Appendix 1. Search Strategy

PubMed (NCBI)
Date of Search: November 27, 2018
Number of results: 415

Search	Search Terms	Results
1	"Postpartum Hemorrhage"[Mesh]	6418
2	"postpartum hemorrhage"[tiab]	3390
3	"postpartum haemorrhage"[tiab]	1610
4	"postpartum hemorrhages"[tiab]	73
5	"postpartum haemorrhages"[tiab]	25
6	"pph"[tiab]	4712
7	"Uterine Hemorrhage"[Mesh]	20319
8	"uterine bleeding"[tiab]	4072
9	OR/ 1-8	27955
10	"Uterine Inertia"[Mesh]	901
11	"uterine inertia"[tiab]	259
12	"uterine atony"[tiab]	739
13	10 OR 11 OR 12	1488
14	"Causality"[Mesh]	758764
15	cause[tiab]	870225
16	causes[tiab]	495323
17	"Epidemiology"[Mesh]	25243
18	epidemiology[tiab]	173955
19	factor[tiab]	1546590
20	factors[tiab]	1837651
21	"Incidence"[Mesh]	236508
22	incidence[tiab]	676019
23	incidences[tiab]	28290

Ende HB, Lozada MJ, Chestnut DH, Osmundson S, Walden RL, Shotwell MS, et al. Risk factors for atonic postpartum hemorrhage: a systematic review and meta-analysis. Obstet Gynecol 2021;137.
The authors provided this information as a supplement to their article.

24	"Prevalence"[Mesh]	260188
25	prevalence[tiab]	550278
26	"Probability"[Mesh]	1253654
27	probability[tiab]	162608
28	"Risk"[Mesh]	1095652
29	risk[tiab]	1836035
30	risks[tiab]	212842
31	"Risk Assessment"[Mesh]	237303
32	"risk assessment"[tiab]	54436
33	"risk assessments"[tiab]	6003
34	"risk factors"[mesh]	745979
35	"risk factor"[tiab]	181739
36	"risk factors"[tiab]	392765
37	"Oxytocin"[Mesh]	18837
38	Oxytocin[tiab]	21942
39	Pitocin[tiab]	216
40	Syntocinon[tiab]	268
41	"Carboprost"[Mesh]	214
42	Hemabate[tiab]	9
43	"carboprost tromethamine" [Supplementary Concept]	15
44	"Methylergonovine"[Mesh]	486
45	Methergine[tiab]	101
46	"Methylergonovine Maleate"[tiab]	39
47	"Misoprostol"[Mesh]	3882
48	Misoprostol[tiab]	4573
49	Cytotec[tiab]	122
50	uterotonic[tiab]	856
51	uterotonics[tiab]	312
52	ecbolic[tiab]	67

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53	OR/ 14-52	6389650
54	9 AND 13 AND 53	497
56	54 AND (English[lang])	415

Appendix 2. Complete List of Studies Reporting on Each Risk Factor With Associated Statistics and Study Characteristics

PATIENT HISTORY AND DEMOGRAPHIC RISK FACTORS						
	Effect Size	Statistic	Number of Patients	Mode of Delivery	Atony Definition	Risk of Bias
Young Age						
Bateman	Ref: 20-34 <20: 1.8 (1.5-2.2)	aOR	876,641	VD, CD	ICD	LOW
Driessen	Ref: 25-35 <25: 0.95 (0.77-1.17)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Lutomski	Ref: 20-29 13-19: 0.98 (0.89-1.07)	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	Ref: 20-24 <20: 1.04 (0.96-1.13)	aOR	371,193	VD, CD	ICD	MOD
Regalia	Ref: 20-40 <20: 1.03 (0.37-2.83)	uOR	10,756	VD	Clinical diagnosis	HIGH
Wetta	Ref: not reported 1.0 (1.0-1.1)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Old Age						
Bateman	Ref: 20-34 35-39: 1.2 (1.0-1.4) ≥40: 1.7 (1.3-2.2)	aOR	876,641	VD, CD	ICD	LOW
Driessen	Ref: 25-35 >35: 0.98 (0.77-1.24)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Lao	Ref: <35 ≥35: 1.1 (0.97-1.28)	uOR	64,886	VD, CD	EBL, criteria for atony not reported	MOD
Lutomski	Ref: 20-29 30-39: 0.95 (0.91-0.98) 40-59: 0.91 (0.83-1.00)	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	Ref: 20-24 25-29: 0.95 (0.91-1.00) 30-34: 1.00 (0.95-1.04) 35-39: 1.05 (0.99-1.11) ≥40: 1.13 (1.04-1.24)	aOR	371,193	VD, CD	ICD	MOD
Regalia	Ref: 20-40 >40: 0.86 (0.42-1.76)	uOR	10,756	VD	Clinical diagnosis	HIGH
Wetta	Ref: not reported 1.0 (1.0-1.1)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH

Hispanic						
Bryant	Ref: White 1.21 (1.18-1.25) 1.44 (1.32-1.58) [with transfusion]	aOR	2,488,974	VD, CD	ICD	LOW
Grotegut	Ref: Caucasian 1.36 (0.41-5.59)	aOR	108	VD, CD	ICD	LOW
Marshall	Ref: White 1.24 (1.20-1.27)	uOR	1,352,691	VD, CD	ICD	MOD
Wetta	Ref: Black 2.26 (1.41-3.62)	aOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Asian						
Bryant	Ref: White Asian/Pacific Islander: 1.31 (1.25-1.38) 1.69 (1.47-1.94) [with transfusion]	aOR	2,488,974	VD, CD	ICD	LOW
Harvey	Ref: White Asian: 1.45 (1.37-1.53) Native Hawaiians and Other Pacific Islanders: 1.40 (1.32-1.48)	aOR	243,693	VD, CD	ICD	LOW
Siddiqui	Ref: Caucasian Asian American and Pacific Islander: 1.41 (1.40-1.42)	uOR	21,898,501	VD, CD	ICD	MOD
Native American						
Chalouhi	Ref: non-native 2.0 (1.1-3.7)	uOR	1,062	VD	Clinical diagnosis AND uterotonic administration	HIGH
African American						
Bryant	Ref: White 0.88 (0.85-0.92) 1.18 (1.07-1.31) [with transfusion]	aOR	2,488,974	VD, CD	ICD	LOW
Marshall	Ref: White 1.14 (1.10-1.18)	uOR	1,352,691	VD, CD	ICD	MOD
Wetta	Ref: White 0.68 (0.42-1.09)	aOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Nulliparity						

Driessen	Ref: Multiparous no prior CD Nulliparous: 1.88 (1.51-2.33) Multiparous prior CD: 1.66 (1.15-2.41)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Feerasta	Ref: Multiparous Nulliparous 1.26 (0.77-2.07)	uOR	332	VD	Not reported	HIGH
Marshall	Ref: Multiparous Nulliparous: 0.41 (0.38-0.43)	uOR	1,352,691	VD, CD	ICD	MOD
Mehrabadi	Ref: parity 1-2 0: 1.29 (1.24-1.34) 3-4: 0.95 (0.88-1.02) ≥5: 0.94 (0.78-1.12)	aOR	371,193	VD, CD	ICD	MOD
Regalia	Ref: Multiparous Nulliparous: 1.49 (1.20-1.82)	uOR	10,756	VD	Clinical diagnosis	HIGH
Wetta	Ref: Multiparous Nulliparous: 1.4 (1.0-2.1)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Prior PPH						
Driessen	1.47 (1.02-2.13)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Feerasta	3.03 (0.40-26.6)	uOR	332	VD	Not reported	HIGH
Oberg	3.3 (3.0-3.5) 5.5 (4.8-6.3) [prior severe PPH] 4.0 (3.6-4.4) [prior atonic PPH]	aRR	538,332	VD	ICD	LOW
Regalia	6.35 (2.99-13.47) [prior atony]	aOR	10,756	VD	Clinical diagnosis	HIGH
Prior Cesarean Delivery						
Bateman 2010	1.10 (0.96-1.26)	uOR	876,641	VD, CD	ICD	LOW
Driessen	1.66 (1.15-2.41)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Mehrabadi	1.02 (0.96-1.10)	aOR	371,193	VD, CD	ICD	MOD
Regalia	0.9 (0.55-1.48)	uOR	10,756	VD	Clinical diagnosis	HIGH
Wetta	1.3 (0.6-2.8)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Blood group O						
Kahr	Ref: Blood group non-O 1.03 (0.63-1.67)	uOR	1,487	VD, CD	Clinical diagnosis, details not reported	MOD
Calcium Channel						

blocker exposure						
Bateman 2013	0.93 (0.58-1.49)	aOR	9,750	VD, CD	ICD	LOW
Antidepressant exposure						
Joseph	1.40 (1.13-1.74)	arr	138,704	VD, CD	ICD	MOD
Aspirin exposure						
Joseph	1.08 (0.70-1.66)	arr	138,704	VD, CD	ICD	MOD
NSAID exposure						
Joseph	1.00 (0.71-1.41)	arr	138,704	VD, CD	ICD	MOD
Doxylamine exposure						
Joseph	1.00 (0.91-1.10)	arr	138,704	VD, CD	ICD	MOD
PATIENT COMORBIDITY RISK FACTORS						
	Effect Size	Statistic	Number of Patients	Mode of Delivery	Atony Definition	Risk of Bias
Hypertension						
Bateman	2.5 (2.1-2.8) [Hypertensive disorders of pregnancy]	aOR	876,641	VD, CD	ICD	LOW
Feerasta	1.67 (0.72-3.38) [Preeclampsia]	uOR	332	VD	Not reported	HIGH
Grotegut	4.90 (1.66-14.43) [Preeclampsia]	uOR	108	VD, CD	ICD	LOW
Joseph	1.63 (1.38-1.92) [Preeclampsia or eclampsia]	urr	138,704	VD, CD	ICD	MOD
Lutomski	1.44 (1.36-1.53) [Hypertension]	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	1.81 (1.61-2.04) [Preeclampsia]	aOR	371,193	VD, CD	ICD	MOD
Regalia	3.01 (1.35-6.71) [Preeclampsia] 2.90 (1.81-4.65) [Pregnancy-induced hypertension]	aOR	10,756	VD	Clinical diagnosis	HIGH
Tran	0.829 (0.174-3.952) [Preeclampsia]	aOR	490	CD	Need for additional intervention to manage blood loss (uterotonic, surgical)	LOW
Wetta	2.61 (1.60-4.25) [Preeclampsia]	aOR	1,798	VD	Diagnosis made “based on the discretion of the treating obstetrical team”	HIGH
Diabetes						
Bateman	1.11 (0.91-1.37) [diabetes]	uOR	876,641	VD, CD	ICