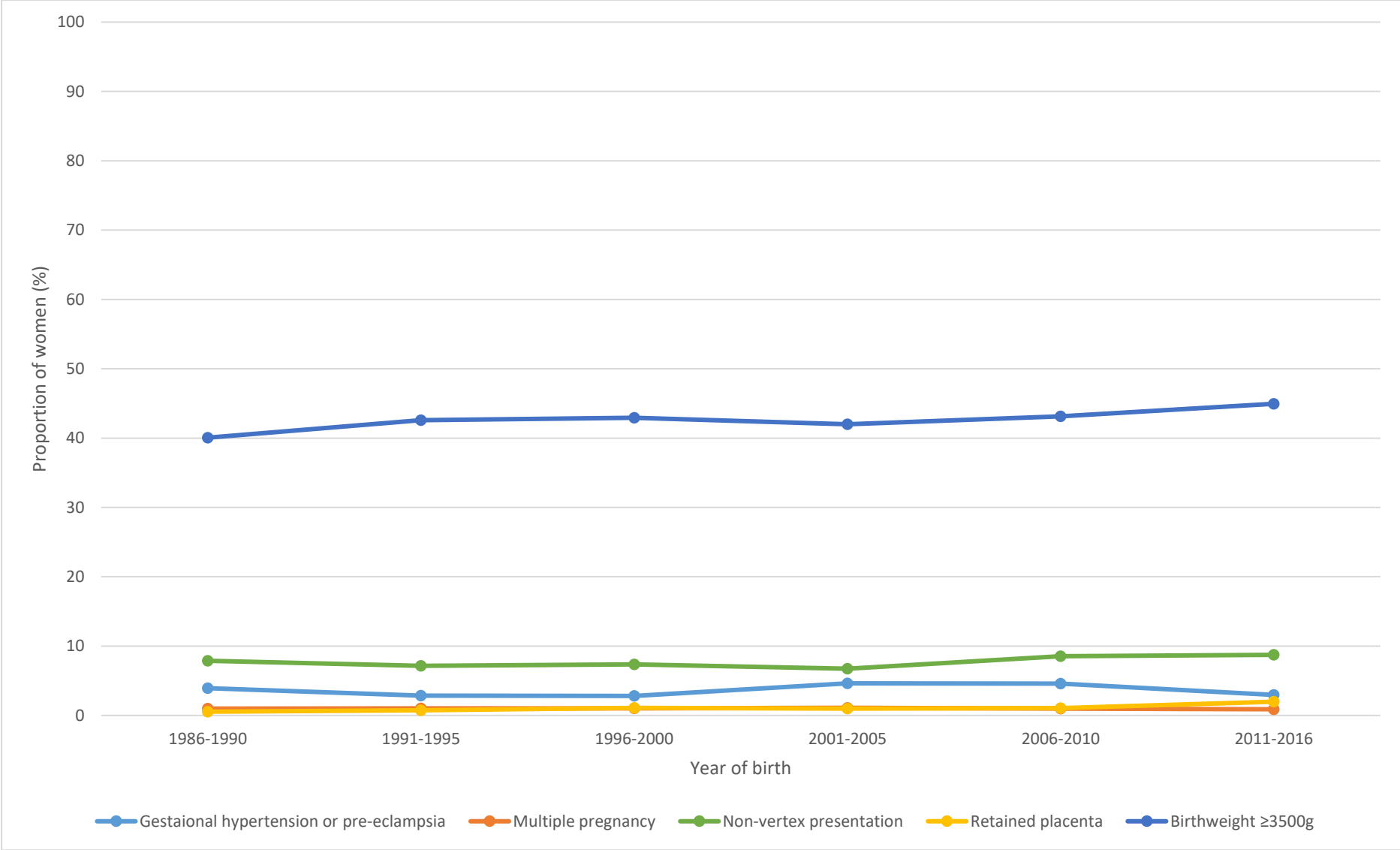


Figure 4.10 Prevalence of non-modifiable, pregnancy- and birth-related risk factors among women who had a vaginal birth, Aberdeen 1986-2016

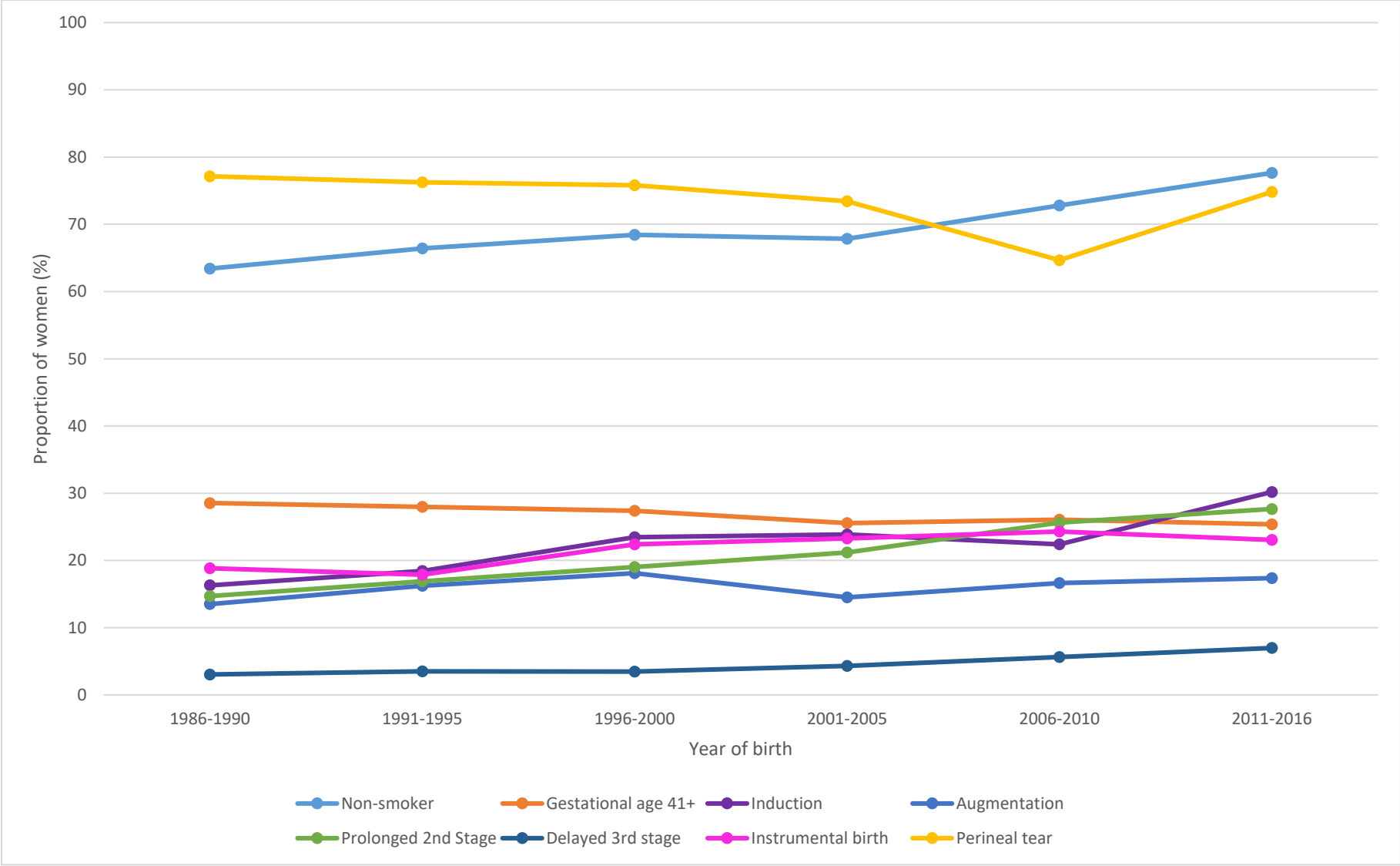


Figure 4.11 Prevalence of potentially modifiable risk factors among women who had a vaginal birth, Aberdeen 1986-2016

4.4.4.2 Prevalence of risk factors over time – caesarean births

The risk factors for PPH over time among women who had a caesarean were similar to those identified in the Model 2. The population attributable fractions for individual risk factors for PPH among women who had a caesarean are presented in Table 4.11. Of the pre-pregnancy, non-modifiable risk factors, no previous caesarean contributed most significantly to the PAF, at 50.4% (95%CI 47.20-53.40). Of the pregnancy-related non-modifiable risk factors, labour before caesarean contributed most to the PAF (21.58%; 95%CI 18.3-24.78) and of the potentially modifiable risk factors, 18.18% of the higher risk could be attributed to not smoking in pregnancy (95% CI 14.5-21.7).

Table 4.11 Population attributable fractions (PAF) for independent risk factors, among all women who had a caesarean birth

Risk factor	*Prevalence (%)*	*Adjusted analysis*		*PAF*	
		OR	*95% CI*	*(%)*[1]	*95% CI*
Pre-pregnancy non-modifiable factors					
Age 30+	55.8	1.32	(1.26-1.39)	17.14	(14.5-19.7)
Black or Asian ethnicity	6.0	1.39	(1.25-1.54)	2.99	(2.12-3.86)
BMI > 25	55.8	1.25	(1.20-1.31)	13.79	(11.2-16.3)
Parity 1	33.7	1.12	(1.06-1.18)	3.14	(1.63-4.63)
Previous PPH	20.4	1.89	(1.75-2.05)	10.49	(9.6-11.4)
No previous CS	73.0	2.23	(2.07-2.40)	50.40	(47.2-53.4)
Pregnancy non-modifiable					
No hypertension	79.8	1.26	(1.19-1.34)	17.28	(13.3-21.1)
Multiple pregnancy	3.9	2.30	(2.01-2.63)	4.96	(4.33-5.58)
Birthweight ≥3500g	41.6	1.20	(1.14-1.27)	19.73	(17.1-22.3)
Head circumference ≥35cm	52.0	1.44	(1.36-1.52)	11.86	(8.64-15.0)
Potentially modifiable					
Non-smoker	73.6	1.26	(1.2-1.33)	18.18	(14.5-21.7)
Induction	24.2	1.29	(1.21-1.38)	9.37	(7.25-11.5)
Gestational age 24-37 weeks	19.4	1.15	(1.08-1.23)	2.28	(1.25-3.30)
CS after labour	59.2	1.36	(1.29-1.44)	21.58	(18.3-24.8)

[1] The proportions add up to more than 100% because many women had more than one risk factor

Figure 4.12 presents the prevalence of pre-pregnancy, non-modifiable risk factors for PPH among caesarean births over time. The prevalence of maternal age ≥30 increased markedly over the study period, from 35% in 1986-1990 to 64.8% in 2011-2016, as did the prevalence of BMI >25, (38.7% to 55.8%), Black or Asian ethnicity (1.1% to 11.9%), and previous PPH (24% to 51%). The prevalence of parity of one increased slightly, from 31.1% to 36.9% and the prevalence of previous caesarean ranged between 41.5% and 49%.

The prevalence of non-modifiable pre-pregnancy factors among women who had caesarean births over time is presented in Figure 4.13. The prevalence of birthweight ≥3500g increased from 35.7% in 1986-1990 to 43.2% in 2011-2016 and similarly head circumference ≥35cm also increased (45.8% to 52.7%). The proportion of women who had no-hypertension in pregnancy increased from 69.7% to 85%. The prevalence of multiple birth remained relatively low throughout the study period but the proportional increase over time was large, from 2.5% to 4.2%.

The proportion of non-smokers increased markedly, from 63% in 1986-1990 to 80% in 2011-2016. Gestational age 24-37 weeks remained very stable, while caesarean after the onset of labour fluctuated between 66.3% and 54.3%. The prevalence of induction increased from 18.2% in 1986-1990 to 25.7% in 2011-2016.

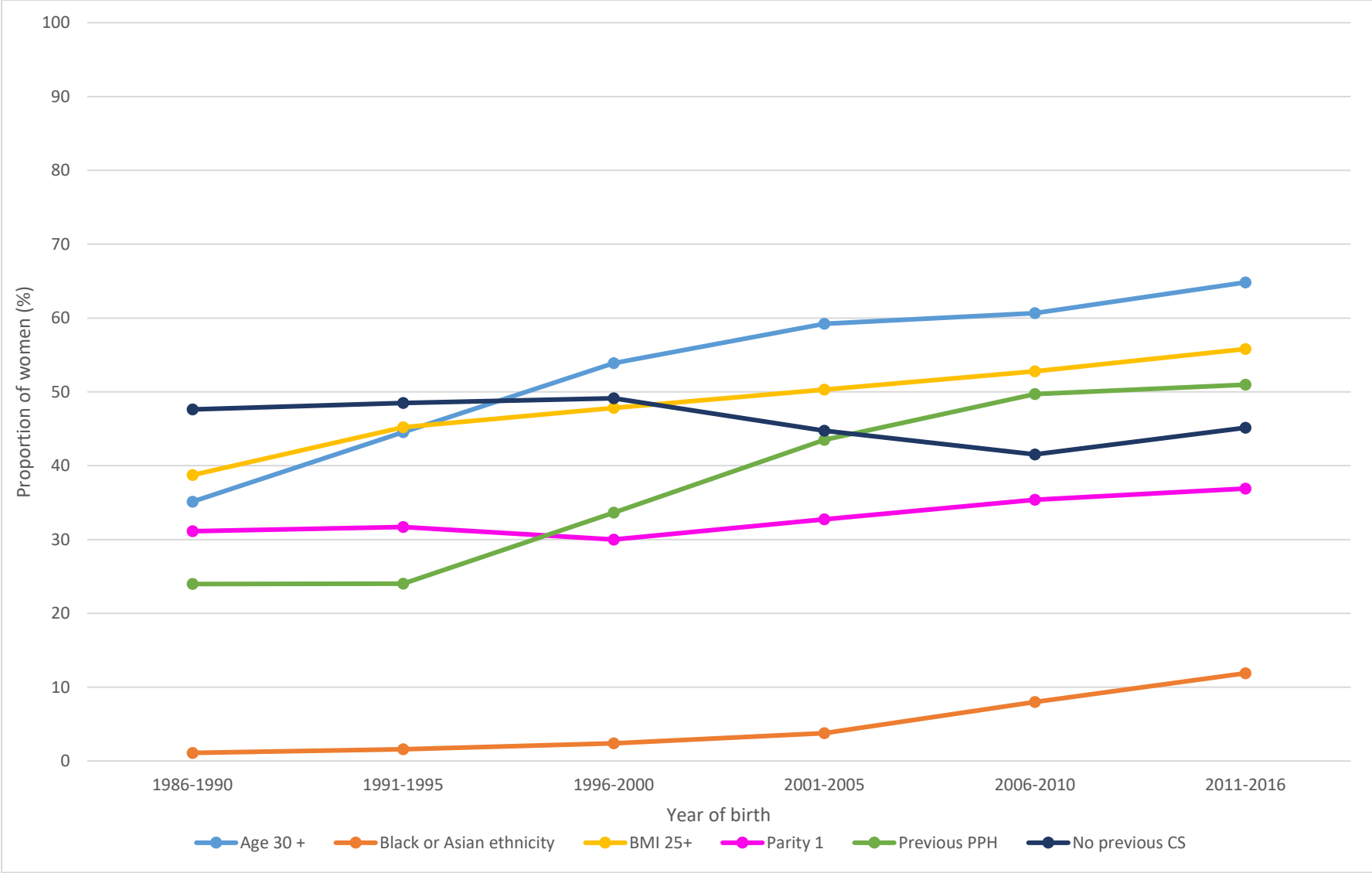


Figure 4.12 Prevalence of non-modifiable, pre-pregnancy risk factors among women who had a caesarean birth, Aberdeen 1986-2016

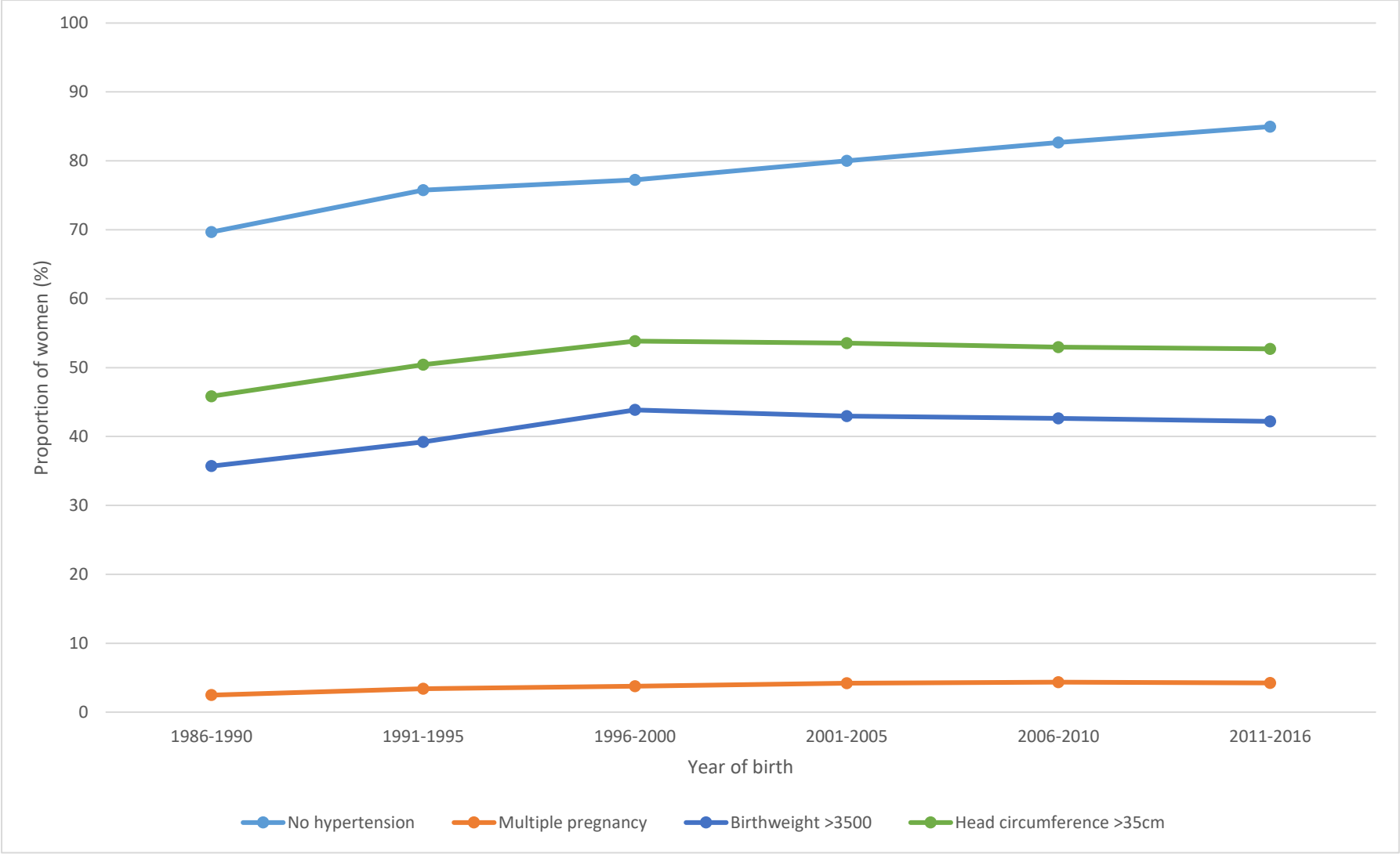


Figure 4.13 Prevalence of non-modifiable pregnancy-related risk factors among women who had a caesarean birth, Aberdeen 1986-2016

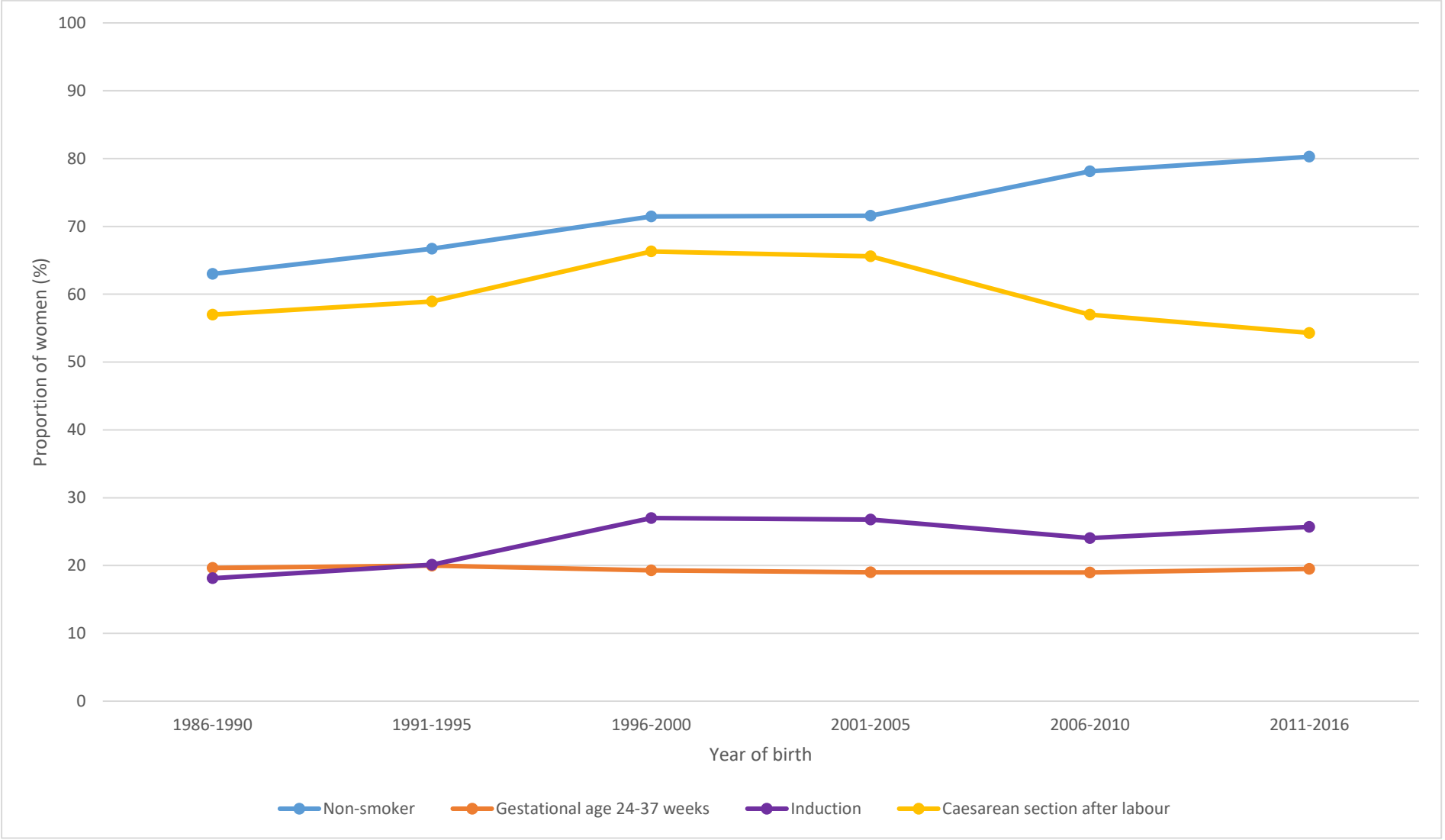


Figure 4.14 Prevalence of potentially modifiable risk factors among women who had a caesarean birth, Aberdeen 1986-2016

4.5 Discussion

4.5.1 Summary

This is the first population-based study to explore the incidence of and risk factors for PPH and SPPH in a UK population over time. This study has demonstrated that the incidence of PPH, and of SPPH, increased significantly in this population between 1986 and 2016, among women who gave birth vaginally and by caesarean, among all women and among women who were categorised as being at low-risk of complications at the start of labour.

The risk factors for PPH and SPPH identified in this study generally align with those found in previous research and as presented in the systematic review. Over the 31-year study period, several risk factors increased in prevalence, including not smoking in pregnancy, induction of labour, prolonged second stage of labour, advanced maternal age and previous PPH. Analysis of the population attributable fraction of independent risk factors for PPH and SPPH and the change in prevalence of these risk factors over time suggests that the increased incidence of PPH and SSPH over time can, in part, be explained by increasing prevalence of key risk factors and the number of risk factors for any individual woman. However, it is evident that the increase in prevalence of risk factors identified in this study cannot wholly account for the increased incidence over time.

4.5.2 Strengths and limitations

The major strength of this study is the population-based design using validated data from a single data source (149). The long study period allowed detailed analysis of the incidence and risk factors for PPH over time and provided sufficient power to perform analyses of risk factors with a relatively low prevalence in the population e.g. multiples among vaginal births.

The Aberdeen population is relatively stable, with low rates of migration (149) and is therefore well suited to exploring changes in incidence of PPH over time, as it is less likely that the changes in incidence can be attributed to significant changes in the population over time.

One of the primary limitations of this study was that it was conducted in a single region of Scotland, which is predominantly White and English speaking, meaning these findings cannot be immediately generalised to other, more-diverse populations in the UK and elsewhere.

Reliable data about the causes of PPH were not available. It was not therefore possible to assess the extent to which these may have changed over time, or whether there is variation in risk factors for PPH with different causes. There were also several risk factors of interest in the AMND that could not be included in the analysis, either because of the way the data were collected or because of issues with data quality. For example, type of anaesthesia administered has been associated with PPH in previous research (52, 111, 121), however, the way this information is collected in the AMND means it was not possible to determine the timing of its administration during the birth episode. It was therefore not possible to identify whether the anaesthesia was administered as part of management of PPH or whether it had been administered prior to significant blood loss. Had this information been available, it may have been possible to further explore the association between some labour and birth-related variables and PPH.

Variability in the methods for estimating the amount of blood lost between modes of birth may have led to misclassification bias among vaginal births. It is also possible that the methods of blood loss estimation changed over the study period and that this contributed to the observed increase in incidence, however, there was no written record of a change in protocol that could be identified that would suggest substantial changes had occurred. This study was underpowered to detect statistically significant associations between many potential risk factors and PPH among low-risk women who had caesarean births.

4.6 Conclusions

The incidence of PPH and SPPH has increased significantly in the past three decades in the Grampian region of Scotland. This trend was observed among women who had vaginal births and those who had caesarean births as well as among all women and low-risk women.

Risk factors identified in this study broadly align with those in previous research. Despite adjustment for independent risk factors, the odds of PPH and SPPH increased significantly over the study period. This suggests there are unmeasured factors that are contributing to the increasing incidence.

Analysis of the contribution of risk factors to the population attributable risk for PPH and the prevalence of risk factors over time suggests that part of the increase is associated with increasing prevalence of risk factors in the population, but that this does not fully explain the increased incidence over time. The role of changes in clinical practices for measuring blood loss, as well as the influence of unexplored risk factors may also have contributed. Findings from this study have important implications for directing future research and efforts to address the increasing incidence of PPH and SPPH.

Chapter 5: Discussion

5.1 Introduction

The overarching aim of this research was to investigate risk factors for PPH in high-income countries, to understand how these may have changed over time and why, to inform changes to clinical practice and policy and ultimately improve outcomes for women. This aim was first addressed through a systematic review to synthesise the existing evidence about risk factors for PPH in high-income countries and identify the gaps in the evidence. The review identified an important gap in the literature related to investigations of risk factors for PPH among low-risk women, and for births that occur outside obstetric units. Addressing this gap, a case-control study was conducted in midwifery units in the UK investigating risk factors for PPH among women who are considered to be at low-risk of complications such as PPH. The findings of the systematic review also informed the risk factors that were investigated in a population-based case-control study of 31 years of births in the Grampian region of Scotland. The study examined how the incidence of PPH and SPPH had changed over time and the extent to which any change was associated with changes in the prevalence of key risk factors.

5.1.1 Why this research was undertaken

The incidence of PPH has increased markedly in high-income countries over the past two decades (8, 10, 12, 67). In England, the rate of PPH increased from 11% in 2012 to 24% in 2021 (69, 77). This increase can be seen across all modes of birth, suggesting that it is not wholly explained by the increase in the rates of instrumental birth and caesarean (69, 77), which have been associated with an increased risk of PPH (10, 13, 46).

Outcomes for women who experience PPH vary widely, from dizziness and impaired recovery following birth to maternal death (31, 152). The rate of maternal death due to PPH has not increased with the increase in incidence in high income countries (21, 153). While this suggests generally good management of PPH, if not managed appropriately PPH can quickly become life threatening and a

high volume of blood loss is associated with significant potential for severe morbidity. Outcomes following a PPH can include anaemia, the need for transfusion, increased risk of sepsis, cardiac arrest, peripartum hysterectomy and difficulty breastfeeding (31, 32). There is also evidence that some negative impacts of severe PPH can persist long-term, for example, increased risk of cardiovascular disease (41). The experience of a PPH can also be distressing for women and their partners (30). In the short term, breastfeeding initiation and maternal wellbeing can be negatively impacted by the experience of PPH (35). In the longer term, women who have a PPH, particularly a SPPH and emergency hysterectomy, may have nightmares and flashbacks associated with the stress of the experience (154).

Taken together, these trends highlight the importance of reducing the incidence through targeted preventive strategies and through appropriate counselling of women and preparation for the event of PPH, for which an accurate understanding of the risk factors for PPH is critical.

5.2 Incidence of PPH

The incidence of PPH varies widely between settings and reported incidence is influenced by the underlying risk profile of the population and the chosen definition and measurement of PPH. The considerable variability of the incidence of PPH reported by studies included in the systematic reviews, even among studies that employed the same definition of PPH, highlights the difficulties in making generalisations about the incidence of PPH across contexts. However, it is evident that, regardless of the definition used, the incidence of PPH has increased over the past three decades in high income countries.

5.2.1 Incidence of PPH requiring transfer in UK midwifery units

The incidence of PPH occurring in UK midwifery units and requiring transfer to obstetric care, as reported in Chapter 3, was 3.9% in AMUs and 2.6% in FMUS, which was higher than expected, based on previous research about births in MU (141). There are limited data against which to compare the results of this study. Data from a national prospective cohort study of maternal outcomes by planned

place of birth in England in 2008-10 (the Birthplace study) estimated that the proportion of women who were transferred from an MU to obstetric care, where the primary reason for transfer was PPH, was 1.0% among women who gave birth in FMUs and 1.0% among women who gave birth in AMUs (141). The results of the Birthplace study, however, are not directly comparable to the UKMidSS study as the former study only included women whose **primary** reason for transfer to obstetric care was PPH, whereas the UKMidSS study, reported in Chapter 3, also included women whose primary or secondary reason for transfer was PPH. Perhaps more importantly, the Birthplace study was conducted between 2008 and 2010. Since then, the incidence of PPH in the UK has increased. In 2010, the overall incidence of PPH among women having a spontaneous vaginal birth in England was 7.2% (155), but by 2021, this has more than doubled to 16.0% (77). While these data relate to the incidence in all NHS hospitals in England, and are not therefore directly comparable to the population in the UKMidSS study, it is likely that this general upward trend in the incidence of PPH has also affected the lower-risk population of women giving birth in MUs.

5.2.1.1 Incidence of PPH requiring transfer in FMUs and AMUs

In the UKMidSS study, the incidence of PPH requiring transfer in AMUs was higher than in FMUs. Women who plan to give birth in FMUs generally have fewer pre-existing and current pregnancy complications compared with women who plan to give birth in AMUs, which may explain the differences in incidence. In the Birthplace study, 2.5% of women who planned birth in an FMU were classified as higher risk, defined in a similar way to the UKMidSS study, while 4.4% of women who planned birth in AMUs were classified as higher risk (141). However, a post hoc analysis of the data from the UKMidSS study, comparing the characteristics of women in each unit type for which data were available, indicated that differences were minimal and thus this seems unlikely to explain the observed difference in incidence.

As the case definition for the UKMidSS study was 'PPH requiring transfer' rather than a threshold of estimated blood loss, it is possible that midwives' decisions about the 'threshold' for transfer differed between FMUs and AMUs. Obstetric care is more readily available in AMUs, compared with FMUs, and therefore it is possible that midwives may be more likely to transfer women at a lower level of blood loss in AMUs, leading to a higher proportion of cases in AMUs. However, a post hoc analysis exploring this possibility revealed that postpartum blood loss was similar among women in FMUs and AMUs, for both cases and controls. This suggests that there was not a higher proportion of women with a PPH whose PPH was managed in FMUs without transfer, and therefore not meeting the case definition of 'PPH requiring transfer'.

Finally, differences in the proportion of complete data between the unit types was considered as a potential explanation for the difference in incidence. This study was the first UKMidSS study that included FMUs, with previous UKMidSS studies only being conducted in AMUs only. Reporting midwives in FMUs may therefore not have been as familiar with the study system as those in AMUs. Cases were only considered as 'confirmed' and included in the numerator for calculating incidence, when sufficiently complete data were received. Data entry completeness in cases reported by FMUs was lower, compared with AMUs (80% vs 91%) and may therefore have contributed to the observed lower incidence of PPH requiring transfer. However, a post hoc analysis comparing the incidence of PPH requiring transfer based on all reported cases (rather than just confirmed cases) was not significantly different to the reported incidence based on complete cases only, for both FMUs and AMUs. Therefore, the lower proportion of data entry completeness in FMUs compared with AMUs seems unlikely to explain the observed difference in incidence between unit types. As the number of births in FMUs is relatively small, compared with AMUs, differences in reporting rates are also unlikely to have significantly impacted the overall results of the study. On balance therefore, it seems likely that there is a true difference in the incidence of PPH in AMUs and FMUs, with incidence of PPH requiring transfer being higher in AMUs compared with FMUs.

5.2.2 Incidence of PPH and SPPH in the Grampian region of Scotland

The overall incidence of PPH and in the Grampian region over the 31-year study period was markedly higher (12% among vaginal births and 62% among caesarean births) than in previous studies conducted in high-income countries. The incidence of PPH was significantly higher among women who gave birth by caesarean, compared with those who had a vaginal birth. This was expected, given the typically higher blood loss during a caesarean than in a vaginal birth (7). The incidence of PPH and SPPH in caesarean births was, however, markedly higher than has been reported in previous studies in high income countries, including in studies using the same definitions of PPH (≥500mL blood loss) and SPPH (≥1500mL blood loss). While it is difficult to compare rates directly due to differences in the inclusion criteria and time period of other studies, the incidence of PPH reported in studies included in the systematic review ranged from 0.43% to 33.7% and for SPPH ranged from 0.1% to 14.4%.

The higher incidence of PPH in the Aberdeen study may be attribute to a higher prevalence of certain risk factors in this study population, compared with other populations. However, another important difference in comparing the data from the Aberdeen study with other estimates of PPH incidence is the method of estimating postpartum blood loss. Aberdeen Maternity Hospital weighs blood that is lost after the birth for births that occur in theatre, including all caesarean births. This is generally considered more accurate than visual estimation of blood loss (54). Visual estimation has been demonstrated to result in an underestimation of the amount of blood lost (156), which may have contributed to an underestimation of blood loss in others studies, which primarily used visual estimation to determine blood loss.

A 2017 study in Wales of over 8680 births used gravimetric and volumetric techniques to quantitatively measure blood loss and reported the incidence of PPH (blood loss ≥500mL) to be 53.0% among elective caesarean births and 60.9% among non-elective caesarean births (55). While these proportions are lower than the incidence of PPH among caesarean births in the later years of the

Aberdeen data (74.2% in 2016), they align more closely to the incidence reported in the Aberdeen study, compared with studies using visual estimation of blood loss. Furthermore, the Welsh study reported a 165% increase in reported blood loss >1500mL following the introduction of quantitative measurement of blood loss, which underscores the magnitude of potential misclassification of severe PPH using visual estimates of blood loss.

The incidence of PPH and SPPH increased significantly among both vaginal and caesarean births in Aberdeen over the study period. This aligns with the general trend of increasing incidence of PPH and SPPH in high-income countries in the past two decades (7, 8, 10, 12). The findings that the prevalence of key risk factors also increased over the 31-year period, suggest that this trend is likely to be partially explained by the increasing prevalence of risk factors over time. It is also possible that undocumented changes in clinical practices over the study period may have contributed to the increasing incidence. For example, it was not possible to ascertain whether blood loss measurement using calibrated drapes for births in theatre was used during the whole study period.

The incidence of PPH and SPPH among low-risk women in Aberdeen who had vaginal births followed a similar pattern in terms of increasing incidence to that seen among all women in the region who had vaginal births. While the incidence of PPH was lower among the low-risk group (7.9% 95% CI 7.7-8.1) compared with all women (11.7% 95% CI 11.5-11.9), it was higher than found in other studies of low-risk populations. However, there are few studies of low-risk women against which to compare these findings. A French study of births in 2004-2006 to low-risk women, defined in a similar way to the NICE guideline employed in this study, reported an incidence of PPH (blood loss ≥500mL) of 4.5% for vaginal and caesarean births combined (105). A Canadian study conducted between 2001 and 2007 investigating low-risk women (defined as those without well-established risk factors for PPH) reported the incidence of PPH (blood loss ≥500mL among vaginal births and ≥1000mL among caesarean births) to be 1.6% (15). This study also noted an increase in the incidence of PPH in the low-risk group over

the study period, from 1.03% in 2001 to 2.45% in 2007. Neither the Welsh nor Canadian study reported how blood loss was estimated, so it is not possible to comment on whether variations in methods contributed to differences in the observed incidences.

It is possible that the higher-than-expected incidence of PPH among low-risk women in Aberdeen can be partially explained by the fact that the definition of 'low-risk' for this study was based on the NICE intrapartum care guideline (146), which was not specifically developed for identifying risk of PPH, but complications in labour and birth generally. While several of the medical and obstetric factors that preclude women from being considered 'low-risk' according to the NICE guideline are risk factors for PPH and were identified as such in the Aberdeen study (obesity, previous PPH, hypertension and, among vaginal births, previous caesarean), several of the risk factors that contributed substantially to the risk of PPH are not exclusion criteria in the NICE guideline (nulliparity, birthweight ≥3500g). Furthermore, as the NICE guideline definition is, by design, for use prior to the birth, it cannot take into account birth-related factors (instrumental birth, prolonged third stage of labour, perineal tear, retained placenta), which have a substantial impact on the odds of PPH and SPPH for vaginal births.

It should also be noted that it was not possible to completely operationalise the risk factors listed in the NICE guideline to identify the low-risk group due to limitations of data availability and data quality (see Appendix C for details about how the NICE intrapartum guideline was operationalises for the Aberdeen study). Most of the risk factors that were not able to be operationalised are uncommon (141), hence the incomplete operationalisation of the NICE guideline definition was unlikely to lead to misclassification of a significant number of higher-risk women as low-risk in this study population. The exception to this was anaemia, which is included in the NICE guideline as 'haemoglobin less than 85 g/litre at onset of labour'. Data about anaemia were available from the AMND, but it was not possible to ascertain the definition and diagnostic criteria for this condition for the entire study period so it was not possible to use anaemia as part of the definition of low-risk women. Given that anaemia is

relatively common in the pregnant population in the UK, estimated to affect one in four pregnancies (157), and that it has been found to be an independent risk factor for PPH in other settings (45, 112), it is possible that the inability to exclude anaemic women from the low-risk analyses may have contributed to the higher than expected incidence of PPH among 'low-risk' women.

The increasing incidence of PPH among low-risk women who had vaginal births is likely explained by increasing prevalence of risk factors that are not accounted for in the NICE guideline. Indeed this is reflected in the increasing incidence of almost all risk factors for PPH among women who had vaginal births, most of which are not included in the NICE guideline. Notwithstanding operationalisation issues discussed above, the unexpectedly high incidence of PPH among low-risk women suggests there may be limited utility for clinicians using the criteria in the NICE guideline to assess a woman's risk of PPH, specifically, though this does not suggest the guidelines is unsuitable for assessing a woman's risk of complications generally.

5.3 Independent risk factors for PPH

The findings of this thesis confirm several well-established factors as independent risk factors for PPH, while calling into question several factors that are often cited as associated with an increased risk of PPH but for which the systematic review demonstrated that evidence is unclear. The inconsistent associations of many of the risk factors across different studies highlights the complexity in assessing risk for PPH and in making comparison across settings and study designs. Generally, risk factors for PPH became more consistently associated and with a higher magnitude of effect with increasing proximity to the birth. For this reason, the discussion of the findings for risk factors investigated in this thesis begin with more distal (maternal sociodemographic) factors, leading to more proximal (intrapartum and birth-related) factors.

5.3.1 Maternal socio-demographic characteristics

5.3.1.1 Maternal age

The association between maternal age and PPH varied between studies included in the systematic review. While several studies reported a significant association between increasing maternal age and higher odds of PPH, this effect was largely attenuated once confounding factors had been adjusted for. Among 36 studies that did adjust for confounding factors, only six reported significantly higher odds of PPH in older age groups, and the magnitude of effect was small, with ORs generally less than 1.7. Three studies reported significantly higher odds of PPH in the youngest age group, after adjusting for confounding factors. Inconsistency in the association between maternal age and PPH was also seen in the two primary research studies reported in this thesis. The apparently mixed results could be partly explained if the true relationship between maternal age and PPH were non-linear. With both younger and older maternal age associated with increased risk of PPH in a small number of studies, after adjustment for confounding factors, it is possible that the true relationship is J-shaped. If this were the case, the dichotomisation of maternal age (e.g. younger than 35 vs 35 and older) employed in most studies included in the systematic review may have masked the association.

In the Aberdeen study, increasing maternal age was an independent risk factor for PPH and SPPH among women who had a caesarean birth but not among women who had a vaginal birth. In all analyses, the magnitude of the effect of maternal age was small once adjusted for confounders. It is possible that the association between maternal age and the risk of PPH is different for vaginal and caesarean birth due to certain indications for caesarean, that are also potential risk factors for PPH, being more common at advanced maternal age. It was not possible from the available data to analyse the association between PPH and SPPH by indication for caesarean. The increased risk may also be a result of the increased prevalence of other risk factors in older mothers for which data were not available in the Aberdeen study. The use of assisted reproductive technology (56) and placenta praevia (158), for example, have been associated with an increased maternal age (118) and were identified as 'likely' risk factors in the systematic review.

5.3.1.2 Maternal race/ethnicity

Race and ethnicity were examined by 16 studies in the systematic review, with most studies there were LRoB reporting a significant association with PPH, resulting in race/ethnicity being rated as 'likely' risk factors. It was unclear in most studies whether ethnicity had been self-reported or assigned at data collection. Furthermore, a range of different categorisations of race and ethnicity were used, but in most studies, Caucasian or White ethnicity was used as the reference group. The different categorisations and different ethnic compositions of study populations make it difficult to compare studies, but in all studies that reported a significant association, being White/Caucasian was associated with lower odds of PPH, compared with minority ethnicities, regardless of how these were defined.

A similar finding was observed in the Aberdeen study with Black and Asian ethnicity associated with an increased risk of PPH and SPPH among vaginal births and for PPH among caesarean births, compared with White ethnicity. A relatively small proportion of women were of Black or Asian ethnicity in Aberdeen, compared with other parts of the UK (159), although the proportion of non-White women increased significantly over the study period. This aligns with a recent UK study using routine clinical data about more than 900,000 women giving birth in maternity units in England from 2015-17, which found that women from ethnic minority backgrounds had an increased risk of severe PPH, after adjusting for available maternal, fetal and birth-related factors (160).

These findings align with a growing body of research indicating that race and ethnicity are associated with a range of maternal health outcomes, with racial and ethnic minorities at higher risk of poor maternal outcomes and severe morbidity (5, 161, 162). The association between ethnicity and PPH does not necessarily suggest a causal or biological association but is more likely a reflection of the

broader health disparities experienced by ethnic minorities related to socioeconomic disadvantage as well as discrimination and inequality in healthcare systems (163-165).

5.3.1.3 Maternal country of birth

Maternal country of birth is sometimes used as a proxy for ethnicity or race, however, it may not accurately reflect an individual's self-identified race or ethnicity and therefore should be viewed with caution when used in this way (166). It may be also used to reflect migrant status, which can have implications for maternal outcomes (167). Five studies in the systematic review examined maternal country of birth, all comparing women born in the study country with women born in other countries. The only two LRoB studies that reported a significant association between country of birth and PPH were both conducted in Australia. Both studies reported that, having adjusted for confounders, women born outside of Australia had higher risk of PPH than those born in Australia. While country of birth may be associated with risk of PPH, these findings should be interpreted with caution as this variable was only significant in one context and may therefore not be generalisable to other settings. It was not possible to examine maternal country of birth in either the Aberdeen or UKMidSS studies.

5.3.1.4 Smoking status

The findings from 13 studies in the systematic regarding an association between smoking and PPH were inconsistent, however, most studies reported no significant association between smoking and PPH, after adjustment for other factors. Two studies reported lower odds of PPH among women who smoked in pregnancy, although one of these studies only conducted univariable analyses without adjusting for potential confounders. A third study reported lower rates of PPH among smokers but did not report whether this was statistically significant.

In both research studies carried out for this thesis smoking was associated with significantly lower odds of PPH, after adjustment for other factors. In the UKMidSS study, women who smoked during pregnancy were almost 30% less likely to experience a PPH requiring transfer than those who did not

smoke. In the Aberdeen study, smoking was associated with lower odds of PPH, but not SPPH, among women who had a vaginal birth and was associated with lower odds of PPH and SPPH among women who had a caesarean birth.

It is possible that the association between smoking and a lower risk of PPH was a result of residual confounding by risk factors not accounted for in either the UKMidSS or Aberdeen analyses. However, given that smoking has been found to be a protective factor for PPH in some previous studies, identified in the systematic review and in other literature (79, 168), these findings may reflect a true association. It is possible that the hypercoagulation effects of smoking contribute to this association (169). It is also possible that the protective effect of smoking is related to the impact of smoking on placental vascularisation. A systematic review of the impact of cigarette smoking on placental vasculature found that women who smoked during pregnancy showed increased vascular resistance on the fetal side of the placenta (170).

While these potential biological mechanisms may contribute to lower blood loss after birth, it is unclear the extent to which it contributes to the occurrence of PPH and whether this association may be differentially associated with the different causes of PPH. Notwithstanding these potential causal mechanisms for a protective effect of smoking in relation to PPH, the systematic review undertaken for this thesis shows that overall the body of literature about this association is unclear, and the results of the two studies reported here would not alter that rating. Furthermore, with some research suggesting that smoking during pregnancy is an independent risk factor for PPH (171), it remains unclear whether maternal smoking is an independent risk or protective factor for PPH.

Clearly, any finding of a protective effect of smoking in terms of PPH should be interpreted with great caution not only because of the potential for a confounded association but also in light of the firmly established negative impacts that smoking has on both the mother and the fetus (170, 172). Exposure to cigarette smoke in pregnancy (both through smoking and passive exposure) has been associated with increased risk of low birthweight, fetal distress and stillbirth (173, 174). There is also strong evidence that in-utero exposure to smoking can have health implications for the child through infancy and longer-term (175).

It should be noted that no study in the systematic review, or in a further search of the literature, that investigated paternal or partner smoking status and risk of PPH could be identified. Given that partner smoking has been associated with a similar range of negative outcomes to maternal smoking (including higher risk of low birthweight, congenital anomaly and stillbirth birth (176, 177), its impact on PPH should be considered as an area for future investigation.

5.3.1.5 Socioeconomic status

Socioeconomic status was variably associated with PPH in the six studies included in the systematic review that examined this factor. Most studies that examined this risk factor found a significant association with PPH after adjustment for other factors, but the direction of the association was inconsistent. Four LRoB studies explored socioeconomic status, variably defined, and PPH with three reporting that lower socioeconomic status was associated with higher risk of PPH but one reporting that higher socioeconomic status was associated with higher risk of PPH. Maternal socioeconomic status was not associated with PPH in any of the multivariable analyses in either the UKMidSS or Aberdeen studies.

It is likely that the different measurements of socioeconomic status (income, area of residence, employment) used across studies have an impact on the association between this risk factor and PPH, which makes it difficult to generalise about the relationship between socioeconomic status and PPH.

This is compounded by the fact that the association between socioeconomic status and health outcomes will differ according to an array of social and environmental factors. However, the relationship between low socioeconomic status and poor maternal outcomes in general is well documented and has been linked with numerous mediating factors such as obesity, psychological stress, environmental hazards including smoking and pollution, and a lack of access to adequate healthcare and social services (178, 179) Therefore, despite the uncertainty around the relationship between socioeconomic status and PPH in this thesis research, this factor should be considered as an important contextual factor in the assessment and development of healthcare policy and practice to address PPH.

5.3.1.6 Maternal education

Maternal education is often used as a proxy for socio-economic status, as level of education is often correlated with income, occupation and other measures of socioeconomic status (180). However, unlike more direct measures of socioeconomic status, education was not found to be a risk factor for PPH by any of the five studies investigating it that were included in the systematic review. Data about maternal education was not available for either the UKMidSS or the Aberdeen studies so it was not possible to investigate this factor in these studies.

5.3.1.7 Civil status

Civil or marital status, i.e. whether a woman was single, married or cohabitating, was examined by five studies included in the systematic review. No studies found a significant association with PPH after adjustment for other factors. Marital status was examined in the Aberdeen study and, again, no significant association was observed after adjustment for confounding factors for any of the analyses. Marital status is therefore not considered to be independently associated with PPH.

5.3.1.8 *Maternal insurance status*

A woman's insurance status may influence her engagement with and access to healthcare both pre-pregnancy and throughout the antenatal period (181, 182). It is therefore possible that this has a bearing on maternal outcomes, including PPH. Five LRoB studies included in the systematic review examined the relationship between insurance status and PPH but with only two studies reporting a significant effect that the multivariable level, it is unclear whether this factor is independently associated with PPH. Given the different definitions/categorisations and the different significance of insurance status across contexts, it is difficult to make generalisations about this variable based on the findings of the systematic review. This factor was not explored in either the UKMidSS or Aberdeen studies.

5.3.2 Medical factors

5.3.2.1 *Hypertensive disorders*

Hypertensive disorders, including pre-pregnancy and gestational hypertension, were associated with higher odds of PPH in most of the studies included in the systematic review that investigated this risk factor. There was a range of categories for this risk factor (for example some studies examined all hypertensive disorders combined, while others differentiated between essential hypertension, gestational and pre-eclampsia) but overall hypertensive disorders were associated with a higher risk of PPH and SPPH, after adjustment for confounding factors.

In the Aberdeen study, the association between PPH and hypertensive disorders varied by mode of birth. Gestational hypertension increased the risk of PPH and SPPH among women who gave birth vaginally, by 35% and 58%, respectively. Among vaginal births, pre-eclampsia/eclampsia was associated with an almost 50% increase in the odds of PPH and more than twice the odds of SPPH. Contrastingly, gestational hypertension and pre-eclampsia/eclampsia appeared to be protective for women who had a caesarean birth. This finding was unexpected, particularly in light of the fact that the occurrence of labour prior to the caesarean was adjusted for in the multivariable analysis. This

indicates that the apparent protective effect of hypertension is unlikely to be driven by the increased likelihood of a planned caesarean among women with hypertensive disorders.

This finding stands in contrast to the association reported in other studies included in the systematic review, which tended to report either no association or an increased risk of PPH among women with hypertension. However, many of the studies that reported no association between hypertension and PPH included both vaginal births and caesarean births in the same analysis. Given that the Aberdeen study found that hypertension was associated with increased odds of PPH in vaginal births but decreased odds in caesarean births, it is possible that other studies that combined the birth methods in the analyses obscured the differential effect of the factor between the birth modes. It is also possible that the apparently anomalous effect observed in the Aberdeen study is a result of residual confounding. Further research is warranted to understand the potential confounding factors or causal contribution of hypertensive disorders in reducing the odds of PPH and SPPH among women who have caesarean births.

5.3.2.2 Diabetes

An independent association between diabetes and PPH was not supported by the findings of the systematic review. Among 14 LRoB studies, a minority of LRoB analyses (15%) reported a significant association between diabetes and PPH/SPPH and these results were in conflicting directions. Two LRoB analyses reported increased odds of PPH among women with diabetes while one reported a marginally protective effect.

In the Aberdeen study, diabetes was associated with a small increase in the odds of PPH and SPPH for both vaginal and caesarean births at the univariable level. However the association was attenuated when confounding factors were added into the model. Diabetes was not significant at the multivariable level for either vaginal or caesarean births.

With only two studies reporting diabetes as a risk factor for PPH in the systematic review and with the association not supported by the findings of the Aberdeen study, it is possible that the association observed in the two studies is product of residual confounding.

5.3.2.3 Maternal weight

The relationship between maternal weight/obesity and PPH was rated as 'unclear' based on the findings of 20 studies included in the systematic review. A minority (20%) of LRoB analyses found a significant association between BMI/obesity and PPH at the multivariable level. Three of fourteen LRoB studies found that higher BMI was associated with higher odds of PPH/SPPH, after adjustment for confounding factors. One study reported weight in kilograms, rather than BMI and found that odds of PPH increased with increasing weight.

In the Aberdeen study, among women who had vaginal births, higher BMI was associated with higher odds of PPH but not of SPPH, in both the analysis of all women and of low-risk women. It is possible that this finding is associated with women who have higher BMIs having higher blood volumes, which may contribute to greater initial blood loss but not necessarily be associated with either natural cessation of blood loss or response to treatment of PPH. Given the increasing proportion of women with high BMIs giving birth, as demonstrated in the Aberdeen study and other research (183), further research into the association between BMI and PPH is warranted.

5.3.2.4 Anaemia

The systematic review provided inconclusive evidence about the association between anaemia or haematocrit/haemoglobin levels and PPH. With five (42%) of 12 LRoB analyses reporting increased risk of PPH among women with anaemia or lower levels of haemoglobin or haematocrit, this risk factor was rated as 'unclear'. The magnitude of effect was relatively large for this risk factor, with odds of SPPH increasing three- to four-fold among women with anaemia/low haemoglobin compared with

those without. The heterogeneity of measures of this risk factor make it difficult to make generalisations across studies.

It was not possible to analyse anaemia as a risk factor in the Aberdeen study due to data availability issues. However, anaemia has been independently associated with PPH in other recent research (184) including a recent systematic review, which concluded that severe prenatal anaemia was associated with increased risk of PPH, although mild and moderate anaemia were not (16). In light of this and the findings of 42% of LRoB analyses in the systematic review reporting a significant association at the multivariable level, anaemia should be considered a possible risk factor for PPH.

5.3.3 Obstetric history

5.3.3.1 Previous PPH

The results of the systematic review indicated that previous PPH is very likely to be an independent risk factor for PPH. Eight studies examined the association between previous PPH and subsequent PPH, with five of six LRoB studies finding an increased risk of PPH at the multivariable level. The magnitude of the effect was higher for this risk factor compared with others explored in the systematic review, with aOR ranging from 2.75 to 8.97. Given that previous PPH is a well-established risk factor for PPH, it was striking that only eight of 53 studies in the systematic review investigated this risk factor. While there is a sizeable body of research investigating previous PPH as a risk factor for subsequent PPH (much of which was not eligible for inclusion in the systematic review because of the study design), it is notable that among this large group of studies, mostly exploring numerous risk factors, only a small number investigated this well-established and highly relevant risk factor. This is potentially a product of the data that is available from routine clinical records and routinely collected data, which served as the source of data in most studies. However, by contrast, previous caesarean birth was investigated by 19 studies. It is notable that this element of obstetric history was available and of interest in more than twice as many studies in the systematic review.

If the relatively limited investigation of previous PPH is a reflection of its availability in clinical records, the findings of this review suggest that these information gaps need to be addressed urgently. The accurate recording of a woman's obstetric history, including any previous PPH as well as the cause and treatment, is vital for identifying women who are at increased risk of PPH and represents an important component of providing counselling about planned place of birth. A New Zealand review of severe maternal morbidity caused by haemorrhage identified 'failure to assess women's risk of PPH in light of previous PPH' as a critical factor in a significant proportion of preventable cases of maternal morbidity (28). An Australian audit of medical records found that previous PPH was under-reported in current pregnancy records by almost 50%, with rates of incomplete history being higher for women who give birth at a different hospital to their first birth (7). The authors concluded that rates of recurrent PPH are likely to be higher than previous studies have estimated, based on the under-reporting of previous PPH in medical records. The extent to which this finding might hold true for the studies included in the systematic review and other research on the risk of PPH is unclear.

In the Aberdeen study, previous PPH was associated with double the odds of PPH and SPPH among women who had vaginal births, after adjusting for confounding factors. Among women who had caesarean births, previous PPH was associated with a 50% increase in the odds of PPH at the multivariable level, however, no significant association with SPPH was observed. In the Grampian region, there is limited migration and thus the vast majority of women who have one birth in Aberdeen will have any subsequent births in Aberdeen (149), meaning that obstetric history is generally reliably recorded in this database.

Recurrent PPH is well established and the risk appears to maintain even after the adjustment for shared maternal characteristics between births (130). While, the risk of PPH by one cause confers high subsequent risk of PPH of the same cause, the risk of a subsequent PPH by any cause is also significantly increased (130, 185). This suggests there is an underlying shared pathology between the

different causes of PPH. However, it was not possible to explore previous cause of PPH in the Aberdeen study. Similarly, studies included in the systematic review did not distinguish between causes of previous PPH and risk of subsequent PPH.

5.3.3.2 Previous caesarean birth

Previous caesarean was found to be variably associated with PPH in the systematic review. This risk factor was investigated by 19 studies, only four of which reported a significant association after adjustment. The direction of the association was also inconsistent, with evidence for both increased risk of PPH in women with a previous caesarean and a protective effect of a previous caesarean. It was difficult to compare the results of these studies because there was a high degree of heterogeneity in terms of inclusion criteria and how previous caesarean was categorised. For example, some studies analysed risk of previous caesarean separately for vaginal births and caesareans while other studies included all modes of birth together. Overall, the evidence rating for this risk factor was 'unclear'.

In the Aberdeen study, previous caesarean was associated with higher risk of PPH and SPPH in a subsequent vaginal birth but a lower risk of PPH and SPPH in a subsequent caesarean birth. After adjusting for confounding factors, previous caesarean was associated with approximately 50% higher odds of PPH and SPPH among women who had vaginal births. Vaginal birth after caesarean (VBAC) has been associated with increased risk of uterine rupture, which can lead to significant blood loss. However, as uterine rupture is rare, occurring in less than 1% of VBACs (186, 187), this association is not likely to drive the increased odds observed in the Aberdeen study.

The association between previous caesarean and PPH was not supported by most studies included in the systematic review and while the high degree of heterogeneity in the study makes it difficult to generalise, previous research investigating outcomes of VBAC suggest that the risk of adverse outcomes for women, including PPH, are low (188). It is possible that the non-significant association

between previous caesarean and subsequent PPH is partially related to many studies analysing vaginal and caesarean births together, which may mask the potentially differential effect of previous caesarean by mode of birth. Future research investigating this risk factor should separate analyses by mode of birth to enable a more thorough investigation of the effect of previous caesarean on subsequent PPH.

Any association between previous caesarean and PPH is potentially a product of increased risk of placental invasion at the site of uterine scarring, which can contribute to higher levels of blood loss (189). A similar mechanism is implicated in the association between previous uterine surgery and PPH (190), discussed below.

5.3.3.3 Previous uterine surgery

Previous uterine surgery was also rated as an 'unclear' risk factor in the systematic review. Seven studies, six of which were LRoB, investigated this risk factor and only one LRoB study found a significant association at the multivariable level. The one HRoB study also reported a significant association with previous uterine surgery being associated with double the odds of SPPH, although the HRoB rating and the fact that no confidence interval was provided, mean these results should be interpreted with caution. Overall, the evidence for this risk factor was rated as 'unclear'. Information about previous uterine surgery was not available for either of the primary studies carried out for this thesis.

Given the increasing rates of myomectomy and caesarean birth (191), future research clarifying the association between these risk factors and PPH is warranted.

5.3.4 Pregnancy factors

5.3.4.1 Parity

Based on the 36 studies that investigated parity in the systematic review, it remains 'unclear' whether parity is independently associated with PPH. Most studies that investigated parity and PPH found no significant association at the multivariable level. Nulliparity is often cited as a risk factor for PPH (35, 83), and indeed of the 11 LRoB analyses that found a significant association, 10 reported higher odds of PPH in nulliparous women. However, one study (109) found that women who had given birth before had 66% higher odds of PPH than nulliparous women, after adjusting for confounding factors. The magnitude of effect was similar across studies that reported higher odds of PPH among primiparous women, with most studies reporting a small increase (around 50%) although one study reported a four-fold increase.

In the Aberdeen study, the relationship between parity and PPH differed by mode of birth. Among women who had vaginal births, nulliparity was associated with double the odds of PPH and SPPH, compared with women who had 2-4 previous births. For women who had one previous birth, the risk of PPH and SPPH increased approximately 20%, although the association was not statistically significant for the SPPH analyses. By contrast, primiparous women who had a caesarean were 50% less likely to have a SPPH, compared with women who had given birth 2-4 times before. Women who had given birth once before were slightly more likely (10%) to have a PPH although this association did not hold for SPPH.

It is possible that the differential effect of parity on PPH by mode of birth is masked in some of the studies included in the systematic review because vaginal births and caesarean births were analysed together in most studies. While the LRoB studies adjusted for confounding variables, including mode of birth, no study reported interaction terms for the effect of mode of birth. The only study in the systematic review (132) that reported odds of PPH for vaginal and caesarean birth separately found higher odds of PPH in nulliparous women giving birth vaginally but reported no association for parity

among women who had caesarean births. However, the potential masking effect of combining modes of birth in analyses cannot completely explain the variability in results for this risk factor because, of 11 studies that included only vaginal births, just two reported a significant effect of parity at the multivariable level.

The relationship between parity and PPH is clearly complex and is likely mediated by other maternal, medical and intrapartum factors. With more than one third of analyses of nulliparity and PPH in the systematic review reporting that nulliparous women have higher odds of PPH, after adjustment for confounding factors, nulliparity should be considered a possible risk factor for PPH. Future research investigating the potential interaction between parity and mode of birth is warranted.

5.3.4.2 Gravidity

While parity and gravidity are clearly correlated, gravidity was rated as 'Not a risk factor' in the systematic review as none of the five studies that investigated this factor reported a significant association at the adjusted level. Gravidity was not explored as a risk factor in the two studies reported in this thesis.

5.3.4.3 Gestational age

The results of the systematic review were equivocal in terms of the relationship between gestational age and PPH. With only a minority (36%) of LRoB analyses reporting a significant association after adjustment for confounding factors, it is 'unclear' whether gestational age is independently associated with PPH. Of the 28 LRoB analyses, five reported that later gestational age was associated with higher odds of PPH, three reported higher odds with earlier gestational age and three reported both earlier and later gestation was associated with higher odds, compared with birth at term. This may suggest the true association between gestational age and PPH is J-shaped, although there was not strong enough evidence of an association to draw conclusions.

The results of the Aberdeen study also suggested a potentially J-shaped association between gestational age with pre-term and post-term births both being associated with increased odds of PPH and SPPH, compared with births at term, regardless of mode of birth. It is likely that the association between gestation and PPH is partially mediated by pregnancy and birth complications that are more prevalent among pre-term births, including placental abnormalities, retained placenta and infection (192, 193), that were not able to be accounted for in the Aberdeen study.

Although the association between post-term birth and PPH has been widely reported in other literature (194, 195), the causal mechanism underlying this association is not well understood. A UK-based study observed reduced uterine contractility among post-date pregnancies, compared with term pregnancies, after adjustment for other factors (196), which may contribute to an increased risk of atonic PPH. A population-based cohort study of births in Sweden and California, USA similarly found that gestational age of 41- 42 weeks was associated with increased risk of PPH, with the association between risk of PPH and gestational age varying by aetiology of PPH (197). Further research is needed to elucidate the biological mechanism behind the association between advanced gestational age and PPH.

5.3.4.4 Multiple pregnancy

Multiple pregnancy was considered a 'very likely' risk factor for PPH, with the vast majority of studies that investigated this factor in the systematic review finding it to be associate with significantly increased risk of PPH, after controlling for confounding factors. The magnitude of effect for this risk factor was generally higher than for other risk factors investigated in the systematic review.

In the Aberdeen study, multiple pregnancy was associated with two to three times the odds of PPH and SPPH, compared with singleton pregnancies, among women who had vaginal births as well as those who had caesarean births. Consistent with other findings presented here, the aOR for SPPH was

higher than for PPH, among both vaginal births and caesareans. The proportion of women giving birth to multiple babies was small, although higher among women who gave birth via caesarean (2.5% of controls and 4.7% of PPH cases) compared with vaginally (0.9% of controls and 2.0% of PPH cases).

Multiple pregnancy has been consistently associated with PPH and SPPH among both caesarean and vaginal births in previous research (78, 198, 199). The findings of this thesis support this association. It is thought that the increased risk of PPH among multiple births is driven by overdistention of the uterus, which can contribute to uterine atony (138). Several physiological adaptations take place to support multiple gestation, including markedly higher increase in blood volume compared to singleton pregnancies and increased cardiac output, which may contribute to higher volumes of postpartum blood loss (200).

5.3.4.5 Placenta praevia

Placenta praevia is a condition in which the placenta partially or completely covers the cervix. This can lead to increased vascularity and can reduce uterine contractility, contributing to high volumes of blood loss following placental separation (201). Placenta praevia was rated as 'very likely' to be a risk factor for PPH/SPPH in the systematic review. Most LRoB studies and all four HRoB studies that investigated the association reported increased odds of PPH among women with placenta praevia. The magnitude of the effect was generally much larger than or other risk factors, ranging from 2.88 to 10.9 for PPH and from 1.93 to 17.1 for SPPH. This reflects the findings observed in other literature investigating this association. A systematic review of the rates of PPH among women with placenta praevia reported that rates of PPH were four times higher than among all women (202). Based on the consistency of evidence presented in the systematic review and the alignment of these findings with other literature, placenta praevia should be considered a key risk factor for PPH.

5.3.4.6 Uterine fibroids

The association between uterine fibroids and PPH was variably reported by studies included in the systematic review. Of the seven LRoB analyses of uterine fibroids and PPH, only one reported a significant association at the multivariable level, with a small magnitude of effect. Of six LRoB studies examining SPPH, three studies reported a significant association between uterine fibroids and SPPH, with high magnitudes of effect (OR ranging from 2 to 11). One HRoB study also reported double the odds of PPH among women with uterine fibroids, however the high risk of bias and no confidence interval for this statistic undermine the reliability of this finding.

Given that a greater proportion of studies investigating SPPH and uterine fibroids reported a significant association compared with PPH, it is possible that uterine fibroids are a risk factor for SPPH but not for PPH. This is supported by the finding that the only two studies that investigated the association between uterine fibroids and both PPH and SPPH reported a significant association for SPPH but not for PPH. While comparing results across studies is difficult due to the high degree of heterogeneity, comparing the association reported within studies is more appropriate because the difference in association between outcomes is not a product of different methods, statistical approaches or underlying populations. However, considering the relatively small number of studies that investigated both PPH and SPPH in the review, it is difficult to draw conclusions based on these findings. It is possible that uterine fibroids impair uterine contractibility and contribute to increased blood loss, however the mechanism underlying the association is not well understood (203).

5.3.4.7 Chorioamnionitis

Chorioamnionitis is an infection of the fetal membranes and the amniotic fluid, and it can lead to inflammation and reduce uterine contractility, which may contribute to PPH (204). As five of the 10 LRoB studies that investigated this risk factor reported higher odds of PPH/SPPH among women with chorioamnionitis, after adjustment for confounding factors, chorioamnionitis was considered a 'likely' risk factor for PPH in the systematic review. The magnitude of effect was small to moderate across

studies that found a significant association. Chorioamnionitis was not included in the Aberdeen analyses, due to data availability issues. Chorioamnionitis is associated with raised temperature in labour (204), which was also rates as a likely risk factor for PPH based on the evidence from the systematic review.

5.3.4.8 Placental abruption

Based on the results of the systematic review, it is 'unclear' whether placental abruption is a risk factor for PPH. Twelve studies investigated the potential association, with only four reporting a significant adjusted association. Overall, it was therefore unclear whether placental abruption is a risk factor for PPH and this risk factor was not investigated in either of the studies reported in this thesis.

It is possible that a lack of significant effect in some of the studies in the systematic review is a product of low statistical power to detect an effect of an uncommon risk factor in small study populations. The LRoB studies that did not report a significant effect at the multivariable level were all relatively small (ranging from N=786 to N=56,394) while those that reported a significant association were all large (ranging from N=364,701 to 55,140,088). The prevalence of placental abruption was estimated in a systematic review to be 0.4-1.0% of pregnancies (205), meaning smaller case-control studies such as those included in the systematic review, may not be best placed to identify the association with PPH. A cohort study examining outcomes of placental abruption in over 57,000 births in France reported that postpartum haemorrhage was more than twice as prevalent in women with placental abruption (12.2%) compared with those without (5.5%) (206). Placental abruption has also been associated with increased risk of blood transfusion (207) and severe maternal morbidity related to haemorrhage (28). Therefore, despite the equivocal results reported in the systematic review, placental abruption should be considered a risk factor for PPH.

5.3.4.9 Assisted conception

Assisted conception was rated as a 'likely' risk factor in the systematic review. Eight studies investigated this risk factor, defined variably, with four reporting increased odds of PPH/SPPH, after adjusting for confounding factors. Assisted conception was not investigated in either of the primary studies reported in this thesis.

The findings of the systematic review align with other literature on assisted conception. A recent study examining risk factors for PPH, eligible for inclusion in the systematic review but published after the search date, reported that the odds of PPH more than doubled among women who used ART (aOR=2.66; 95% CI 1.77-3.88) (208). A meta-analysis of studies examining assisted conception and maternal outcomes reported an increased risk of PPH among women who conceived through in vitro fertilization or intracytoplasmic sperm injection (RR 1.29, 95% CI 1.06–1.57). However only two studies were included in this meta-analysis and the authors noted substantial heterogeneity among the studies (I^2 = 65%) (209). Assisted conception is associated with increased risk of a range of poor maternal (209) and perinatal outcomes (210, 211). It is possible that the association between assisted conception and PPH is driven by increased risk of placenta praevia in pregnancies that results from IVF (212, 213). It is also possible that the mechanical placement of embryos causes the release of prostaglandin, which may contribute to uterine contractility (214). The mechanisms behind the association are not well understated and indeed several mechanisms may drive this association. Given the increasing proportion of pregnancies resulting from assisted conception in high-income countries (215), further research into this mechanism is important.

5.3.4.10 Polyhydramnios

Based on the eight studies that examined polyhydramnios in the systematic review, it was 'unclear' whether polyhydramnios is an independent risk factor for PPH. Three LRoB studies reported an increased risk of PPH, all with small magnitudes of effect (aOR ranging from 1.15 to 1.47).

Polyhydramnios is characterised by an abnormal increase in the volume of amniotic fluid during pregnancy and has been linked to higher rates of perinatal morbidity and mortality (216). While the mechanism driving this association is not well understood, it is thought that polyhydramnios may lead to uterine overdistention, which can limit the ability of the uterus to contract sufficiently after the birth.

5.3.4.11 Antepartum haemorrhage

Antepartum haemorrhage (APH) was rated as a very likely risk factor for PPH based on eight studies in the systematic review that examined this factor. Two of the three LRoB studies that investigated this risk factor found that APH increased the risk of PPH while the third reported no association at the multivariable level. Three of the four LRoB studies that investigated APH and SPPH reported higher odds of PPH among women with APH, compared with those without. Four of seven LRoB studies reported higher odds of PPH/SPPH associated with APH.

This finding aligns with previous literature as well as the findings of related variables in this systematic review, namely placenta praevia, which was also rated as a 'very likely' risk factor and is a cause of APH. Placental abruption is also a cause of APH and has previously been associated with increased risk of PPH, though the rating for that risk factor in this review was 'unclear'.

5.3.5 Labour factors

5.3.5.1 Induction of labour

Induction of labour was rated as a 'likely' risk factor based on the results of 40 studies included in the systematic review. Most LRoB studies reported that induction of labour was associated with higher odds of PPH/SPPH, after adjustment for confounding factors. Most studies that investigated this risk factor compared any induction to spontaneous labour, with only a minority reporting on specific method of induction. The most commonly examined of these was oxytocin for induction of labour, of which four of six studies found an increased risk of PPH/SPPH, compared with no oxytocin.

In the Aberdeen study, induction of labour was similarly significantly associated with PPH and SPPH among women who had vaginal births and those that had caesareans. The study examined the number of methods of induction finding that odds of PPH and SPPH were even higher when two or more methods of induction had been used. However, it was not possible to determine whether this association was driven by the effects of combining induction methods or by the indication for multiple methods of induction.

The association between induction of labour and PPH is well established in both observational and experimental research (78, 105, 217). One potential mechanism that has been proposed to drive the association is the over-exposure to oxytocin during labour (through induction or augmentation) leading to desensitisation of oxytocin receptors and potentially compromising the effectiveness of oxytocin in promoting uterine contractility after delivery (218). However, methods of induction other than oxytocin have also been associated with increased risk of PPH (105). Several observational and experimental studies have explored the association between different methods of induction and PPH, but no significant difference in blood loss between mode of induction has been reported (219, 220).

5.3.5.2 Augmentation of labour

The results of the systematic review were inconclusive in terms of the relationship between augmentation of labour and PPH. Nine of 22 LRoB analysis of augmentation of labour reported increased risk of PPH, after adjustment for confounding factors. Oxytocin was the most commonly investigated specific method of augmentation, with a minority of these studies reporting a significant association at the multivariable level.

Among women who had vaginal births, augmentation of labour was associated with moderately higher (25-50%) odds of PPH and SPPH in the Aberdeen study. This was consistent across all women

and low-risk women and is congruent with previous research. Due to lack of data availability, it was not possible to analyse the association by method of labour augmentation in this study. It is unclear whether the association observed was driven by particular methods of augmentation or whether it may be associated with the indication for augmentation.

In the Aberdeen study, augmentation was not investigated as a potential risk factor for PPH among women who had a caesarean birth. This decision was made because for women who had a caesarean birth after the onset of labour, it was not possible to determine at which stage of labour, or after what duration, the woman's birth occurred. It was therefore not possible to distinguish women who had no labour augmentation because it was not indicated, from those women who had no augmentation because they had already been transferred for caesarean. This would have made any potential association between augmentation of labour and PPH or SPPH potentially misleading.

Previous research has suggested that oxytocin use for augmentation is associated with PPH (218). As with induction of labour, it is thought that exposure to excessive oxytocin in labour through augmentation may downregulate myometrial oxytocin receptors during the third stage of labour impairing the ability of the uterus to contract (218, 221).

5.3.5.3 Pre-labour rupture of membranes

The evidence for an independent association between pre-labour rupture of membranes (PROM) was equivocal in the systematic review. Twelve studies investigated the risk factor, with a variety of definitions used, and only one reported a significant association at the multivariable level. A recent case control study examining risk factors for poor uterine contractility also reported no associated between PROM and postpartum haemorrhage (221). Given the relatively limited evidence for PROM being independently associated with PPH, this factor was not considered appropriate for investigation in the Aberdeen or UKMidSS studies.

5.3.5.4 Analgesia/anaesthesia

The use of anaesthesia and analgesia were variably associated with PPH across studies included in the systematic review. Twenty-three studies explored epidural use and PPH and several reported an association at the univariable level, generally reporting higher odds of PPH associated with epidural. However, the three studies that reported an aOR all identified a protective effect of epidural use. General anaesthesia was investigated by three LRoB studies and the association was also unclear with only one reporting a significant association at the multivariable level. With a minority of studies reporting a significant association between anaesthesia/analgesia use and PPH, this risk factor was rated as 'unclear'.

In the Aberdeen study, it was not possible to determine the timing of the administration of anaesthesia/analgesia in relation to the birth so it was not possible to include this variable in the analysis. Epidural analgesia has been associated with increased duration of the second stage of labour, which is considered a likely risk factor for PPH (222).

A recent case-control study in Israel investigating blood transfusion reported a positive association between general anaesthesia and overall blood transfusion rate, however, this was only significant at the univariable level (223). It is likely that the indications for general anaesthesia play an important role in the relationship between this risk factor and PPH, however, none of the studies included in the systematic review reported on indications for general anaesthesia.

5.3.5.5 Maternal intrapartum pyrexia

Intrapartum fever or maternal pyrexia was rated as 'very likely' to be a risk factor for PPH with five of the six LRoB studies that examined this risk factor finding higher odds of PPH/SPPH, compared with no fever, at the multivariable level. The magnitude of the effect was moderate to very large, ranging from aOR 1.6 to 5.26. Data were not available to investigate the association between maternal pyrexia and PPH in the Aberdeen study.

Maternal pyrexia in labour can be a sign of chorioamnionitis, which is considered a 'likely' risk factor for PPH. Raised temperature in labour has also been associated with the use of epidural analgesia (224), which has been variably associated with PPH, as identified in the systematic review.

5.3.5.6 Overall duration of all labour

The evidence for an independent association between duration of all labour and PPH was inconclusive based on studies included in the systematic review. Fifteen studies examined duration of labour using a variety of definitions and categories to assess this risk factor, including categories based on number of hours and the assessment of 'prolonged labour' or 'obstructed labour'. Nine studies were considered LRoB and the majority of these did not report a statistically significant association between duration of labour and PPH/SPPH. The four LRoB studies that reported a statistically significant association found increased odds of PPH among women with a longer duration of labour compared with shorter durations.

The high degree of heterogeneity in terms of definitions and assessment of duration of labour makes it difficult to draw conclusions about the potential association between overall duration of labour and PPH. Furthermore, the absence of a universally accepted definition to determine the precise onset of the first stage of labour, coupled with variations in symptoms experienced by women during labour initiation, presents challenges in accurately measuring the overall duration (225). As a result, data concerning this risk factor should be interpreted with caution.

5.3.5.7 Duration of first stage of labour

The association between duration of first stage of labour and PPH was inconsistent across studies in the systematic review. There was a high degree of heterogeneity in terms of definitions and categories used to assess the association. Studies that did report a significant association found that longer first stage of labour was associated with higher odds of PPH, however, only 40% of LRoB analysis reported a significant association after adjustment for confounding factors so it was 'unclear' whether duration

is first stage is independently associated with PPH. As with the duration of all labour, described above, differences in the assessment of the start of labour make comparisons between studies challenging (225).

In the Aberdeen study, prolonged first stage of labour was found to be an independent risk factor for PPH among women who had a vaginal birth, but not SPPH and not among women who had caesarean births. The analysis of all women who had a vaginal birth was the largest population in this study and therefore had the greatest power to detect associations with statistical significance. Given the large number of variables in this analysis, it is also possible that the observed association is the result of chance or the influence of unmeasured variables. With 40% of LRoB analyses reporting a significant association between longer duration of first stage of labour and PPH, further investigation into this risk factor is warranted.

5.3.5.8 Duration of second stage of labour

Duration of the second stage of labour was rated 'very likely' to be independently associated with PPH, based on the 20 studies that examined this risk factor in the systematic review. Most (72%) of the LRoB analyses that investigated this risk factor reported a significant association at the multivariable level. While a range of definitions and categories were used to investigate this risk factor, the general trend across all significant results was that longer duration, however defined, was associated with increased odds of PPH. Similarly, in the Aberdeen study, possibly prolonged second stage of labour was significantly associated with PPH and SPPH among women who had vaginal births.

The different definitions of this variable between studies and the complex relationship between other intrapartum factors and labour duration make it difficult to draw conclusions about the length of second stage of labour before the risk for PPH is expected to increase. The expected duration of second stage of labour (before it would be considered possibly prolonged) is also influenced by whether a woman has given birth previously, with women who have given birth before generally

having shorter a second stage of labour than women giving birth for the first time (146). Other factors such as whether or not a woman had induced or augmented labour may influence how long the second stage goes on before the risk of PPH begins to increase (226). As the association is thought to be driven by increased uterine muscle fatigue contributing to uterine atony (132), clinicians should be aware that a long second stage of labour may increase a woman's risk of PPH.

5.3.5.9 Duration of third stage

The results of the systematic review supported the well-established association between prolonged third stage of labour and increased risk of PPH. With six of the seven studies reporting a significant association, third stage of labour was rated as 'very likely' to be independently associated with PPH. While there was a range of categories used to explore this variable, the general trend of longer third stage of labour being associated with higher odds of PPH was demonstrated in all significant analyses. The most common category analysed was third stage of labour lasting longer than 30 minutes, which was reported by four studies and was consistently associated with higher odds of PPH compared with shorter durations, with large magnitudes of effect (aOR ranging from 2.6 to 10.9).

It is notable that among a large group of studies investigating multiple risk factors, only eight explored the association between duration of third stage and PPH and no studies explored the association between third stage duration and SPPH. This is particularly striking in light of the fact that 20 studies explored the relationship between duration of second stage and PPH, although again none of the studies examining SPPH explored second stage duration. It is unclear why information on duration of second stage of labour would be available and/or of interest for investigation more frequently than duration of third stage. Given that duration of third stage of labour is widely acknowledged to be an important risk factor for PPH (35, 43, 44), this finding was unexpected.

In the Aberdeen study, a third stage of labour lasting 30 minutes or more was associated with more than four times the odds of PPH and nearly seven times the odds of SPPH, after adjustment for confounding factors. This aligns with the generally large magnitude of effect seen in studies in the systematic review that examined third stage lasting longer than 30 minutes. A prolonged third stage of labour can contribute to postpartum blood loss due to prolonged bleeding from the placental site and from unrepaired perineal trauma (33). The optimum duration of third stage of labour is difficult to assess, given a number of intrapartum factors as well as the impact of planned management of the third stage. A case-control study examining the impact of length of uncomplicated third stage of labour in Israel found a third stage longer than 30 minutes increased the risk of blood transfusion by three-fold and concluded that a third stage lasting longer than 17 minutes was associated with an increased risk of blood transfusion (227). The study, however, excluded women whose third stage of labour lasted longer than 60 minutes. The NICE intrapartum care guideline (146) suggests that a third stage of labour should be diagnosed as prolonged if it lasts longer than 30 minutes in active management, or longer than 60 minutes of physiological management. While it is beyond the scope of this thesis to suggest an optimum duration of third stage of labour, the findings presented here highlight the importance of increasing vigilance by clinicians with increasing duration of the third stage of labour.

5.3.5.10 Third stage management

Appropriate management of the third stage of labour is widely recognised as an important component of minimising postpartum blood loss (84). Various methods of third stage management were analysed by five studies in the systematic review, with most LRoB analyses finding a significant association after adjustment for other factors. There was a high degree of heterogeneity terms of the method of third stage management that was examined, rendering generalisations about this risk factor based on the systematic review inappropriate.

In the UKMidSS study, data were collected about the administration of Syntocinon or Syntometrine as part of active management of the third stage of labour, however, it was not possible to determine the chronology of administration in relation to blood loss; that is, whether administration was part of planned active management or whether it was indicated for management of a high volume of blood loss. As a consequence, this variable was not included in the multivariable analysis, despite its significance in the univariable analysis, because of problems with interpreting any apparent association between the administration of Syntocinon or Syntometrine and PPH. For similar reasons, data on administration of oxytocin in the third stage of labour were not included in the Aberdeen analysis. The difficulty of determining the timing of and indication for administration of drugs in the third stage of labour in observational research may explain why only a small number of studies in the systematic review examined this risk factor, despite its well-established association with PPH. A Cochrane systematic review including 20 randomised or quasi-randomised trials found that active management of the third stage of labour using prophylactic oxytocin was more effective in preventing high volumes of blood loss and the need for transfusion than expectant management (85). While the evidence for the association between third stage management and PPH presented in this thesis research is limited, the general trend appears to align with other previous research and supports the emphasis on active third stage management in current clinical guidelines for the prevention and management of PPH (84).

5.3.6 Birth factors

5.3.6.1 Caesarean birth

The results of the systematic review were inconclusive in terms of whether caesarean birth is a risk factor for PPH. While most studies that analysed caesarean birth reported a significant association, results were in conflicting directions. Seven LRoB analyses found caesarean (a mix of planned and unplanned) to be associated with increased odds of PPH/SPPH, however, five reported a protective effect of planned caesarean and one reported a protective effect of emergency caesarean, compared with vaginal birth. Caesarean was therefore rated as ‘unclear’ as a risk factor for PPH/SPPH.

In the Aberdeen study, caesarean births were analysed separately from vaginal births and a multivariable analysis investigating the odds of PPH associated with caesarean birth was not conducted. However, the incidence of PPH and SPPH was markedly (six-fold) higher among women who had a caesarean birth, compared with women who had a vaginal birth. This trend was consistent across the 31-year study period. Although of note, this finding may be partially explained by the different methods of blood loss measurement between the two birth modes in Aberdeen Maternity Hospital.

The higher incidence of PPH among caesarean births, compared with vaginal births, is likely to be partly driven by the different methods of estimating blood loss between birth modes, with blood loss following caesarean births being measured while blood loss following vaginal birth usually being visually estimated in Aberdeen Maternity Hospital. However, given that the markedly higher incidence was also observed for SPPH, which is calculated among vaginal births, the overall trend likely reflects a true higher incidence of PPH among caesarean births compared with vaginal births.

The relationship between caesarean birth and PPH is likely medicated by a number of interrelated factors, including the indication for caesarean, the occurrence and progression of labour. It is difficult to draw conclusions about the direct effect of caesarean birth across studies that adjusted for these factors variably.

5.3.6.2 Instrumental birth

The findings of the systematic review supported the widely-cited association between instrumental birth and PPH. Instrumental birth was rated as a very likely risk factor for PPH, with the vast majority of LRoB analyses finding higher odds of PPH compared with spontaneous vaginal birth. There was a range of categories analysed, with some studies analysing forceps separately from vacuum extraction and others combining the two procedures. Generally, the magnitude of effect was higher for instrumental birth than for caesarean birth ranging from aOR 1.1 to 6.6.

In the Aberdeen study, instrumental birth was an important risk factor for PPH and SPPH. Compared with spontaneous vaginal birth, women who had an instrumental birth were 2.5 times more likely to have a PPH and three times more likely to have an SPPH, after adjustment for confounding factors. Some caution is needed when interpreting the association between instrumental birth and PPH due to variability in the methods of estimating blood loss between instrumental and non-instrumental vaginal births. As previously described, in the Aberdeen Maternity Hospital, blood loss is calculated for births occurring in theatre (including instrumental births) and visually estimated for births occurring outside of theatre, unless an SPPH is diagnosed. This may have led to the misclassification of cases of PPH as controls being more likely in the non-instrumental birth group. As blood loss for instrumental births at Aberdeen Maternity Hospital is calculated, rather than visually estimated, it is more likely that a higher amount of blood loss would be recorded, compared with births that occurred out of theatre and were therefore visually estimated. However, as the effect observed in this study aligns with the results of previous research, it is considered likely that the association reported in this study reflects a true association between instrumental birth and PPH.

The risk of PPH following an instrumental birth is well-established in the existing literature (35, 46, 68). Trauma to the genital tract caused by the use of instruments may contribute directly to increased volume of blood loss and is discussed below.

5.3.6.3 Genital tract trauma

Genital tract trauma was rated as a 'very likely' risk factor for PPH based on the findings of 31 studies reporting on this factor in the systematic review. A wide range of injuries were included in this category, from lacerations to third and fourth degree perineal tear, as well as cervical tears and high vaginal lacerations and combinations of these. Regardless of the category used, the odds of PPH/SPPH were significantly higher among women with genital tract trauma. Seven studies investigated the risk

of PPH by degree of trauma and six of these reported that a higher degree of trauma was associated with higher odds of PPH. Generally, the magnitude of effect was higher for this risk factor, compared with other included in the systematic review, which aligns with the trend observed in this thesis research of risk factors occurring in closer proximity to the birth being more reliably associated with PPH and at a higher magnitude.

In the Aberdeen study, the odds of PPH and SPPH were significantly higher for women who had a perineal tear, compared with those who did not. Women who had a severe tear (third or fourth degree) has 4.5 times the odds of PPH and 3.2 times the odds of SPPH, compared with those who had lower degree of tearing or episiotomy.

The association between perineal/genital tract trauma and PPH is well documented in the literature, as reflected in the finding of the systematic review. Trauma can be a direct cause of PPH, but also occurs alongside non-pathological blood loss (13, 51, 105, 121) and in a systematic review of the literature on atonic PPH, was found to be associated with increased risk of PPH caused by uterine atony (78) . This supports the investigation of perineal trauma as a risk factor for PPH despite the fact that it can be a direct cause of PPH.

5.3.6.4 Episiotomy

Episiotomy was rated as an 'unclear' risk factor for PPH based on the results of 16 studies in the systematic review that investigated the association. Most studies that investigated episiotomy and PPH reported a higher risk compared with no episiotomy, with moderate effect sizes ranging from aOR of 1.3 to 2.6. However, two studies found episiotomy to be protective, reporting approximately 10% lower odds of PPH. It is unclear why these two studies found associations in the opposite direction from other studies. It is possible that clinical practice around indication for or method of episiotomy differed in the settings of these two studies, which may have contributed to a protective effect (228, 229). It is also possible that this association was due to chance or residual confounding.

The data available in the AMND did not allow for episiotomy to be analysed separately from perineal trauma (the variable was constructed as combined categories), so it was not possible to explore the association of episiotomy in that study.

Episiotomy is a form of genital tract trauma and may contribute directly to increased blood loss at the site of the surgical incision (46). However, a systematic review of selective episiotomy compared with no episiotomy found no increased risk of perineal trauma associated with selective episiotomy (230). Therefore, while there is a plausible mechanism driving the association between episiotomy and PPH, it remains unclear whether this should be considered an independent risk factor for PPH.

5.3.6.5 Presentation

The association between presentation of the baby and PPH was inconsistent in the systematic review, resulting in an 'unclear' rating for this risk factor. Of the ten studies that compared vertex presentation to non-vertex presentations, variably categorised, four reported a significantly higher odds of PPH/SPPH associated with non-vertex presentation. The magnitude of effect varied widely between studies, from a 90% higher odds of PPH among those with a compound presentation to a 12-fold increase for non-cephalic presentation. The latter study was limited to women with placenta praevia, however, and had very wide confidence intervals. Two studies (12, 139) reported a protective effect of breech presentation compared with cephalic presentation, but only one of these adjusted for confounders.

In the Aberdeen study, non-vertex presentation was associated with a moderate increase in the odds of PPH and SPPH among women who had vaginal births (21% and 30% higher odds, respectively). Among women who had a caesarean, non-vertex presentation was not independently associated with PPH but was associated with 14% higher odds of SPPH, after adjustment for confounding factors.

Women with a non-vertex presenting baby are generally considered higher risk because of potential maternal and neonatal morbidity associated with labour and birth in this position (231). This influences the way their birth and labour is managed, which may have implications for the risk of PPH.

5.3.6.6 Retained placenta

The results of the systematic review supported the well-established association between retained placenta and PPH. Ten studies investigated the risk factor with eight being considered LRoB. Six (75%) of eight LRoB studies reported significantly higher odds of PPH among women who had a retained placenta or manual removal of placenta, compared with those who did not. The four studies that did not report multivariable analyses for this variable all reported significant associations at the unadjusted level, including two studies reporting a 30-fold increase in the odds of PPH among those who had a manual removal of placenta. Results from the Aberdeen study concurred with those from the systematic review, with retained placenta being significantly associated with higher odds of PPH and SPPH. The magnitude of the effect was markedly higher for SPPH, compared with PPH, almost 20-fold and almost 6-fold, respectively.

Retained placenta is widely accepted as a key risk factor for PPH and guidelines for the management and prevention of PPH agree that when the placenta is not delivered spontaneously, manual removal of the placenta is indicated (84). Retained placenta has also been associated with a high risk of recurrent retained placenta and associated PPH (130, 185).

5.3.7 Baby characteristics

5.3.7.1 Birthweight

Higher birthweight is a well-established risk factor for PPH and this association was confirmed by the findings of the systematic review, with birthweight rated as ‘very likely’ to be independently associated with PPH. Of the 26 LRoB studies that examined birthweight and PPH, 18 (69%) reported a

significant association, with all reporting higher odds of PPH associated with higher birthweight, after adjusting for confounding factors. Three of eight LRoB analyses of birthweight and SPPH found significant associations, again reporting that higher birthweight was associated with higher odds of PPH.

Similarly, the Aberdeen study identified increasing birthweight associated with higher odds of PPH and SPPH among both vaginal and caesarean births, after adjustment for confounding factors. Low birthweight, less than 3000g, was associated with 15-30% lower odds of PPH and SPPH, compared with birthweights of 3000-3499g. Women who had babies born at 3500-3999g had 31-57% higher odds of PPH and SPPH. Birthweight >4000g was associated with a two- to three-fold increase in odds of PPH and SPPH. Birthweight is correlated with gestational age, however, the increased odds associated with increased birthweight persisted in models that adjusted for gestational age.

Higher birthweight is generally accepted as a risk factor for PPH (35, 46, 78). Increased birthweight is associated with overdistention of the uterus caused by stretching of the uterine fibres, which can contribute to uterine atony (78). Larger babies are also associated with larger placental separation sites, which can contribute to increased blood loss from the placental site(232).

5.3.7.2 Sex

The systematic review identified five studies that examined sex of the baby as a potential risk factor for PPH. While male sex has been associated with higher birthweight and therefore may be associated with increased risk of PPH, no studies in the systematic review found sex to be associated with PPH at the multivariable level. Sex was also not identified as a risk factor in either of the primary studies conducted for this thesis. Sex is therefore not considered likely to be an independent risk factor for PPH.

5.3.7.3 Birth status

Three studies included in the systematic review investigated stillbirth as a risk factor for PPH, with all three reporting a significantly higher risk of PPH among women who had a stillbirth. The magnitude of effect in these studies was moderate to very large, ranging from aOR 1.69 to 7.70. In the Aberdeen study, stillbirth was inconsistently associated with PPH and SPPH across the analyses. Among women who had a vaginal birth, stillbirth was associated with a four-fold increase in the odds of SPPH but was not independently associated with PPH. Similarly, stillbirth was not associated with PPH among low risk-women but was associated with a moderate (20%) increase in the odds of SPPH in this population. However, among women who had a caesarean birth, stillbirth was not associated with PPH or SPPH at the multivariable level.

Studies that examined stillbirth as a risk factor did not provide information or analysis on the timing of stillbirth, i.e. whether the intrauterine death occurred antepartum or intrapartum. This information may have been important for understanding the association and potential confounding factors or driving mechanisms behind the association. Higher rates of retained placenta have been observed among women who have a stillbirth, which may contribute to the association between stillbirth and postpartum haemorrhage (233)

5.4 Risk factors among low-risk women

While considerable research has been undertaken investigating the risk factors for PPH among the general birthing population, the systematic review highlighted that relatively little research has been conducted on the risk factors for PPH among women who might be considered low-risk at the start of care in labour. Previous research has identified that many women who experience PPH do not have any of the identified risk factors (52, 234). This warranted an investigation into risk factors for PPH among low-risk women and consideration of whether the factors associated with higher risk of PPH in this population might be different compared with the general birthing population. To address this question, the UKMidSS study and a sub-group analysis of the Aberdeen study were conducted. Most low-risk women give birth vaginally (141). The sub-group analysis of the Aberdeen study also investigated the risk factors for PPH among low-risk women who had a caesarean birth but there was limited power to detect associations given the size of this population and the results are therefore not discussed in this section.

Broadly speaking, risk factors identified in the UKMidSS analysis and in the low-risk Aberdeen analysis were similar to those that were identified in the general population in the Aberdeen study and those synthesised in the systematic review. Many of the risk factors identified in the general birthing population are not applicable to the low-risk population (e.g. multiple birth, hypertension) because of the criteria used to define a woman as low-risk, but the risk factors that are applicable to both groups of women generally showed similar associations in the two populations. For example, among all women, in the Aberdeen study, nulliparity was associated with double the odds of PPH, compared with 2-4 previous births, and this was also the case for low-risk women. There were no risk factors identified in the Aberdeen study that were statistically significantly associated with PPH in the low-risk population that were not also identified as associated with PPH in the analyses of all women.

In the UKMidSS study, the following risk factors were independently associated with higher risk of PPH:

- Nulliparity
- Not smoking during pregnancy
- Previous PPH
- Previous pregnancy complication other than PPH
- Post-term gestation
- Instrumental birth
- Prolonged third stage of labour
- 3rd or 4th degree perineal tear, and
- Birthweight 3500g or more.

With the exception of previous complications other than PPH, which were not examined, and post-term birth, which was not applicable because post-term was an exclusion criterion for the Aberdeen low-risk sample, all of the above risk factors were also associated with higher odds of PPH among low-risk women in the Aberdeen study. The following additional risk factors were independently associated with PPH among low-risk women in the Aberdeen study:

- Black or Asian ethnicity
- BMI of 25 or more
- One previous birth
- Augmentation of labour
- Prolonged second stage of labour
- Head circumference of 35cm or more, and
- Retained placenta.

It is evident that risk factors for PPH among low-risk women are similar to those among the general birthing population. While the Aberdeen study found similar magnitudes of effect for each individual risk factor compared with those found for all women, the absolute risk of PPH for low-risk women with any given risk factor was lower than among all women. This pattern was consistent across all risk factors analysed in the study. With almost half (49%) of woman giving birth vaginally being considered low-risk in the Aberdeen study and similar proportions reported in other studies (81, 90, 91) this is an

important group to consider. Understanding the risk factors relevant to low-risk women is particularly important in the context of this group being more likely to be eligible to consider planning birth outside of an obstetric unit, either in an MU or at home.

Risk factors that are evident prior to the onset of labour are important for informing decisions about planned place of birth. For example, women who are otherwise considered low-risk but who have a higher BMI, have had a previous PPH or are giving birth for the first time may wish to consider how these factors impact their potential risk of PPH. In particular, the risk of PPH following a previous PPH should be considered, as this was strongly associated with subsequent PPH. In the Aberdeen study, previous PPH was associated with more than double the odds of PPH among low-risk women and the odds of SPPH were 2.7 times higher among women with a previous PPH, at the multivariable level. The NICE intrapartum care guideline (CG190) lists 'Previous PPH requiring additional treatment or transfusion' as a risk factor suggesting increased risk during labour and birth (146). For the Aberdeen study, in the absence of data about treatment and transfusion around the previous PPH, this was operationalised as a previous PPH of at least 1500mL. This means that it is likely that some women who had a previous PPH that required additional treatment or transfusion with a blood loss <1,500mL and would therefore have been misclassified as low-risk. This may have contributed to the relatively large effect size for this risk factor among low-risk women.

In the UKMidSS study, among women who had given birth at least once before, a previous PPH nearly tripled the odds of a woman having a PPH requiring transfer. This finding is supported by a national cohort study of women admitted to AMUs for labour care following a PPH in a previous pregnancy, which reported that having a previous PPH was associated with a 65% higher risk of a subsequent PPH requiring transfer, compared with other multiparous women who had not had a PPH before (92). The absolute risk of a subsequent PPH requiring transfer among women who had a PPH in a previous pregnancy was low, at 4%, compared with 2% in other multiparous women (92). These results suggest

that women who have had a previous PPH should be informed about their increased relative risk of a subsequent PPH. While the absolute risk among women who plan to give birth in a MU and have had a previous PPH is low, nevertheless this should be taken into consideration during counselling.

Nulliparity emerged as another important antenatal risk factor, in terms of magnitude of effect, for determining an otherwise low-risk woman's potential risk of PPH. In both the Aberdeen and UKMidSS studies, nulliparity was associated with double the odds of PPH. This aligns with other research on all women giving birth, as identified in the systematic review. While the risk of PPH among primiparous women in the UKMidSS study was higher than in women who had given birth before, and primiparous women make up a considerable proportion of cases, the absolute risk of PPH following birth in an MU remains low for primiparous women. Primiparous women have higher rates of PPH than multiparous women, both in England (NHS Digital 2021) and in other high-income countries (13, 107, 235). Furthermore, the results of the UKMidSS study do not suggest that women giving birth for the first time were more likely to need enhanced treatment or care, compared with multiparous women.

In the UKMidSS study, outcomes were generally good among women who had PPH requiring transfer. One in four cases of PPH requiring transfer received 'enhanced treatment or care' (transfer to higher-level care or blood transfusion). The vast majority of women who had a PPH requiring transfer and required higher-level care were admitted to higher-level care for observation and stayed for 1 day or less, which may reflect a precautionary approach. Although difficulty with breastfeeding has been associated with PPH in previous research (236), breastfeeding initiation before discharge was similar among cases and controls in the UKMidSS study. Based on the multivariable analysis comparing women who had enhanced care with those who did not, it was not possible to determine based on pre-labour or intrapartum factors which women might be at higher risk of receiving 'enhanced treatment or care'. However, this may be a consequence of lack of power to detect significant associations. Overall, these findings suggest that women who are otherwise low-risk and eligible to

consider planning birth in a MU, including nulliparous women and those who have had a previous PPH, should consider this option. The Aberdeen study did not examine outcomes for women who had a PPH and therefore it is not possible to comment on whether outcomes for low-risk women are different from all women in this population. Additionally, while the Aberdeen Maternity Hospital has an AMU, it was not possible to determine from the available data whether a woman had planned or given birth in the AMU. Such information would have enabled a more comprehensive comparison of the two studies.

5.5 Number of risk factors and odds of PPH

In the Aberdeen study, for both vaginal and caesarean births, the greater number of risk factors a woman had, the higher her odds of having a PPH. The influence of each additional risk factor on the odds of PPH was considerable. For example, among women who had vaginal births, the odds of PPH more than doubled for women who had three risk factors and more than tripled for women who had four risk factors, compared to those with just one risk factor. Risk factors were not weighted to reflect their magnitude of the effect, however, which may limit the applicability of this finding. While this trend may be intuitive, there is limited previous research against which to compare these findings. One US study of vaginal births found significantly higher proportions of women who had a PPH had three or more risk factors, compared with controls (35% and 15% respectively) while a smaller proportion of women who had a PPH had no identified risk factors, compared with controls (9% and 22%, respectively) (52).

Over the 31-year study period of the Aberdeen study, the proportion of women who had multiple risk factors increased markedly. In 1986-1990, 45% of women giving birth vaginally had between zero and four risk factors, compared with 35% in 2011-2016. Notably, the proportion of women with nine or more risk factors almost doubled over that period, from 6% to 11%. Given that the odds of PPH were 25 times higher among women with nine risk factors and 35 times higher among women with 10 or more risk factors, compared to women with one risk factor, the increasing proportion of women with multiple risk factors for PPH is notable. A similar pattern was observed for women who had caesarean births. The proportion of women who had between zero and four risk factors declined from almost 50% in 1986-1990 to 20% in 2011-2016. The incremental influence of each additional risk factor was smaller for caesarean births, compared with vaginal births but still statistically significant. Women who had five or more risk factors had more than double the odds of PPH compared to women who had one risk factor. It seems likely that these patterns have played an integral role in the increasing incidence of PPH and SPPH over time.

5.6 Prevalence of risk factors over time

It has been suggested that one of the key drivers of the increased incidence of PPH in recent decades is the increase in the prevalence of key risk factors in the population (7, 10, 12) . These include maternal factors such as including increasing BMI, increasing maternal age, and higher prevalence of hypertensive disorders and increased obstetric intervention in labour and birth including induction of labour, augmentation, instrumental birth and caesarean birth. While there is considerable evidence for increased prevalence of these factors in recent years (7, 10, 33) and some evidence that this has contributed to increased incidence of PPH (7, 11, 12) , research that has controlled for increasing prevalence of risk factors has still noted an increase in the incidence of PPH (7, 10) This includes the studies carried out for this thesis.

In the Aberdeen study, the incidence of PPH and SPPH increased significantly across all population groups during the 31-year study period. Among vaginal births, the incidence of PPH increased by 3.7-fold and SPPH increased by 10-fold, from 1986-2016. Among caesarean births, the incidence of PPH almost doubled and SPPH increased by 4.6 fold. It is likely that this trend is explained, at least in part, by the fact that the prevalence of almost every risk factor for PPH also increased over the study period. The population attributable fractions (PAF) calculated for both vaginal and caesarean births provide important context for interpreting the changes in the prevalence of risk factors over time. Taken together, these analyses suggest that there are several risk factors for PPH that contribute a relatively high proportion of the PAF and that have increased in prevalence over the study period, which is likely to have contributed to the increasing incidence of PPH and SPPH.

Among vaginal births, nulliparity, birthweight more than 3500g, perineal tear and being a non-smoker each contributed 15% or more to the overall incidence of PPH. The prevalence of both high birthweight and being a non-smoker increased markedly over the study period and likely contributed considerably to the increase in PPH over the study period. Maternal age of 30 or more, BMI above 25,

induction of labour, and instrumental birth each contributed approximately 6% to the PAF. All of these risk factors became markedly more common over the 31-year period and thus, despite the relatively lower contribution to the prevalence individually, they each likely contributed to the increased incidence of PPH.

The PAF and the prevalence of risk factors over time also help to put into context the contribution of risk factors that are associated with a very high odds of PPH, but that have a relatively low prevalence on the population. For example, among vaginal births, retained placenta increased the odds of a PPH almost six-fold; however, the prevalence of retained placenta in the population has remained relatively low throughout the study period. Therefore, despite a very strong association with PPH and the very high proportional increase (0.5% in 1986-1990 to 2.0% in 2016), the prevalence of retained placenta, with a PAF of 0.1%, is unlikely to have substantially contributed to the increasing prevalence of PPH. Notwithstanding the potentially small contribution of retained placenta to PPH incidence overall, the quadrupling of this important risk factor over the study period is noteworthy in itself.

Among women who had caesarean births, maternal age of 30 or more, being a non-smoker, BMI of 25 or more, not being hypertensive, birthweight of 3500g or more, head circumference of 35cm or more, previous PPH, induction of labour, and caesarean after labour onset all contributed substantially to the incidence of PPH and all increased markedly over the study period. Of particular note are the increases in the prevalence of higher maternal age and previous PPH. The prevalence of previous PPH among women having caesareans doubled from 24% in 1986-1990 to 51% in 2011-2016. The prevalence of maternal age of 30 or more almost doubled during the study period (from 35.1% in 1986-1990 to 64.8% in 2011-2016).

That the increase over the study period in the odds of PPH remained significant, among both vaginal and caesarean births, even after adjustment for all independent risk factors, suggests that risk factors

that were not accounted for in these analyses likely played a role in the increased incidence of PPH over time. Previous research, for example, has suggested that uterine fibroids, placental disorders and chorioamnionitis all increase the risk of PPH and each has increased in prevalence in recent years (9, 12), however, the research conducted for this thesis was unable to investigate these factors. As discussed above, the fact that the odds of PPH increased dramatically as the number of risk factors a woman had increased, and that the number of risk factors women had increased markedly over the 31-year study period may also be important for explaining increasing incidence. Given the cumulative effect of each risk factor, it may be that the rise in incidence of PPH is a consequence of the increase in the number of risk factors each woman has.

5.7 Strengths and limitations

The major strengths of the systematic review were the robust search strategy; the use of two reviewers for article screening, data extraction and risk of bias assessment; and the pragmatic approach to defining outcomes and exposures, which enabled a comprehensive overview of the risk factors for PPH. The heterogeneity seen in the systematic review, in terms of definitions of PPH, definitions of risk factors, factors considered for inclusion and the general heterogeneity of populations rendered meta-analysis inappropriate and highlights the difficulty in making generalisations about risk factors for PPH. However, there were several factors for which there is strong evidence for an independent association with PPH and the generalisability of these findings was considered to be high. Given the high degree of heterogeneity of the studies included in the review, factors that were rated as 'very likely' and 'likely' risk factors, because of the consistency of associations, are considered likely to be risk factors across a wide range of populations and settings. The heterogeneity in the systematic review served to triangulate the evidence and enhance confidence in these findings and their likely relevance to a range of settings. The high degree of heterogeneity of included studies was also a limitation, making it difficult to draw comparisons across studies where overall results were unclear. The exclusion of articles published in languages other than English contributed to regional bias and limits the generalisability of the findings.

The major strengths of the UKMidSS study were its robust design, capturing information not collected previously and the high (98%) participation rate of MUs in the UK. A limitation of the study was the case definition of PPH requiring transfer, which limits the potential to compare the findings with other research that uses different definitions of PPH. The small sample size, which was unavoidable given the early termination of data collection in light of the burden COVID-19 placed on the healthcare system, limited the power of analyses of risk factors that are uncommon among women who give birth in MUs.

In the Aberdeen study, the major strengths included the population-based design using a comprehensive and validated data source. The inclusion of 31-years of data allowed analysis of trends in incidence and risk factors for PPH over time in a relatively stable population. The study was sufficiently powered to perform analyses of risk factors with a relatively low prevalence in the population. The key limitations were that it was geographically limited to one predominantly White and English-speaking region of the UK which limits its generalisability to more diverse populations.

Overall, this thesis has presented a comprehensive overview of the risk factors for PPH in high-income countries. It has also addressed a key gap in the literature by investigating risk factors for PPH among low-risk women. It is limited by the focus on births in the UK across both analytical studies, which restricts the generalisability of the findings. It is also limited by the reliance on observational research, both in the primary studies and the systematic review, and the inherent issue of residual confounding associated with this research design.

5.8 Implications for practice

There are several implications for clinical practice and areas for future research that have been highlighted through this research. Generally, the risk factors that were identified as 'likely' or 'very likely' on the basis of the systematic review are already included in national and international guidelines from professional bodies on the treatment and management of PPH. This suggests that guidelines that specify particular risk factors clinicians need to be aware of are broadly appropriate. Where there is consistent evidence for an association between risk factors and PPH, guidelines that do not already refer to important risk factors should be amended to reflect this understanding, although any amendments to current guidance should be based on the most relevant evidence for the context in which the guideline is intended to be applied. Updating clinical guidance to reflect the most recent research is critical for improving clinicians' awareness and ensuring that policies for treatment and prevention are appropriate. This is important for informed counselling of women in the antenatal

period in terms of planning place of birth and, where necessary, planning for potential increased blood loss though monitoring blood indices and intrapartum and postpartum management to minimise blood loss.

The results of this thesis also suggest that many risk factors that have been regularly referred to as 'well-established' risk factors, may not be independently associated with PPH, particularly not across all contexts and settings. Factors such as maternal age, high BMI, previous caesarean birth, augmentation of labour and caesarean birth do not show consistent associations with PPH. The bearing these risk factors have on an individual woman's risk of PPH is unclear and therefore these factors should be considered in the context of other risk factors a woman presents with, both antenatally and intrapartum.

In terms of directing research and public health efforts towards addressing risk factors for PPH, the clear factors of interest are those that are potentially modifiable and that contribute an important proportion to the population attributable risk. There are a number of risk factors identified in this thesis that may be suitable for public health intervention, based on their relatively high contribution to the PAF reported in the Aberdeen study and potential modifiability. In terms of clinical practice, the increasing prevalence of medical intervention in the intrapartum period over time has been associated with the increasing risk of PPH, as seen in the Aberdeen study and elsewhere (9, 12, 132). Practices relating to induction of labour and use of instruments to assist vaginal birth should be reviewed in terms of their contribution to the incidence of PPH and balanced in terms of their benefits for maternal and perinatal outcomes.

The significant risk of recurrent PPH is clear across all three studies comprising this thesis. While previous PPH is a well-recognised risk factor and is included in most clinical guidelines, the relatively limited investigation into this risk factor by studies in the systematic review raises questions about the

recording of this risk factor in health records. A multidisciplinary review of severe maternal morbidity (SMM) in New Zealand revealed that postpartum haemorrhage was the most common cause of SMM and that over a third of cases were potentially preventable, due to delayed or failure of diagnosis (28). The review found that a significant proportion of preventable PPH SMM was attributable to a lack of recognition of high-risk patients, including a considerable underreporting of previous PPH. This underscores the need for an accurate recording of a woman's obstetric history as well as any emerging risk factors for PPH.

By increasing awareness of the key risk factors that contribute to a woman's cumulative risk of PPH, including pre-existing and emerging risk factors that occur during childbirth, the speed of diagnosis and treatment of PPH could improve, potentially preventing cases of severe morbidity due to haemorrhage. Furthermore, as a significant proportion of the risk factors with the highest magnitude of effect identified in this thesis relate to events occurring during labour and birth, clinicians should remain aware of emerging risk factors, in addition to those already known, and be able to identify and respond to a woman's increasing level of risk.

5.9 Future research

This thesis has highlighted several priorities and considerations for future research. First, future studies investigating risk factors for PPH should analyse vaginal births and caesarean births separately. Most studies included in the systematic review included analyses of vaginal and caesarean births together; however, the results of this research suggest that there may be a differential effect of several risk factors on the risk of PPH based on mode of birth. Consequently, a clearer picture of risk factors would be provided by separating investigations by mode of birth. Consideration should also be given to the separate analysis of caesarean births based on whether or not labour occurred. Factors related to labour, including induction and progression of labour, as well as different indications for caesarean between women with planned and unplanned caesarean, may influence the associations between

other risk factors and PPH. This suggests separate investigation of risk factors among women who have a caesarean birth based on the presence of labour is warranted. Secondly, investigation of risk factors by cause of PPH would be helpful in elucidating areas for potential intervention. A large multi-centre or national study that has sufficient power to detect potential associations among the different causes of PPH would be suitable for such an investigation.

The systematic review revealed a paucity of research investigating risk factors among low-risk women, particularly among those who give birth in midwifery units. While the primary research carried out for this thesis was designed to help fill that gap, the findings of these studies have limited generalisability outside of the UK. Future research in other settings would be informative for understanding the risk factors among low-risk women.

While there are clear areas for potential future research and public health initiatives to reduce the prevalence of some key risk factors, many risk factors that substantially impact the incidence of PPH are, for practical purposes, immutable. Factors such as not smoking during pregnancy, nulliparity, maternal age greater than 30, larger birthweight, ethnicity and multiple births are not suitable candidates for public health initiatives. Further investigation as to the association each of these has with potential causes of PPH, however, may reveal avenues for targeted intervention.

Finally, given that the rate of PPH and SPPH has increased over time, despite adjustment for independent risk factors in the Aberdeen study and in other research, it is probable that additional risk factors, or changes to clinical practice, that were unaccounted for in these studies have contributed to the increased in incidence. Future research that explores the potential contribution of as yet unexplored risk factors would enhance our understanding the underlying reasons for the increased incidence and provide some insight into the direction of this trend in future. In particular,

studies that investigate the genetic contribution to PPH and environmental factors that may explain this concerning trend and, potentially, assist in reversing it.

5.10 Conclusion

This thesis provides a comprehensive synthesis of the available evidence about risk factors for PPH in high-income countries. The findings confirm several risk factors for PPH that have been previously documented in the literature and incorporated into clinical guidelines for risk assessment. Factors that were rated as likely or very likely risk factors were: maternal race/ethnicity, hypertensive disorders, previous PPH, multiple pregnancy, assisted conception, antepartum haemorrhage, induction of labour, prolonged second stage of labour, prolonged third stage of labour, maternal pyrexia in labour, instrumental birth, genital tract trauma, retained placenta and larger birthweight. However, many risk factors remain unclear in terms of their independent relationship with PPH, including some risk factors that are currently included in clinical guidelines for the assessment of risk of PPH, including: maternal age, BMI, previous caesarean birth, parity, augmentation of labour, caesarean birth and episiotomy. The lack of clear findings for many risk factors, identified by the systematic review, partially reflects the high degree of heterogeneity of studies in terms of study design, study population, definition and measurement of PPH, and adjustment for different risk factors in multivariable models. It also reflects the complexity of identifying risk factors for an outcome that has multiple potential aetiologies and where the risk factors have both interactive and independent contributions.

The significant increase in incidence of PPH over the past three decades is likely explained, in part, by the significant rise in prevalence of almost all identified risk factors for PPH. However, even after accounting for this, there remains an unexplained increase that warrants further investigation. The results of this thesis indicate that risk factors for PPH are significantly cumulative. Thus, a small increase in the number of risk factors among women in the birthing population may contribute to a

large increase in the overall incidence of PPH. This is of particular concern in light of the increasing prevalence of many risk factors in recent years.

It is evident that risk factors among low-risk women are broadly similar to those identified in studies of the general population of women giving birth. The results of individual studies as well as the results of the systematic review revealed a noticeable pattern of increasing consistency and magnitude of effect as risk factors become more proximal to the birth. Thus, while accurately identifying a woman's potential risk of PPH antenatally is important for enabling informed decisions about planned place of birth, and potentially preparing for the occurrence of PPH, the significant contribution of emerging risk factors during labour and birth underscores the importance of reassessing risk as labour and birth progress and ensuring that policies and guidelines support appropriate rapid treatment, and transfer where necessary, in all birth settings.

The findings of this thesis shed light on the complexities surrounding identifying risk factors for PPH and emphasise the urgent need for proactive measures to address increasing incidence. The identification and understanding of risk factors associated with PPH play a crucial role in developing targeted interventions, enhancing risk assessment protocols, and implementing preventive strategies. By recognising the cumulative nature of risk factors and the increasing prevalence observed in recent years, healthcare systems can strive to implement comprehensive approaches that encompass early detection, timely intervention, and appropriate management of PPH to improve maternal health outcomes.

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Appendix A: Chapter 2

Appendix A.1: Search terms for identifying relevant articles

Table A.1.1 Terms used to search Medline for systematic review

1. exp Postpartum Hemorrhage/
2. ((postnatal or post-natal) adj2 h?emorrhag*).mp.
3. (obstetric adj2 h?emorrhag*).mp.
4. ((postpart* or post-part*) adj2 h?emorrhag*).mp.
5. ((postnatal or post-natal) adj2 (bleeding or blood loss)).mp.
6. ((postpart* or post-part*) adj2 (bleeding or blood loss)).mp.
7. (obstetric adj2 (bleeding or blood loss)).mp.
8. pph.mp.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. risk* or factor* or character* or 492irectly492*).mp.
11. (epidemiolog*).ti.
12. 10 or 11
13. 9 and 12

Table A.1.2 Terms used to search Embase for systematic review

1. exp Postpartum Hemorrhage/
2. ((postnatal or post-natal) adj2 h?emorrhag*).mp.
3. (obstetric adj2 h?emorrhag*).mp.
4. ((postpart* or post-part*) adj2 h?emorrhag*).mp.
5. ((postnatal or post-natal) adj2 (bleeding or blood loss)).mp.
6. ((postpart* or post-part*) adj2 (bleeding or blood loss)).mp.
7. (obstetric adj2 (bleeding or blood loss)).mp.
8. pph.mp.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. (risk* or factor* or character* or 492irectly492*).mp.
11. (epidemiolog*).ti.
12. 10 or 11
13. 9 and 12

Table A.1.3 Terms used to search Web of science for systematic review

1. TS=((postnatal or post-natal) NEAR/2 h$emorrhag*)
2. TS=(obstetric NEAR/2 h$emorrhag*)
3. TS=((postpart* or post-part*) NEAR/2 h$emorrhag*)
4. TS=((postnatal or post-natal) NEAR/2 (bleeding or blood loss))
5. TS=((postpart* or post-part*) NEAR/2 (bleeding or blood loss))
6. TS=(obstetric NEAR/2 (bleeding or blood loss))
7. TS=(pph)
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. TS=(risk* or factor* or character* or 492irectly492*)
10. TI=(epidemiolog*)
12. 9 or 10
13. 8 and 11

Table A.2: Modified Risk of Bias Assessment tool for Non-Randomised Studies (RoBANS)

	Domain	Adapted criteria	
		Low risk of bias[1]	High risk of bias[1]
1	Participant selection	The following criteria should be considered for participant's selection: **All studies** • Women with and without PPH were selected from the same population group(s) and time period(s) • All participants were assessed for PPH • The selection of participants was independent of exposure status (i.e. risk factors under investigation) **Case-control studies** • In the case that not all women without a PPH were included in the sample, selection and recruitment of controls is clearly explained and justified.	The following criteria should be considered for participant's selection: **All studies** • Women with or without PPH were selected from different population groups and/or time periods (e.g. historical unexposed cohort) • Not all women in the study were assessed for PPH • The selection of participants was not independent of exposure status (i.e. risk factors under investigation) **Case-control studies** • In the case that not all women without a PPH were included in the sample, selection and recruitment of controls was not clearly explained or justified.
2	Confounding variables	The major confounding variables were adequately considered and adjusted in the study design (through participant restriction/exclusion or matching) and/or in the analysis.	The major confounding variables were not considered in the study design or analysis (i.e. the study did not confirm or adjust for the potential confounders such as maternal age, maternal education or socio economic status, BMI, Parity etc.) The study only conducted/presented univariable analyses
3	Exposure measurement	The following criteria should be considered for exposure (risk factor) measurement • Exposures were evaluated using established diagnostic/classification criteria or validated tool or laboratory tests • Exposures evaluation was performed in a standardised fashion by qualified assessors (e.g. midwives, doctors, psychologists) • The timing of outcome assessment was comparable for all participants • The data source/s from which information about exposures/ risk factors is derived is the same for cases and controls	Any of the following • Exposures were established using non-established criteria or self-reported exposures where clinical/laboratory findings would be appropriate (e.g. self-reported iron deficiency not confirmed by lab results) • The data source/s from which information about exposures/ risk factors is derived is different for cases and controls • The timing of exposure assessment was different for cases/controls

4	Blinding and outcome measurement	The following criteria should be considered • PPH was defined using standardised diagnostic criteria, for example using definitions of WHO, RCOG, ACOG, or ICD-10 codes. • PPH evaluation was performed in a standardised fashion by qualified assessors (e.g. midwives, doctors) • The timing of PPH assessment was comparable for all participants • Outcome assessors were blinded to women's medical history/record for PPH or were blinded to the research question.	Any of the following PPH was defined using non-standard or unclear criteria or tools with uncertain validity/reliability (including self-reporting using such tools) or diagnostic criteria were not clear • The measurement of PPH was not comparable among all study participants. • The assessors of PPH (OB, midwife) were not blinded to the research question.
5	Incomplete data	The following criteria should be considered • The proportion and causes of missing data were similar between cases and controls • The potential impact of missing data was corrected in the analysis • The study results were demonstrated to be robust to the presence of missing data (e.g. via sensitivity analyses)	• The proportion and causes of missing data differed between participants with or without PPH (or cases and controls), and these differences were not addressed in the analysis • The study results were influenced by the missing data
6	Selective reporting (within study)	The following criteria should be considered • If a study protocol is available, the pre-defined primary/secondary analyses were described as planned or justified in the study report if there were any legitimate changes from the protocol. • Analyses of all of the outcomes/exposures that are relevant to the study objectives were reported (e.g. check the outcomes mentioned in the methods section and the reported results, or consider missing report of the measures which are usually collected together e.g. SBP and DBP) • The effect estimates reported do not seem to have been selected from (i) alternative outcome/exposure measurements, (ii) multiple analytic approaches, or (iii) multiple subgroups	• The pre-defined primary analyses were not fully reported or reported as planned in a protocol or not justified for the differences. • Additional analyses that were not pre-specified or 494irectly relevant to the study objectives were included (e.g. subgroup analyses, secondary variables), except for those with a clear justification • Some analyses of exposures/outcomes that are relevant to the study objectives were not reported • The effect estimates reported seem to have been selected from (i) alternative outcome/exposure measurements, (ii) multiple analytic approaches, or (iii) multiple subgroups

[1] If there is insufficient information to determine whether the risk of bias is low or high, it should be classified as "unclear".

Appendix A.3: Covidence data extraction form

Study information	
Author	
Year published	
Country	
Setting	
Methods	
Study design	
Data source	
Aim of study	
First year of included births	
Last year of included births	
Description of population	
Inclusion criteria	
Exclusion criteria	
Definition of PPH	
Definition of SPPH	
Assessment of PPH	
Results	
Total number in population	
Number of PPH cases	
Number of SPPH cases	
Incidence of PPH	
Incidence of SPPH	
Comment	

Table A.4: Bespoke Excel data extraction form for study results

Covidence #	Study, Year	Statistical methods	Variables adjusted for in the multivariable analysis	Risk factor group (e.g. Maternal characteristics)	Risk factor name	Type of statistic (e.g. mean, proportion, OR, aOR)	Result	Significance level	Comments

Appendix A.5: Risk factors not included in narrative synthesis

Table A.5.1: Included studies investigating various maternal characteristics as potential risk factors for postpartum haemorrhage

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Maternal height			
Kramer, 2011	**PPH:** < 160cm: 2.1% 160-170cm: 2.2% >170cm: 2.3% **SPPH:** < 160cm: 0.20% 160-170cm: 0.19% >170cm: 0.08%	PPH/SPPH rate (%)	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726
Looft, 2017	**Height (cm)** **All:** ≤154: 1507 155-164: 19128 165-174: 29424 ≥175: 6622 Missing: 586 **PPH:** ≤154: 415 155-164: 5250 165-174: 8646 ≥175: 2084 Missing: 159	n	NA	VB	**PPH:** EBL ≥500mL	57,267
Oberg, 2014b	**<160cm:** ref **160-169:** 1.16 (1.08-1.24) **≥170:** 1.39 (1.30-1.49)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Drug use			
Lisonkova, 2016	**PPH:** 1 (0.27%) **CTL:** 2 (0.54%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393
			Legal status - French or legal immigrant			
Firmin, 2019	**PPH:** 63.5% **CTL:** 69.2%	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154
			Maternal language			
Firmin, 2019	**French:** 0.68 (0.38-1.23) **Other language:** ref	uOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154

Table A.5.2: Included studies investigating various medical factors as potential risk factors for postpartum haemorrhage

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Anticoagulant medication			
Endo-Kawamura, 2016	**Mid-pregnancy blood test:** Antithombin activity <90%: 1.62 (0.94-2.79) **Pre-delivery blood test:** Antithombin activity <85%: 1.84 (1.05-3.21)	aOR aOR	Sig Sig	VB	**PPH:** EBL ≥700mL	1,032
Nyflot, 2016	**Medication - anticoagulant:** 3.75 (2.22-6.35)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 115 **CTL:** 82
Nyflot, 2017a	**Medication - anticoagulant:** 4.79 (2.72-8.41)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059
			Pro-thrombic alleles: TFPI			
Biguzzi, 2014	**F2:** 0.70 (0.42-1.15) **No F2:** ref	aOR	NS	VB	**PPH:** EBL ≥500mL	3,219
Biguzzi, 2014	**GP1BA:** 1.07 (0.87-1.33) **GP1BA:** ref	aOR	NS	VB	**PPH:** EBL ≥500mL	3,219
Biguzzi, 2014	**TFPI:** 0.91 (0.76-1.10) **No TFPI:** ref	aOR	NS	VB	**PPH:** EBL ≥500mL	3,219
			Asthma			
Merriam, 2018	**PPH 1:** Asthma:1.02 (0.99-1.05) No asthma: ref **PPH 2:** Asthma: 1.10 (1.06-1.15) No asthma: ref	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088
Noguchi, 2017	**PPH:** Asthma: 7 **CTL:** Asthma: 371	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Blood disorders			

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Magan, 2005a	**Elective CS:** PPH: 1.77 (1.04-2.92) SPPH: 3.22 (1.50-6.92)	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837
Magan, 2005b	**Blood disorders:** 1.3 (1.1-1.6)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868
			Coagulopathy			
Oberg, 2014a	**Coagulopathy:** 1.45 (1.29-1.43)	uOR	Sig	VB, CS	**PPH:** ICD codes, typically EBL ≥1000mL	583,332
Oberg, 2014b	**Coagulopathy:** 1.57 (1.22-2.02)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756
			Human Placental Protein 13 (PP13)			
Farina, 2017	**PPH:** 1.44 (0.42) **CTL:** 1.00 (0.59) p=0.029	Multiple of mean	Sig	VB	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390
Farina, 2017	**PPH:** 25.8 (2.68) **CTL:** 13.54 (7.59) p <0.001	Ranks sum	Sig	VB	**PPH:** EBL ≥1000mL	**PPH:** 15 **CTL:** 390
			Hypervascularity			
Lee, 2017	**Hypervascularity:** 6.23 (2.13-18.22)	aOR	Sig	CS	**SPPH:** intraoperative blood loss ≥2000mL	210
Lee, 2018	**Hypervascularity:** 4.51 (2.30-8.83)	aOR	Sig	CS	**SPPH:** intraoperative blood loss ≥2000mL	506
			Laboratory findings; ++			
Koopmans, 2014	**Proteinuria ++:** 1.0 (0.55-2.3) **Negative:** ref	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Koopmans, 2014	Proteinuria **+++:** 1.8 (0.91-5.5) **Negative:** ref	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
			Platelets			
Biguzzi, 2011	**Platelets (30x10^3 uL increment) [within one month before delivery]:** 0.96 (0.93-0.99)	aOR	Sig	VB	**PPH:** EBL ≥500mL	6,011
Koopmans, 2014	**Platelets (x10^9/L):** 0.997 (0.99-1.0)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
			Prepartum Amplitude of clot firmness 10 mins after clotting (EXTEM A10)			
Kaufner, 2016	≤57: 1.33 (0.36-4.88) 58-61: 1.71 (0.48-6.19) 62-65: 1.55 (0.43-5.54) 66+: ref	uOR	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
			Alanine aminotransferase (U/L)			
Koopmans, 2014	**Alanine aminotransferase (U/L):** 1.00 (0.98-1.02)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
			Antiphospholipid antibody syndrome			
Noguchi, 2017	**PPH:** 0 **CTL:** 7	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Aspartate amniotransferase (U/L)			
Koopmans, 2014	**Aspartate amniotransferase (U/L):** 0.99 (0.97-1.01)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
			Blood pressure			
Koopmans, 2014	**Systolic:** 0.67 (0.99-1.02) **Diastolic:** 1.01 (0.98-1.04)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Blood type			
Biguzzi, 2011	Blood group O: 0.93 (0.81-1.07) non-O: ref	aOR	NS	VB	**PPH:** EBL ≥500mL	6,011
			Chronic kidney disease			
Noguchi, 2017	**PPH:** 0 **CTL:** 17	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Circulatory system disorders			
Magan, 2005a	**Emergency CS:** PPH: 3.92 (1.12-11.48) SPPH: 2.11 (0.32-13.71)	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837
			Creatine			
Koopmans, 2014	**Creatinine (umol/L):** 1.003 (0.99-1.01)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
			D-dimer			
Endo-Kawamura, 2016	**Mid-pregnancy blood test:** D-dimer ≥1.9 ug/mL: 2.59 (1.68-3.99) **Pre-delivery blood test:** D-dimer ≥2.7 ug/mL: 2.03 (1.29-3.19)	aOR aOR	Sig Sig	VB	**PPH:** EBL ≥700mL	1,032
			EXTEM Clot-formation time (s)			
Kaufner, 2016	**CTL:** 75 (64.5-89.5) **PPH:** 78 (66-97) p=0.516	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Fibrinogen levels			
Endo-Kawamura, 2016	**Mid-pregnancy blood test:** Fibrinogen <3.8 g/L: 1.83 (1.09-3.07) **Pre-delivery blood test:** Fibrinogen <4.0 g/L: 1.96 (1.18-3.27)	aOR aOR	Sig Sig	VB	**PPH:** EBL ≥700mL	1,032
			Group B Streptococcus positive			
Lisonkova, 2016	**PPH:** 36 (6.79%) **CTL:** 23 (6.01%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393
			Heart disease			
Noguchi, 2017	**PPH:** 2 **CTL:** 53	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Hematologic disease			
Noguchi, 2017	**PPH:** 1 **CTL:** 25	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Hepatitis			
Noguchi, 2017	**PPH:** 0 **CTL:** 42	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Hyperthermia			
Firmin, 2019	**Hyperthermia:** 2.11 (0.72-6.17) **No hyperthermia:** ref	uOR	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154
			Laboratory findings; Proteinuria+			
Koopmans, 2014	**Proteinuria+:** 1.1 (0.72-2.2) **Negative:** ref	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Laboratory findings; Trace			
Koopmans, 2014	**Trace proteinuria:** 1.2 (0.64-2.4) **Negative:** ref	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
			Lactate dehydrogenase (U/L)			
Koopmans, 2014	**Lactate dehydrogenase (U/L):** 1.00 (1.00-1.00)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
			Lead poisoning			
Firmin, 2019	**Lead poisoning:** 2.04 (1.01-4.10) **No lead poisoning:** ref	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154
			Maternal infection			
Lisonkova, 2016	**PPH:** 60 (15.79%) **CTL:** 51 (13.46%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393
			Medication - Antibiotics in pregnancy			
Briley, 2013	**Antibiotics in pregnancy:** 1.14 (0.77-1.66)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937
			Medication – Antidepressant (30 day exposure)			
Salkeld, 2008	SSRI: 1.33 (0.94-1.89) Non-SSRI: 1.29 (0.58-2.84) None: ref	aOR	NS	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943
			Medication – Antidepressant (60 day exposure)			
Salkeld, 2008	SSRI: 1.40 (1.04-1.88) Non-SSRI: 1.11 (0.55-2.22) None: ref	aOR	NS	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Medication – Antidepressant (90 day exposure)						
Salkeld, 2008	SSRI: 1.32 (1.03-1.70) Non-SSRI: 1.04 (0.61-1.75) None: ref	aOR	NS	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943
Medication – Antidepressant (180 day exposure)						
Salkeld, 2008	SSRI: 1.30 (0.98-1.72) Non-SSRI: 1.12 (0.62-2.01) None: ref	aOR	NS	VB, CS	**PPH:** ICD 9 and ICD 10 codes	**PPH:** 2,460 **CTL:** 23,943
Medication - Antihypertensives in pregnancy						
Briley, 2013	**Antihypertensives in pregnancy:** 0.66 (0.33-1.32)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937
Medication - Diabetic Rx in pregnancy						
Briley, 2013	**Diabetic Rx:** 1.20 (0.43-3.37)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937
Medication - Steroids for fetal reasons						
Briley, 2013	**Steroids for fetal reasons:** 1.23 (0.69-2.18)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937
Postpartum activated partial thromboplastin time (aPTT)						
Kaufner, 2016	**CTL:** 30.8 (29.1-32.4) **PPH:** 30.5 (28.5-31.8) p=0.570	Mean (SD)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
Postpartum EXTEM a-angle ANGLE						
Kaufner, 2016	**CTL:** 76 (73-78) **PPH:** 75 (70.5-78) p=0.451	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
Postpartum EXTEM Clotting time						
Kaufner, 2016	**CTL:** 43 (38-50.5) **PPH:** 42 (39.5-44) p=0.615	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
Postpartum Prothombin time (s)						

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Kaufner, 2016	**CTL:** 101.5 (9.5) **PPH:** 94.8 (5.77) p=0.006	Mean (SD)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
Postpartum Fibrinogen (g/L)						
Kaufner, 2016	**CTL:** 4.31 (0.74) **PPH:** 3.83 (0.95) p=0.021	Mean (SD)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
Postpartum FIBTEM Mx clot firmness (mm)						
Kaufner, 2016	**CTL:** 22 (20-26) **PPH:** 20 (18-24) p=0.169	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
Prepartum activated partial thromboplastin time (aPTT)						
Kaufner, 2016	**Prepartum Activated partial thromboplastin time (s):** **CTL:** 30.4 (29.0-31.9) **PPH:** 29.9 (28.9-32.0) P=0.370	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
Prepartum EXTEM a-angle (degrees)						
Kaufner, 2016	**CTL:** 76 (73-78) **PPH:** 76 (74-78) p=0.808	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
Prepartum EXTEM Clot-formation time (s)						
Kaufner, 2016	**CTL:** 76 (64-88) **PPH:** 73 (66-84) p=0.952	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
Prepartum EXTEM Clotting time						
Kaufner, 2016	**CTL:** 42 (38-48) **PPH:** 43 (40-48) p=0.441	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Prepartum Fibrinogen (g/L)			
Kaufner, 2016	**≤3.5:** 2.33 (0.37-14.73) **>3.5-4.5:** 1.41 (0.31-6.39) **>4.5-5.5:** 0.90 (0.20-4.14) **>5.5:** ref	aOR	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
			Prepartum FIBTEM Mx clot firmness (mm)			
Kaufner, 2016	**≤20:** 1.58 (0.49-5.08) **21-23:** 1.28 (0.38-4.34) **24-26:** 1.26(0.36-4.44) **27+:** ref	uOR	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
			Prepartum Platelets (10^9/L)			
Kaufner, 2016	**CTL:** 221 (181-267) **PPH:** 214 (173-257) p=0.494	Median (IQR)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
			Prepartum Prothombin time (s)			
Kaufner, 2016	**CTL:** 107 (10.8) **PPH:** 106 (9.0) p=0.558	Mean (SD)	NS	VB, CS (urgent only)	**PPH:** EBL ≥500mL	217
			Pro-haemorrhagic alleles: ACE			
Biguzzi, 2014	**Pro-haemorrhagic alleles ACE:** 1.05 (0.92-1.19)	aOR	NS	VB	**PPH:** EBL ≥500mL	3,219
			Pro-haemorrhagic alleles: ITGA2			
Biguzzi, 2014	**Pro-haemorrhagic alleles ITGA2:** 0.92 (0.81-1.04) **no ITGA2:** ref	aOR	NS	VB	**PPH:** EBL ≥500mL	3,219
			Pro-thrombic alleles: F3			
Biguzzi, 2014	**F3:** 0.79 (0.69-0.90) **No F3:** ref	aOR	Sig	VB	**PPH:** EBL ≥500mL	3,219
			Pro-thrombic alleles: F5			

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Biguzzi, 2014	**F5:** 0.99 (0.59-1.66) **No F5:** ref	aOR	NS	VB	**PPH:** EBL ≥500mL	3,219
			Pro-thrombic alleles: ITGA2			
Biguzzi, 2014	**ITGA2:** 0.98 (0.86-1.12) **No ITGA2:** ref	aOR	NS	VB	**PPH:** EBL ≥500mL	3,219
			Psychiatrics			
Noguchi, 2017	**PPH:** 0 **CTL:** 122	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Seizure			
Noguchi, 2017	**PPH:** 1 **CTL:** 73	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Systemic lupus erythematosus			
Noguchi, 2017	**PPH:** 1 **CTL:** 12	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Thromboprophylaxis (any)			
Lisonkova, 2016	**PPH:** 20 (5.26%) **CTL:** 23 (6.04%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393
			Thromboprophylaxis with heparin			
Lisonkova, 2016	**PPH:** 16 (4.21%) **CTL:** 20 (5.25%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393
			Thyroid disease			
Noguchi, 2017	**PPH:** 6 **CTL:** 150	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Uric acid			
Koopmans, 2014	**Uric acid (mmol/Lx10):** 1.01 (0.78-1.3)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014

Table A.5.3: Included studies investigating various obstetric history factors as potential risk factors for postpartum haemorrhage

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Previous abortions			
Koopmans, 2014	**Previous abortion:** 1.1 (0.68-1.7)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
Lisonkova, 2016	**0:** ref **1-2:** 0.62 (0.40-0.94) **≥3:** 1.21 (0.47-3.15)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393
Noguchi, 2017	**Recurrent pregnancy loss:** **PPH:** 10 **CTL:** 220	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
Sheiner, 2009	**Recurrent abortions:** **PPH 1:** 8.0% **PPH 2:** 4.5% **PPH 3:** 9.5% **CTL:** 4.9%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645
			Previous D&C			
Butwick, 2017	**Pre-labour CS:** Previous D&C or D&E: 1.88 (1.17-3.0)	aOR	Sig	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** Case: 269 CTL: 550
Lee, 2017	**Previous D&C:** 4.47(1.29-15.48) **No previous D&C:** ref	aOR	Sig	CS	**SPPH:** intraoperative blood loss ≥2000mL	210
Lee, 2018	**Previous D&C:** 1.45 (0.81-2.63)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506
			History of infertility			
Suzuki, 2007	**History of infertility:** 2.06 (0.70-6.06)	uOR	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 132

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			History of myectomy			
Butwick, 2017	**Pre-labour CS:** **CTL:** Prior history of myectomy: 27 (4.9%) **SPPH:** Prior history of myectomy: 13 (4.8%) p=0.96	%	NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** Case: 269 CTL: 550 **Intrapartum CS** Case: 278 CTL: 572
			Previous pre-eclampsia			
Noguchi, 2017	**PPH:** 4 **CTL:** 120	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Prior macrosomia			
Noguchi, 2017	**PPH:** 0 **CTL:** 23	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Prior placenta abruption			
Noguchi, 2017	**PPH:** 1 **CTL:** 29	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Prior preterm birth			
Noguchi, 2017	**PPH:** 6 **CTL:** 179	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Prior stillbirth			
Noguchi, 2017	**PPH:** 3 **CTL:** 75	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Prior uterine cervix conization			

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Noguchi, 2017	**PPH:** 2 **CTL:** 93	n	NS	VB, CS	**SPPH:** EBL ≥1500g	4,829
			Uterine anomaly			
Nyflot, 2017a	**Uterine anomaly:** 2.40 (1.15-5.01)	uOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	**SPPH:** 1,064 **CTL:** 2,059

Table A.5.4: Included studies investigating various pregnancy factors as potential risk factors for postpartum haemorrhage

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Placenta accreta			
Davey, 2019	54.9 (30.8-97.8)	aOR	Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701
Lisonkova, 2016	**PPH:** 2 (0.52%) **CTL:** 0	%	NA	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393
Sheiner, 2009	**PPH:** 3.3 (1.7-6.4)	aOR	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153, 645
			Antenatal care			
Briley, 2013	**Any antenatal day unit attendance:** 0.95 (0.72-1.26)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937
Buzaglo, 2014	**No antenatal care:** **PPH:** 3.6% **CTL:** 5.1% p=0.088	%	NS	VB	**PPH:** EBL ≥500mL	56,394
			Loss of hypoechoic retroplacental zone			
Lee, 2017	**Loss of hypoechoic retroplacental zone:** 2.09 (0.73-6.00)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210
Lee, 2018	**Loss of hypoechoic retroplacental zone:** 1.38 (0.78-2.55)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Placenta multiple lacunae			
Lee, 2017	**Placenta multiple lacunae:** 1.77 (0.63-4.97)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210
Lee, 2018	**Placenta multiple lacunae:** 2.77 (1.54-4.99)	aOR	Sig	CS	**SPPH:** intraoperative blood loss ≥2000mL	506
			Placental anterior location			
Lee, 2018	**Placental anterior location:** 2.74 (1.54-4.89)	aOR	Sig	CS	**SPPH:** intraoperative blood loss ≥2000mL	506
Magan, 2005a	**Elective CS:** **PPH:** 2.48 (1.06-5.24) **SPPH:** 2.81 (0.89-8.84)	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837
			Abnormally invasive placenta			
Kaelin Agten, 2017	**Abnormally invasive placenta:** 10.4 (9.5-11.5)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	739,444
			Adherent placenta			
Buzaglo, 2014	**PPH:** 1.8% **CTL:** 0.7%	%	NS	VB	**PPH:** EBL ≥500mL	56,394
			Admission >24 weeks			
Briley, 2013	**Admission >24 weeks:** 0.82 (0.53-1.29)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Antenatal transfusion			
Magan, 2005a	**Emergency CS:** **PPH:** 4.80 (1.02-20.67) **SPPH:** 9.01 (1.94-41.94)	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837
			Generally unwell			
Briley, 2013	**Generally unwell:** 1.33 (0.69-2.60)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937
			Gross placental pathology			
Kramer, 2011	**PPH:** Normal: ref Infarction: 1.2 (0.8-1.8) Marginal cord insertion: 1.5 (1.2-1.8) Circimvallate placenta: 1.5 (1.0-2.3) Chorangioma: 0.9 (0.7-1.2) Other abnormality: 1.5 (1.3-1.9)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726
	SPPH: Normal: ref Infarction: 3.9 (0.4-34.0) Marginal cord insertion: 1.6 (0.5-5.0) Circimvallate placenta: 2.0 (0.3-16.1) Chorangioma: 1.1 (0.1-8.4) Other abnormality: 2.8 (0.8-9.0)	aOR	NS			

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Monochrorionic twins			
Suzuki, 2007	**Monochrorionic twins:** 0.6 1 (0.27-1.35)	uOR	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 135
			Oligohydramnios			
Hiersch, 2016	**PPH:** Oligohydramnios: 3.1% **CTL:** Oligohydramnios: 1.9% 0.24	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154
Kramer, 2011	**PPH:** Normal: ref Oligohydramnios: 0.8 (0.7-1.1) **SPPH:** Normal: ref Oligohydramnios: 0.2 (0.002-1.3)	aOR aOR	NS NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726
Sheiner, 2009	**PPH 1:** Oligohydramnion: 2.2% **PPH 2:** Oligohydramnion: 2.4% **PPH 3:** Oligohydramnion: 1.5% **CTL:** Oligohydramnion: 2.1%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Placental abnormalities			
Ford, 2007	**1994-1995** 3.81 (3.22-4.50) **2002** 4.29 (3.38-5.45)	aOR aOR	Sig Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374
			Pre-eclampsia screen			
Briley, 2013	**Pre-eclampsia screen:** 1.04 (0.57-1.91)	aOR	NS	VB, CS	**PPH:** EBL ≥500mL	9,937
			Retroplacental hematoma			
Firmin, 2019	**Retroplacental hematoma:** PPH: 3.2% CTL: 0 p=0.001	%	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000	**PPH:** 308 **CTL:** 154
			Suspected large fetus			
Lisonkova, 2016	**PPH:** Suspected large fetus: 13 (3.4%) **CTL:** Suspected large fetus: 7 (1.83%)	%	NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393
			Twin-twin transfusion syndrome			
Magan, 2005b	**Twin-twin transfusion syndrome:** 5.1 (1.5-15.7)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868
			Vitamin use in pregnancy			
Lisonkova, 2016	**Vitamin use in pregnancy:** 1.84 (1.12-3.02)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Weight gain during pregnancy			
Fukami, 2019	**CTL:** <9.9 Kg: 56.6% 10.0-14.9 Kg: 34.6% >15.0: 8.8% **PPH:** <9.9 Kg: 38.7% 10.0-14.9 Kg: 43.0% >15.0: 18.3%	%	NS	VB	**PPH:** CBL ≥1000mL	1,608

Table A.5.5: Included studies investigating various labour factors as potential risk factors for postpartum haemorrhage

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Magnesium infusion			
Butwick, 2017	**Pre-labour CS:** na **Intrapartum CS:** 1.26 (0.6-2.64)	aOR	NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS:** Case: 269 CTL: 550 **Intrapartum CS:** Case: 278 CTL: 572
Koopmans, 2014	**Use of magnesium sulfate:** 1.29 (0.68-2.4)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1014
Lisonkova, 2016	**Magnesium sulfate:** 10.8 (1.19-98.8)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393
Miller, 2017	**Magnesium infusion:** 1.44 (0.70-2.97)	aOR	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318
			Shoulder dystocia			
Buzaglo, 2014	**PPH:** 0.2% **CTL:** 0.1%	%	NS	VB	**PPH:** EBL ≥500mL	56,394
Hiersch, 2016	**PPH:** 0.7% **CTL:** 0.9% p=1.0	%	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154
Magan, 2005a	**Elective CS:** na **Emergency CS:** PPH: 1.79 (1.19-2.67) SPPH: 1.61 (0.91-2.86)	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Sheiner, 2009	**PPH 1:** 0% **PPH 2:** 0.6% **PPH 3:** 0% **CTL:** 0.2%	%	NS	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645
Intrapartum haemorrhage						
Magan, 2005a	**Emergency CS:** PPH: 3.06 (1.89-4.94) SPPH: 2.27 (1.18-4.39)	aOR	Sig	CS	**PPH:** CBL≥1000mL and/or transfusion **SPPH:** CBL≥1500mL and/or transfusion	4,837
Magan, 2005b	**Intrapartum haemorrhage:** 1.5 (1.0-2.3)	aOR	NS	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868
Using tocolytics just before delivery						
Lee, 2017	**Using tocolytics just before delivery:** 0.00 (0.00-0.00)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210
Lee, 2018	**Using tocolytics just before delivery:** 1.54 (0.44-5.40)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506
Abnormal labour						
Ford, 2007	**1994-1995:** 1.24 (1.13-1.37) **2002:** 1.46 (1.30-1.65)	aOR aOR	Sig Sig	VB, CS	**PPH:** ICD 9 and 10 codes	752,374
Antibiotic use during delivery						
Lisonkova, 2016	Antibiotic use during delivery	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Cervical dilation prior to CS						
Butwick, 2017	**Intrapartum CS:** **CTL:** 1-9cm: 384 (67.15) 10cm: 152 (25.6%) Missing: 36 (6.3%) **SPPH:** 1-9cm: 204 (73.4%) 10cm: 61 (21.9%) Missing: 13 (4.7%)	%	NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** Case: 269 CTL: 550 **Intrapartum CS** Case: 278 CTL: 572
Indication for induction of labour						

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Khireddine, 2012	**All women** **PPH 1:** Spontaneous: ref Standard indication: 1.28 (1.06-1.55) Non-standard indication: 1.11 (0.89-1.40)	aOR	Sig	VB,CS	**PPH 1:** EBL ≥500mL **PPH 2:** Hb ≥4 g/dL or RBC transfusion ≥2 units	**CTL:** 1,744 **PPH 1:** 4,450 **PPH 2**: 1,125
	PPH 2: Spontaneous: ref Standard indication: 1.33 (1.04-1.71) Non-standard indication: 0.96 (0.68-1.36)	aOR	Sig			
	Pimiparas: **PPH 1:** Spontaneous: ref Standard indication: 1.35 (1.04-1.74) Non-standard indication: 1.43 (1.04-1.97)	aOr	Sig			
	PPH 2: Spontaneous: ref Standard indication: 1.33 (1.04-1.71) Non-standard indication: 0.96 (0.68-1.36)	aOR	Sig			

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Suture interval after vaginal birth			
Briley, 2013	**Suture interval after vaginal birth (hours):** 2.03 (1.65-2.50) **Suture interval not recorded:** 2.2 (1.32-3.69)	aOR	Sig	VB, CS	**PPH:** EBL ≥500mL	9,937
			Tocolytic therapy			
Kramer, 2011	**PPH:** 1.3 (1.1-1.5) **SPPH:** 0.4 (0.1-2.2)	aOR aOR	Sig NS	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL **SPPH:** EBL ≥1500mL, transfusion and/or hysterectomy	103,726
			Use of intravenous antihypertensives			
Koopmans, 2014	**Use of intravenous antihypertensives:** 1.50 (0.77-2.9)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
			Use of oxytocin			
Koopmans, 2014	**Intrapartum use of oxytocin:** 1.02 (0.70-1.5)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
			Use of prostaglandins			
Koopmans, 2014	**Intrapartum use of prostaglandins:** 0.91 (0.61-1.3)	uOR	NS	VB, CS	**PPH:** EBL ≥1000mL	**N:** 1,132 **PPH:** 118 **CTL:** 1,014
			Fetal distress			
Combs, 1991a	**Fetal distress:** PPH: 34 (17.3%) CTL: 87 (14.8%)	%	NS	CS	**PPH:** Haematocrit decreased of 10 points or more between admission and postpartum measurements or blood transfusion.	**PPH:** 196 **CTL:** 588

Table A.5.6: Included studies investigating various birth factors as potential risk factors for postpartum haemorrhage

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Placental weight			
Biguzzi, 2011	**Placenta weight (100g increments):** 1.24 (1.13-1.36)	aOR	Sig	VB	**PPH:** EBL ≥500mL	6,011
Biguzzi, 2014	**Placental weight (100g increments):** 1.32 (1.21-1.45)	aOR	Sig	VB	**PPH:** EBL ≥500mL	3,219
Lee, 2017	**Placental weight (g):** 1.00 (0.99-1.00)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210
Lee, 2018	**Placental weight (g):** 1.00 (0.99-1.00)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506
			Annual delivery volume of hospital			
Dionne, 2015	**Annual number of deliveries in the unit:** **PPH 1:** ≤1500: 0.83 (0.46-1.50) 1501-3000: 0.80 (0.44-1.46) >3000: ref	aOR	NS	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	CTL: 762 PPH: 3,852 SPPH: 1,048
	PPH 2: ≤1500: 0.73 (0.40-1.34) 1501-3000:0.73 (0.40-1.34) >3000: ref	aOR	NS			

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Merriam, 2018	**Annual delivery volume:** **PPH 1:** < 1000: 1.14 (1.04-1.25) 1000-2000:1.04 (0.97-1.13) >2000: ref **PPH 2:** < 1000: 1.10 (0.99) 1000-2000: (0.94-1.14) >2000: ref	aRR aRR	Sig NS	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088
Short cervical length before delivery (<2.5cm)						
Lee, 2017	**Short cervical length before delivery (<2.5cm):** 1.45 (0.35-6.07)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210
Lee, 2018	**Short cervical length before delivery (<2.5cm):** 2.01 (0.92-4.75)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506
Time of delivery						
Butwick, 2017	**Pre-labour CS:** Weekday daytime: ref Weekday nightime: 0.98 (0.4-2.39) Weekend: 1.64 (0.83-3.24) **Intrapartum CS:** Weekday daytime: ref Weekday nightime: 0.64 (0.39-1.03) Weekend: 1.05 (0.63-1.73)	aOR aOR	NS NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** Case: 269 CTL: 550 **Intrapartum CS** Case: 278 CTL: 572

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Miller 2017	**PPH:** Weekday daytime: 40 (25.2%) Weekday nighttime: 69 (43.4%) Weekend: 50 (31.5%) **CTL:** Weekday daytime: 88 (27.7%) Weekday nighttime: 138 (43.4%) Weekend: 92 (28.9%)	%	NS	VB	**PPH:** EBL ≥500mL	**PPH:** 159 **CTL:** 318
Uterine contraction at caesarean section						
Lee, 2017	**Uterine contraction at caesarean section:** 0.00 (0.00-0.00)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	210
Lee, 2018	**Uterine contraction at caesarean section:** 0.69 (0.21-2.27)	aOR	NS	CS	**SPPH:** intraoperative blood loss ≥2000mL	506
Year of birth						

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Merriam, 2018	**PPH 1:** 1998: ref 1999: 0.98 (0.93-1.03) 2000: 0.99 (0.94-1.05) 2001: 1.01 (0.96-1.07) 2002: 1.03 (0.98-1.09) 2003: 1.08 (1.02-1.14) 2004: 1.09 (1.03-1.15) 2005: 1.08 (1.02-1.14) 2006: 1.09 (1.03-1.15) 2007: 0.95 (0.89-1.00) 2008: 0.96 (0.90-1.03) 2009: 1.01 (0.95-1.07) 2010: 1.04 (0.98-1.11) 2011: 1.06 (0.99-1.13)	aRR	Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088
	PPH 2: 1998: ref 1999: 1.00 (0.91-1.09) 2000: 1.11 (1.01-1.22) 2001: 1.17 (1.06-1.29) 2002: 1.30 (1.18-1.44) 2003: 1.45 (1.31-1.60) 2004: 1.51 (1.37-1.66) 2005: 1.68 (1.51-1.88) 2006: 1.84 (1.68-2.02) 2007: 1.99 (1.81-2.19) 2008: 2.10 (1.91-2.31) 2009: 2.34 (2.12-2.58) 2010: 2.51 (2.28-2.76) 2011: 2.82 (2.54-3.12)	aRR	Sig			

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
Oberg, 2014b	1997-2000: ref 2001-04: 1.09 (1.04-1.14) 2005-09: 1.15 (1.10-1.20)	uOR	Sig	VB	**PPH:** ICD codes, typically EBL ≥1000mL	307,756
Cervical incompetence						
Sheiner, 2009	**PPH 1:** 1.5% **PPH 2:** 0.6% **PPH 3:** 2.0% **CTL:**0.5%	%	Sig	VB, CS	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥500mL and revision of birth canal under anaesthesia **PPH 3:** EBL ≥500mL and blood transfusion	**PPH:** 137 **PPH2:** 330 **PPH3:** 199 **CTL:** 153,645
Hospital bed size						
Merriam, 2018	**PPH 1:** Small: ref Medium: 0.99 (0.92-1.06) Large: 0.91 (0.85-0.97) Unknown: 0.80 (0.61-1.06)	aRR	Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088
	PPH 2 Small: ref Medium: 0.99 (0.89-1.09) Large: 0.86 (0.87-1.06) Unknown: 0.56 (0.26-1.23)	aRR	Sig			
Hospital location						
Merriam, 2018	**PPH 1:** Rural: ref Urban: 1.33 (1.24-1.42)	aRR	Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088
	PPH 2 Rural: ref Urban: 1.14 (1.05-1.25)	aRR	Sig			

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Hospital region			
Merriam, 2018	**PPH 1:** Northeast: ref Midwest: 1.15 (1.06-1.25) South: 0.83 (0.76-0.91) West: 1.21 (1.11-1.32)	aRR	Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088
	PPH 2 Northeast: ref Midwest: 0.89 (0.79-1.01) South: 0.99 (0.90-1.10) West: 0.88 (0.78-0.99)	aRR	Sig			
			Hospital status			
Dionne, 2015	**PPH 1:** Public university: 30.3% Public non-university: 51.2% Private: 18.5% **PPH 2:** >Public university: 30.2% Public non-university: 51.4% Private: 18.3% **CTL:** Public university: 21.3% Public non-university: 49.1% Private: 29.7%	%	NS	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	CTL: 762 PPH: 3,852 SPPH: 1,048

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Hospital teaching			
Merriam, 2018	**PPH 1:** Non-teaching: ref Teaching: 0.95 (0.88-1.02) **PPH 2:** Non-teaching: ref Teaching: 0.84 (0.77-0.92)	aRR aRR	NS Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088
			Incomplete placenta/ membranes ragged			
Henry, 2005	**PPH 1:** Complete placenta: ref Incomplete placenta/ membranes ragged: 3.56 (1.52-8.36) **PPH 2:** Complete placenta: ref Incomplete placenta/ membranes ragged: 7.86 (2.66-23.17)	aOR aOR	Sig Sig	VB	**PPH 1:** EBL ≥500mL **PPH 2:** EBL ≥1000mL or admission to High Dependency Ward, return to operating theatre, or blood transfusion	**CTL:** 125 **PPH 1:** 125 **PPH 2:** 50
			Intertwin time interval >30minutes			
Suzuki, 2007	**Intertwin time interval >30minutes:** 1.58 (0.68-3.70)	uOR	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 145

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Level of the maternity unit			
Dionne, 2015	**PPH 1:** Level 1: 28.4% Level 2: 49.3% Level 3: 22.3% **PPH 2:** Level 1: 28.0% Level 2: 48.5% Level 3: 23.6% **CTL:** Level 1: 33.5% Level 2: 51.2% Level 3: 15.4%	%	NS	VB	**PPH 1:** EBL ≥500mL or peripartum haemoglobin decrease ≥2g/dL **PPH 2:** Transfusion of ≥2 units RBC or peripartum haemoglobin decrease ≥4g/dL	**CTL:** 762 **PPH:** 3,852 **SPPH:** 1,048
			One placenta			
Suzuki, 2007	**One placenta:** 0.66 (0.32-1.33)	uOR	NS	VB	**PPH:** EBL ≥1000mL	**PPH:** 41 **CTL:** 146
			Short cervical length before delivery (<2.0cm)			
Lee, 2017	**Short cervical length before delivery (<2.0cm):** 7.13 (1.01-50.25)	aOR	Sig	CS	**SPPH:** intraoperative blood loss ≥2000mL	210
			Uterine incision			
Butwick, 2017	**Pre-labour CS:** Uterine incision: Transverse: ref Other: 4.12 (2.05-8.26) **Intrapartum CS:** Uterine incision: Transverse: ref Other: 2.75 (0.95-8.01)	aOR aOR	Sig NS	CS	**SPPH:** EBL ≥ 1500mL or transfusion within 48 hrs	**Pre-labour CS** Case: 269 CTL: 550 **Intrapartum CS** Case: 278 CTL: 572

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Uterine rupture			
Mehrabadi, 2013	**Uterine rupture:** 10.6 (8.67-12.9)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Or as diagnosed by healthcare provider	2,193,425
			VBAC			
Lisonkova, 2016	**Vaginal delivery without prior CS:** Ref **Vaginal delivery with prior CS:** 3.70 (1.08-12.7) **CS without prev CS:** 0.53 (0.32-0.88) **CS with prior CS:** 0.47 (0.24-0.95)	aOR	Sig	VB, CS	**PPH (VB):** EBL ≥500mL **PPH (CS):** EBL ≥1000mL Atonic PPH only	**PPH:** 393 **CTL:** 393

Table A.5.7: Baby characteristics

Study	*Effect size & definitions*	*Stat*	*Sig*	*Delivery*	*Definition of PPH*	*Number of women*
			Birth Status			
Davey, 2019	**All women:** Liveborn: ref Stillbirn: 1.88 (1.4-2.5) **Women who experienced labour:** Liveborn: ref Stillborn: 1.69 (1.2-2.4)	aOR aOR	Sig Sig	VB, CS	**SPPH:** EBL ≥1500mL	364,701
Magan, 2005b	**Intrauterine fetal death:** 2.6 (1.1-5.7)	aOR	Sig	VB	**PPH:** CBL≥1000mL and/or transfusion	13,868
Merriam, 2018	**PPH 1:** Stillbirth: 3.25 (3.13-3.39) **PPH 2:** Stillbirth: 7.79 (7.31-8.67)	aRR aRR	Sig Sig	VB, CS	**PPH 1:** ICD codes for PPH **PPH 2:** ICD codes for PPH and/or transfusion	55,140,088
			Head Circumference			
Hiersch, 2016	**PPH:** 34.7 (1.3) **CTL:** 34.5 (1.3) p=0.16	Mean (SD)	NS	VB (vacuum only)	**PPH:** EBL ≥500mL, haemoglobin drop ≥3 g/dL	1,154

Appendix B: Chapter 3

Appendix B.1: Members of the UKMidSS Steering Committee

UK Midwifery Study System Steering Group (in addition to RR and JJK):

Mervi Jokinen (Chair), Royal College of Midwives; Philippa Cox (Vice Chair, from February 2022), Homerton University Hospital; Meena Bhatia (from June 2019), Oxford University Hospitals NHS Foundation Trust; Posy Bidwell, The Royal College of Obstetricians and Gynaecologists (until Feb 2020); Jan Butler (until December 2018), Cambridge University Hospitals NHS Foundation Trust; Karen Joash (from June 2019), Imperial College Healthcare NHS Trust; Eddie Morris (until May 2020), Royal College of Obstetricians and Gynaecologists; Jackie O'Neill (from February 2019), South Eastern Trust; Dharmintra Pasupathy, Faculty of Medicine and Health, University of Sydney; Rachel Plachcinski, Independent parent, patient and public involvement consultant; Jane Rogers, Consultant Midwife; formerly at University Hospitals Southampton; Aung Soe (until October 2021), Medway NHS Foundation Trust; Anna Temke (from February 2019), James Cook University Hospital; Catherine Williams, Independent parent, patient and public involvement consultant; Phillis Winter, Midwifery Team Manager at NHS Tayside (until Feb 2019).

Table B.2: UKMidSS data collection form

Data item	*Details*
Maternal socio-demographic information	
Age at delivery	
Ethnicity	01. White British 02. White Irish 03. Any other White background 04. Mixed White & Black Caribbean 05. Mixed White & Black African 06. Mixed White & Asian 07. Any other mixed background 08. Indian 09. Pakistani 10. Bangladeshi 11. Any other Asian background 12. Black Caribbean 13. Black African 14. Any other Black background 15. Chinese 16. Any other ethnic group 17. Not recorded For analysis, these were categorised as: 1. White (UK and Ireland) 2. White (other) 3. Asian 4. Black 5. Other
Woman's employment status	
Woman's occupation	This was a free text question. Responses were coded using the Office of National Statistics Occupation Coding Tool. This tool allows users to code occupation titles against the Standard Occupational Classification 2010. The title of the woman's occupation, provided as free text, was entered into the search bar in the coding tool and the associated NS-SEC CLASS code was assigned to the record. NS-SEC CLASS codes were categorised as follows: NS-SEC CODES 1.1, 1.2, 2 = 'Higher managerial' NS-SEC CODE 3 = 'Intermediate' NS-SEC CODE 4 = 'Small employers' NS-SEC CODE 5 = 'Lower supervisory/tech' NS-SEC CODE 6 & 7 = 'Semi-routine' Categories for which there was not NS-SEC CODE were: 'Employed, but occupation unrecorded/uncodable' 'Unemployed/student' 'Employment status unknown'
Partner's employment status	

Data item	*Details*
Partner's occupation	This was coded as per woman's occupation, above. Where a woman was unemployed or her occupation was not able to be coded, the partner's occupation, if any, was used to determine socioeconomic status.
Children in Low-income Families Measure score	Midwives entered maternal postcodes and derived the corresponding CLFM.
Pre-existing clinical characteristics	
Height	Height in cm at booking
Weight	Weight in kg at booking
BMI	Number between 15-40, provided to one decimal place. For analysis, these were categorised as: 1. <18.5 2. 18.5-24.9 3. 25-29.9 4. 30-35 5. >35
Smoking status at delivery	01. Never smoked 02. Gave up prior to pregnancy 03. Gave up during pregnancy 04. Current smoker 05. Not recorded Categorised as: Smoked during pregnancy Did not smoke during pregnancy
Previous pregnancies	Y/N
Number of pregnancies >24 weeks gestation	
Number of pregnancy losses <24 weeks gestation	
Complications in previous pregnancies	01. Primary postpartum haemorrhage needing treatment or transfusion 02. Retained placenta requiring manual removal 03. Caesarean section 04. Uterine surgery (excluding Caesarean section) 05. Other, please specify* 06. None of the above
Clinical characteristics arising during pregnancy	
Assisted conception	Y/N
Estimated date of delivery	DD/MM/YY
Gestational age	Completed weeks

Data item	*Details*
Medical conditions known prior to admission	01. Essential hypertension 02. Confirmed cardiac disease 03. Thromboembolic disorder 04. Atypical antibodies 05. Hyperthyroidism 06. Diabetes 07. Renal disease 08. Epilepsy 09. Other, please specify* 10. None of the above
Risk factors identified antenatally	01. BMI at booking >35kg/m^2 02. Post-term (>42 weeks) 03. Anaemia (haemoglobin <105g/litre) 04. Group B Streptococcus 05. Antepartum haemorrhage 06. Pre-eclampsia / pregnancy induced hypertension 07. Gestational diabetes 08. Malpresentation (breech or transverse lie) 09. Other, please specify* 10. None of the above
Intrapartum factors	
Labour dates and times	Midwives entered dates and times to generate the duration of the following variables: 01. Duration of labour care (hours) 02. Time between birth and oxytocic administration 03. 3rd stage duration (hours) 04. Time from birth to decision to transfer/escalate for PPH 05. Time from decision to transfer to start of transfer for PPH 06. Time from start of transfer to arrival in obstetric unit 07. Time from arrival in obstetric unit to first seen by obstetrician for PPH 08. Overall time from decision to transfer for PPH to first seen by OB for PPH 09. Maternal postnatal length of stay
Induced labour	Y/N

Data item	*Details*
Complications identified at the start of labour care	01. Maternal tachycardia 02. Essential hypertension 03. Proteinuria 04. Maternal pyrexia 05. Vaginal blood loss 06. Prolonged rupture of membranes 07. Significant meconium 08. Reported pain differing from pain normally associated with contractions 09. Abnormal presentation, including cord presentation 10. Transverse or oblique lie 11. High or free-floating head 12. Suspected fetal growth restriction or macrosomia 13. Suspected anhydramnios or polyhydramnios 14. Fetal heart rate abnormality 15. Deceleration in fetal heart rate 16. Reduced fetal movements in the last 24 hours 17. None of the above
Stage of labour at start of care	01. Latent stage 02. Active 1st stage 03. Passive 2nd stage 04. Active 2nd stage
Immersion in water for pain relief in labour	Y/N
Complications identified during labour care	01. Maternal tachycardia 02. Hypertension 03. Maternal pyrexia 04. Vaginal blood loss 05. Prolonged rupture of membranes 06. Significant meconium 07. Reported pain differing from pain normally associated with contractions 08. Confirmed/suspected delay in first stage of labour 09. Confirmed/suspected delay in second stage of labour 10. Obstetric emergency 11. Abnormal presentation, including cord presentation 12. Transverse or oblique lie 13. High or free-floating head 14. Fetal heart rate abnormality 15. Deceleration in fetal heart rate 16. None of the above
Transfer to obstetric care	Y/N

Data item	*Details*
Reason for transfer to obstetric care	01. Maternal tachycardia 02. Hypertension 03. Maternal pyrexia 04. Prolonged rupture of membranes 05. Significant meconium 06. Confirmed/suspected delay in first stage of labour 07. Confirmed/suspected delay in second stage of labour 08. Abnormal presentation, including cord presentation 09. Transverse or oblique lie 10. High or free-floating head 11. Fetal heart rate abnormality 12. Deceleration in fetal heart rate 13. Other, please specify*
Birth factors	
Mode of birth	01. Spontaneous vertex birth 02. Vaginal Breech 03. Ventouse 04. Forceps
Birth in water	Y/N
Syntocinon or Syntometrine as part of active management in 3rd stage	Y/N
3rd or 4th degree tear	Y/N
Duration third stage of labour	Derived from labour durations, above
Birthweight	Baby's weight at birth in grams
Maternal outcomes	
Estimated blood loss	mL
Treatment for PPH	01. Bimanual compression 02. Catheterisation 03. Cannulation/IV fluids 04. First-line uterotonics, e.g. syntocinon, syntometrine, misoprostol, ergometrine, prostaglandin 05. Second-line uterotonics, e.g. Hemabate, Carboprost 06. Blood products/transfusion or iron transfusion 07. Tranexamic acid 08. Invasive procedure, e.g. intra-abdominal packing, intrauterine balloons or packing, interventional radiology, brace suture, hysterectomy 09. Other, please specify* 10. Not recorded
Major obstetric haemorrhage called	Y/N
Blood transfusion received	Y/N
Units of blood received	

Data item	*Details*
Primary cause of PPH	01. Uterine atony 02. Genital tract trauma 03. Retained products / morbidly adherent placenta 04. Other, please specify* 05. Not recorded
Higher level care received within 48 hours of birth	Y/N
Highest level of care received	01. Enhanced maternity care (high dependency) 02. Intensive care 03. Other higher level care, please specify (free text)
Main reason for higher level care	Free text*
Maternal morbidity	Free text*
Maternal death	Y/N
Neonatal outcomes	
Sex	01. Male 02. Female 03. Indeterminate
Stillbirth	Y/N
Apgar score at 5 minutes	
Breastfed before discharge	Y/N
Admitted to higher level care within 48 hours	Y/N
Reason for admission	01. Respiratory problems 02. Suspected perinatal asphyxia 03. Hypoglycaemia 04. Physical trauma/birth injury 05. Feeding problems 06. Suspected infection 07. Meconium aspiration 08. Jaundice 09. Congenital anomaly 10. Maternal admission to higher level care 11. Maternal substance-misuse 12. Other, please specify
Neonatal morbidity	Free text*
Neonatal death	Y/N
Notes	Any other information Details provided here were used to check eligibility and case status and to validate or confirm data provided in other fields

Appendix B.3: Coding dictionary for 'Other' categories

Previous pregnancy complications

Code **PREV_COMP_05_OTH_coded** using the following:

1. Primary PPH needing treatment of transfusion
2. Retained placenta requiring manual removal
3. Caesarean section
4. Uterine surgery (excluding CS)
5. Other*
6. None of the above

**Valid options for 5 (Other):*

- Pre-eclampsia requiring preterm birth
- Placental abruption with adverse outcome
- Eclampsia
- Uterine rupture
- Unexplained stillbirth/neonatal death or previous death related to intrapartum difficulty
- Previous baby with neonatal encephalopathy
- Shoulder dystocia

If not a valid option, code as 'None of the above'

Medical risk factors

Code **MED_RF_09_OTH_coded** using the following:

1. Hypertension
2. Confirmed cardiac disease
3. Thromboembolic disorder
4. Atypical antibodies
5. Hyperthyroidism
6. Diabetes
7. Renal disease
8. Epilepsy
9. Other*
10. None of the above

**Valid options for 9 (Other):*

- Asthma requiring an increase in treatment or hospital treatment
- Haemoglobinopathies - sickle-cell disease, beta-thalassaemia major
- Immune thrombocytopenia purpura or other platelet disorder
- Hepatitis B/C with abnormal liver function tests

If not a valid option, code as 'None of the above'

NOTE: Check for any risk factors listed here which are actually **current pregnancy risk factors** which should be coded under **PREG_RF_06_OTH_coded**

Current pregnancy risk factors

Code **PREG_RF_09_OTH_coded** using the following:

1. BMI at booking of greater than 35 kg/m2
2. Post-term (>42 weeks)
3. Anaemia (haemoglobin <85 g/litre)
4. Group B Streptococcus
5. Antepartum haemorrhage
6. Pre eclampsia or pregnancy induced hypertension
7. Gestational diabetes
8. Malpresentation (breech/transverse lie)
9. Other *
10. None of the above

**Valid options for 9 (Other):*

Preterm labour or preterm prelabour rupture of membranes

- Substance misuse or alcohol dependency
- Small for gestational age
- Multiple birth
- Placenta praevia
- Anaemia – haemoglobin less than 85g/litre at onset of labour
- Induction of labour
- Recurrent antepartum haemorrhage

If not a valid option, code as 'None of the above'

'Other' primary reason for transfer

Code **OBSTRANOTH** using the following:

1. Maternal tachycardia
2. Hypertension
3. Maternal pyrexia
4. Prolonged rupture of membranes
5. Significant meconium
6. Confirmed/suspected delay in first stage of labour
7. Confirmed/suspected delay in second stage of labour
8. Abnormal presentation, including cord presentation
9. Transverse or oblique lie
10. High or free-floating head
11. Fetal heart rate abnormality
12. Deceleration in fetal heart rate
13. Other

Common categories in other coded as new categories:

14. Shoulder dystocia
15. Antepartum haemorrhage

Treatment for PPH

1. Bimanual compression
2. Catheterisation
3. Cannulation/IV fluids
4. First-line uterotonics
5. Second-line uterotonics
6. Blood products/transfusion
7. Tranexamic acid
8. Invasive procedure
9. Other

Code BLOODTRT_09_OTH using the following:

0. No additional treatment (includes Uterine massage, and FBC)
1. Vaginal pack
2. Repair of tear/Suturing
3. Manual removal of placenta
4. Evaluation under anaesthesia

Underlying cause of PPH

Main categories

1. Uterine atony
2. Genital tract trauma
3. Retained products/morbidly adherent placenta
4. Other
5. Not recorded

Code PPHCAUSEOTH using the following:

6. Thrombin (including placental abruption, hypertension, pre-eclampsia, von Willebrand's disease, haemophilia A/B, ITP or acquired coagulopathy i.e. DIC, HELLP.)
7. Unknown (including 'physiological third stage', 'lscs', 'clots')

What was the highest level of care the woman received?

1. Enhanced maternity care (high dependency)
2. Intensive care
3. Other higher-level care

Others coded as:

1. Enhanced maternity care (1-1 care, AOCU, High dependency on LW)
2. Not higher level care (Delivery unit, Maternal obc/hb, maternal delivery suite)

Main reason for admission to higher level maternal care

These are all free-text. Code as:

1. PPH (include observation following PPH, Routine care following PPH, Transfusion, MROP)
2. Recovery from theatre procedure
3. Observation (where PPH not mentioned)
4. Sepsis/pyrexia
5. Other/not clear

Maternal morbidity

These are all free-text. Derived categories and codes below:

1. Readmission secondary PPH/ retained placenta
2. Pyrexia/sepsis
3. Anaemia
4. Urinary retention
5. Other
6. None of the above

Reason for admission to neonatal unit

Code NICU_REAS_OTH _coded using the following:

1. Respiratory problems
2. Suspected perinatal asphyxia
3. Hypoglycaemia
4. Physical trauma/birth injury
5. Feeding problems
6. Suspected infection
7. Meconium aspiration
8. Jaundice
9. Congenital anomaly
10. Maternal admission to higher level care
11. Maternal substance-misuse
12. Other*

**Valid options for 12 (Other):*

- Persistent hypothermia, jaundice, MSL
- Observation for low Apgar
- Full resuscitation
- Macrosomia
- Bowl obstruction
- Blood in nappy 4x occasions
- Baby transferrer to a London hospital
- Baby sent for cooling in a tertiary unit, suspected HIE
- ABO isoimmunisation and jaundice

Neonatal morbidity

These are all free-text. Derived categories and codes below:

1. Birth injury (fracture and pulsy)
2. Congenital anomaly
3. Jaundice
4. Sepsis/ Infection
5. Meconium at birth
6. Respiratory distress
7. Other

Appendix B.4 Univariable and multivariable analysis of low-risk women

Tables B.1-5 present the unadjusted analysis of pre-existing clinical, clinical characteristics arising during pregnancy, intrapartum and birth related factors associated with PPH requiring transfer among low-risk women.

The sociodemographic profiles of cases and controls were similar among women who were considered low-risk (Table B.1, below). As seen in the main analysis, smoking status was significantly associated with PPH requiring transfer among low-risk women (OR=0.75; 95% CI 0.58-0.96).

Table B.3.1 Sociodemographic characteristics of mothers among low-risk women

	Controls (n = 1268)		***Cases (n = 1219)***		***Unadjusted ORs***		***p value***
	n	***%***	***n***	***%***	***OR***	***95% CI***	
Maternal age							0.808
<20	44	3.5	40	3.3	0.98	(0.65-1.5)	
20-24	189	14.9	177	14.2	1.01	(0.77-1.33)	
25-29	369	29.1	341	28.0	1	.	
30-34	428	33.8	447	36.7	1.13	(0.91-1.4)	
35-40	219	17.3	198	16.2	0.98	(0.75-1.27)	
>40	19	1.5	16	1.3	0.91	(0.45-1.85)	
Missing	0		0		.	.	
Smoking status							0.025
Did not smoke during pregnancy	1099	86.7	1090	89.4	1	.	
Smoked during pregnancy	141	11.1	106	8.7	0.76	(0.60-0.97)	
Missing	28	2.2	23	1.9	.	.	
Area deprivation quintile							0.171
1st (least deprived)	283	22.4	313	25.9	1	.	
2nd	272	21.6	249	20.6	0.82	(0.67-1.00)	
3rd	254	20.1	215	17.8	0.75	(0.61-0.94)	
4th	234	18.6	219	18.1	0.81	(0.66-1.00)	
5th (most deprived)	218	17.3	214	17.7	0.89	(0.71-1.11)	
Missing	7	.	9		.	.	
Ethnicity							0.995
White (UK and Ireland)	854	67.4	818	67.1	1	.	
White (other)	150	11.8	148	12.1	1.03	(0.80-1.33)	
Asian	139	11.0	138	11.3	1.04	(0.80-1.33)	
Black	52	4.1	49	4.0	0.98	(0.67-1.44)	
Other	73	5.8	66	5.4	0.94	(0.63-1.42)	
Socioeconomic status							0.064
Higher managerial	376	29.0	419	35.0	1	.	
Intermediate	253	19.6	217	17.6	0.77	(0.61-0.96)	
Routine and manual	300	24.3	274	22.3	0.82	(0.68-0.99)	
Employed, occupation unknown	88	7.1	86	6.9	0.88	(0.64-1.19)	
Unemployed/student	87	6.9	59	5.3	0.61	(0.42-0.89)	
Not recorded	164	13.2	164	12.9	0.90	(0.72-1.12)	

Giving birth for the first time increased the odds of PPH requiring transfer (OR=1.82; 95% CI 1.56-2.14) (Table B.2), while having given birth 2 or more times decreased the odds of PPH requiring transfer (OR=0.74; 95% CI 0.59-0.93), compared with women who had given birth once before.

Table B.2 Pre-existing clinical characteristics among low-risk women

	Controls (n = 1315)		*Cases (n = 1286)*		*Unadjusted ORs*		*p value*
	n	*%*	*n*	*%*	*OR*	*95% CI*	
BMI at booking							0.829
< 18.5	38	3.0	34	2.8	0.94	(0.6-1.49)	
18.5-24.9	706	55.7	671	55.1	1.00	(0-0)	
25-29.9	357	28.2	339	27.8	1.00	(0.83-1.2)	
30-35	127	10.0	139	11.4	1.15	(0.9-1.47)	
>35	0	0	0	0			
BMI not recorded	40	3.1	36	3.0	0.95	(0.64-1.39)	
Parity[1]							<0.001
0	479	37.8	666	54.7	1.83	(1.56-2.14)	
1	537	42.4	409	33.6	1		
2 or more	252	19.9	144	11.8	0.75	(0.59-0.95)	
Missing	0	.	0	.	.	.	

[1] Number of previous pregnancies carried to at least 24 completed weeks' gestation

Low-risk women who gave birth after 41 weeks' gestation had increased odds of PPH requiring transfer (OR=1.40; 95% CI 1.13-1.75) compared with women who gave birth at 40 weeks' gestation, while giving birth at gestational ages <40 weeks reduced the odds of PPH requiring transfer (Table B.3).

Table B.3 Clinical characteristics arising during pregnancy among low-risk women

	Controls (n = 1314)		*Cases (n = 1286)*		*Unadjusted ORs*		*p value*
	n	*%*	*n*	*%*	*OR*	*95% CI*	
Sex of baby							0.714
Male	620	49.1	588	48.4	1.03	(0.88-1.19)	
Female	644	50.1	628	51.6	1	.	
Missing	4		3	.			
Gestational age (weeks)							<0.001
36-37	56	4.4	31	2.5	0.55	(0.34-0.91)	
38	147	11.6	114	9.4	0.78	(0.59-1.02)	
39	352	27.8	293	24.0	0.83	(0.71-0.98)	
40	514	40.5	513	42.1	1		
41-42	199	15.7	268	22.0	1.35	(1.07-1.7)	
Missing	0	.	0	.	.	.	

Intrapartum risk factors among low-risk women were broadly similar to the main analysis, Table B.4. Induction of labour increased the odds of PPH among low-risk women (OR=1.52; 95% CI 1.01-2.27). Maternal complications identified at the start of labour care, and maternal and fetal complications identified during labour (before the birth) were all significantly associated with increased odds of PPH requiring transfer among low-risk women, p<0.05 for all variables.

Table B.4 Intrapartum factors among low-risk women

	Controls (n =1315)		Cases (n = 1286)		Unadjusted ORs		
	n	%	n	%	OR	95% CI	p value
Stage of labour at start of care							0.440
Latent stage	228	18.0	224	18.4	1.00	(0.79-1.26)	
Active 1st stage	896	70.8	880	72.4	1	.	
Passive 2nd stage	46	3.6	40	3.3	0.89	(0.59-1.33)	
Active 2nd stage	95	7.5	71	5.8	0.77	(0.54-1.07)	
Missing	3	.	4	.	.	.	
Maternal complications identified at the start of labour care[1]							<0.001
None	1254	99.2	1184	97.5	1	.	
One or more	10	0.8	31	2.6	3.28	(1.68-6.44)	
Missing	4	.	4	.	.	.	
Fetal complications identified at the start of labour care[2]							0.20
None	1240	98.1	1183	97.4	1	.	
One or more	24	1.9	32	2.6	1.40	(0.82-2.40)	
Missing	4	.	4	.	.	.	
Maternal complications identified during labour (before birth)[3]							<0.001
None	1249	98.5	1181	96.9	1	.	
One or more	19	1.5	38	3.1	2.11	(1.41-3.18)	
Missing	0	.	0	.	.	.	
Fetal complications identified during labour (before birth)[4]							0.066
None	1185	93.5	1117	91.7	1	.	
One or more	83	6.6	102	8.4	1.30	(0.98-1.73)	
Missing	0	.	0	.	.	.	

[1] Maternal tachycardia, hypertension, proteinuria, maternal pyrexia, vaginal blood loss, prolonged rupture of membranes, and reported pain differing from pain normally associated with contractions.
[2] Significant meconium, abnormal presentation, high or free-floating head, suspected anhydramnios or polyhydramnios, fetal heart rate abnormality, deceleration in fetal heart rate, and reduced fetal movements in the last 24 hours.
[3] Maternal tachycardia, hypertension, maternal prexia, vaginal blood loss, prolonged rupture of membranes.
[4] Significant meconium, confirmed/suspected delay in first stage of labour, confirmed\suspected delay in second stage of labour, obstetric emergency, abnormal presentation, fetal heart rate abnormality, and deceleration in fetal heart rate.

Women who had an instrumental birth had increased odds of PPH requiring transfer compared with those with a spontaneous vertex birth (OR=3.66; 95% CI 2.36-5.66) (B.5). Third stage of labour lasting ≥60 minutes also increased odds (OR=4.46; 95% CI 3.09-6.42), as did perineal trauma (OR=4.98; 95% CI 3.36-7.38), Syntocinon/ Syntometrine administered for 3rd stage management (OR 1.46 95% CI

1.15-1.85) and giving birth to a baby weighting 3500-3999g (OR=1.61; 95% CI 1.34-1.94) or ≥4000g (OR 1.94 95% CI 1.52-2.51), compared with giving birth to a baby weighing 3000-3499g.

Table B.5 Birth-related factors among low-risk women

	Controls (n =1314)		*Cases (n =1315)*		*Unadjusted ORs*		*p value*
	n	*%*	*n*	*%*	*OR*	*95% CI*	
Labour/birth in water							0.061
No immersion in water	694	54.9	646	53.2	1	.	
Immersion in water for labour, land birth	191	15.1	217	17.9	1.22	(1.02-1.46)	
Birth in water	380	23.0	353	29.0	1.00	(0.85-1.16)	
Missing	3	.	4	.		.	
Birth mode							<0.001
Spontaneous vertex birth	1253	99.1	1181	97.5	1	.	
Vaginal breech	<5	<0.4	0	0	.	.	
Instrumental	9	0.7	30	2.5	3.54	(2.22-5.63)	
Missing	<5	.	8	.		.	
Duration of third stage of labour							<0.001
< 60 minutes	1201	94.7	1014	83.2	1	.	
≥ 60 minutes	47	3.7	177	14.5	4.46	(3.10-6.42)	
Missing	20	1.6	28	2.3	1.65	(0.91-3.04)	
Perineal trauma							<0.001
<3rd degree tear or no tear	1223	96.7	1035	85.2	1	.	
3rd or 4th degree tear	42	3.3	180	14.8	5.06	(3.41-7.53)	
Missing	3	.	4	.			
Syntocinon/ Syntometrine for 3rd stage management							0.002
No	246	19.5	171	14.1	1	.	
Yes	1019	80.6	1044	85.9	1.47	(1.16-1.87)	
Missing	3	.	4	.	.	.	
Birthweight (g)							<0.001
<3000	176	13.9	93	7.7	0.68	(0.51-0.91)	
3000-3499	548	43.4	426	35.0	1	.	
3500-3999	417	33.0	511	42.0	1.58	(1.31-1.90)	
≥4000	123	9.7	186	15.3	1.95	(1.51-2.52)	
Missing	4	.	3	.	.	.	

Appendix B.5 Analysis of risk factors for PPH among cases and controls by unit type

Table B.6 Risk factors for PPH requiring transfer to obstetric care among cases according to the type of unit in which women gave birth

	FMU *n = 99*		*AMU* *n = 1,402*		*p value*
	n	*%*	*n*	*%*	
Smoking status					<0.001
Did not smoke during pregnancy	87	87.9	1264	90.2	
Smoked during pregnancy	5	5.0	116	8.3	
Missing	7	7.1	22	1.6	
Parity					0.640
0	54	54.6	696	49.6	
1	33	33.3	515	36.7	
2+	12	12.1	191	13.6	
Missing	0	.	0	.	
Previous pregnancy complication[1]					0.214
No previous complication	41	95.4	609	89.4	
Previous PPH	2	4.7	72	10.6	
Previous complication other than PPH	2	3.9	25	3.9	
Missing	0	.	0	.	
Gestational age					0.531
36-37	4	4.0	34	2.4	
38	12	12.1	131	9.3	
39	27	27.3	331	23.6	
40	34	34.3	555	39.6	
41+	22	22.2	351	25.0	
Missing	0	.	0	.	
Birth mode					0.110
Spontaneous vertex or vaginal breech birth	99	100.0	1357	97.5	
Instrumental birth	0	0	35	2.5	
Missing	0	.	10	.	
Duration of third stage of labour					<0.001
< 60 minutes	77	77.8	1163	82.9	
≥ 60 minutes	12	12.1	215	15.3	
Missing	10	10.1	24	1.7	
Syntocinon/ Syntometrine for 3rd stage management					0.462
Yes	83	16.2	1208	86.5	
No	16	83.8	189	13.5	
Missing	0	.	5	.	
Perineal tear					0.319
<3rd degree tear or no tear	82	82.8	1208	86.4	
3rd or 4th degree tear	17	17.2	190	13.6	
Missing	0	.	4	.	
Birthweight (gm)					0.417
<3000	6	6.1	106	7.6	
3000-3499	27	27.3	481	34.3	
3500-3999	47	47.5	581	41.5	
≥4000	19	19.2	231	16.5	
Missing	0	.	3	.	

[1] Among multiparous women only

Table B.7 Risk factors for PPH requiring transfer to obstetric care among controls according to the type on unit in which they gave birth

	FMU		*AMU*		
	n = 94		*n = 1381*		*p value*
	n	*%*	*n*	*%*	
Smoking status					0.390
Did not smoke during pregnancy	77	81.9	1197	86.7	
Smoked during pregnancy	15	16.0	156	11.3	
Missing	2	12.1	28	2.0	
Parity					0.262
0	40	42.6	473	34.3	
1	37	39.4	617	44.7	
2+	17	18.1	291	21.1	
Missing	0	.	0	.	
Previous PPH[1]					0.421
Previous PPH	1	1.9	36	4.0	
No previous complication	53	98.1	856	96.0	
Missing	0	.	0	.	
Problems in a previous pregnancy, excluding PPH[1]					0.320
Previous complication other than PPH	0	0.0	16	1.8	
No previous complication	53	100.0	856	98.2	
Missing	0	.	0	.	
Gestational age					0.728
36-37	3	3.2	63	4.6	
38	14	14.9	153	11.1	
39	22	23.4	377	27.3	
40	39	41.5	552	40.0	
41-43	16	17.0	235	17.0	
Missing	0	.	1	.	
Birth mode					0.410
Spontaneous vertex or vaginal breech birth	93	100.0	1368	99.3	
Instrumental birth	0	0	10	0.7	
Missing	1	.	3	.	
Duration of third stage of labour					<0.001
< 60 minutes	79	84.0	1320	95.6	
≥ 60 minutes	10	10.6	43	3.1	
Missing	5	5.3	18	1.3	
Syntocinon/ Syntometrine for 3rd stage management					0.010
Yes	66	71.0	1128	81.8	
No	27	29.0	251	18.2	
Missing	1	.	2	.	
Perineal tear					0.600
<3rd degree tear or no tear	91	97.9	1336	96.9	
3rd or 4th degree tear	2	2.1	43	3.1	
Missing	1	.	2	.	
Birthweight (gm)					0.061
<3000	20	21.5	172	12.5	
3000-3499	34	36.6	610	44.3	
3500-3999	32	34.4	453	32.9	
≥4000	7	7.5	143	10.4	
Missing	1	.	3	.	

[1] Among multiparous women only

Appendix C: Chapter 4

Table C.1 Operationalisation of medical risk factors (NICE CG190 Table 6) to exclude women at higher risk of complications

Disease area	*Medical condition*	*Operationalisation in dataset*
Cardiovascular	Confirmed cardiac disease	Record includes ICD 9 codes *390-459*
	Hypertensive disorders	Record includes *hypertensio*n indicator
Respiratory	Asthma requiring an increase in treatment or hospital treatment	Data unavailable for some or all years
	Cystic fibrosis	Record includes ICD 9 code *277.0*
Haematological	Haemoglobinopathies – sickle-cell disease, beta-thalassaemia major	Record includes ICD 9 code *282.6 or 282.44*
	History of thromboembolic disorders	Record includes ICD 9 code *451-459*
	Immune thrombocytopenia purpura or other platelet disorder or platelet count below 100×109 /litre	Record includes ICD 9 code *451-459*
	von Willebrand's disease	Record includes ICD 9 code *286.4*
	Bleeding disorder in the woman or unborn baby	Record includes ICD 9 code *280-289*
	Atypical antibodies which carry a risk of haemolytic disease of the newborn	Data unavailable for some or all years
Endocrine	Hyperthyroidism	Record includes ICD 9 code *244.9, 242.9*
	Diabetes	Record includes ICD 9 codes 250 *or 648.8*
Infective	Risk factors associated with group B streptococcus whereby antibiotics in labour would be recommended	Data unavailable for some or all years
	Hepatitis B/C with abnormal liver function tests	Record includes ICD 9 codes *70.21, 70.31, 70.41 or 70.5*
	Carrier of/infected with HIV	Record includes ICD 9 code *233.6*
	Toxoplasmosis – women receiving treatment	Record includes *Toxoplasmosis* indicator
	Current active infection of chicken pox/rubella/genital herpes in the woman or baby	Record includes ICD 9 codes *056.9, 054.10, 052.9 or 052.0*
	Tuberculosis under treatment	Record includes ICD 9 codes *011.90 or 010-018*
Immune	Systemic lupus erythematosus	Record includes IC9 code *710.0*
	Scleroderma	Record includes ICD 9 codes *710.1*
Renal	Abnormal renal function	Record includes ICD 9 codes *794.4 or 593.9*

Disease area	*Medical condition*	*Operationalisation in dataset*
	Renal disease requiring supervision by a renal specialist	Record includes ICD 9 code *585.0*
Neurological	Epilepsy	Record includes ICD 9 codes *345.1 or 345.9*
	Myasthenia gravis	Record includes ICD 9 codes *358.00 or 358.01*
	Previous cerebrovascular accident	Data unavailable or poor quality
Gastrointestinal	Liver disease associated with current abnormal liver function tests	Record includes ICD 9 codes *570.0-573.9*
Psychiatric	Psychiatric disorder requiring current inpatient care	Data unavailable for some or all years

Table C.2 Operationalisation of medical risk factors (NICE CG190 Table 6) to exclude women at higher risk of complications

Factor	*Additional information*	*Operationalisation in dataset*
Previous complications	Unexplained stillbirth/neonatal death or previous death related to intrapartum difficulty	Record includes *Previous unexplained stillbirth* indicator
	Previous baby with neonatal encephalopathy	Record includes *Previous baby encephalopathy* indicator
	Pre-eclampsia requiring preterm birth	Record includes *Previous pre-eclampsia* indicator
	Placental abruption with adverse outcome	Record includes *Previous Placental Abruption* indicator
	Eclampsia	Record includes *Previous pre-eclampsia* indicator
	Uterine rupture	Record includes *Previous uterine rupture* indicator
	Primary postpartum haemorrhage requiring additional treatment or blood transfusion	Record includes *Previous blood loss >1500mL* indicator
	Retained placenta requiring manual removal in theatre	Record includes *Previous retained placenta* indicator
	Caesarean section	Record includes *Previous caesarean section* indicator
	Shoulder dystocia	Data unavailable for some or all years
Current pregnancy	Multiple birth	Record includes number of births in this pregnancy > 1
	Placenta praevia	Record includes *placenta praevia* indicator
	Pre-eclampsia or pregnancy-induced hypertension	Record includes P*re-eclampsia or gestational hypertension* indicator
	Preterm labour or preterm prelabour rupture of membranes	Record includes *Preterm, prelabour rupture of membranes* indicator
	Placental abruption	Record includes *placental abruption* indicator
	Anaemia – haemoglobin less than 85 g/litre at onset of labour	Data unavailable for some or all years
	Confirmed intrauterine death	Data unavailable for some or all years
	Induction of labour	Record includes *Induction* indicator
	Substance misuse	Data unavailable for some or all years
	Alcohol dependency requiring assessment or treatment	Data unavailable for some or all years
	Onset of gestational diabetes	Data unavailable for some or all years
	Malpresentation – breech or transverse lie	Record includes non-vertex presentation
	BMI at booking of greater than 35 kg/m2	Calculated BMI at booking > 35
	Recurrent antepartum haemorrhage	Record includes *Recurrent antepartum haemorrhage* indicator
	Small for gestational age in this pregnancy (less than fifth centile or	Data unavailable for some or all years

Factor	*Additional information*	*Operationalisation in dataset*
	reduced growth velocity on ultrasound)	
	Abnormal fetal heart rate/doppler studies	Data unavailable for some or all years
	Ultrasound diagnosis of oligo-/polyhydramnios	Record includes O*ligohydramnios /polyhydramnios* indicator
Previous gynaecological history	Myomectomy	Record includes Myomectomy indicator
	Hysterotomy	Record includes Hysterotomy indicator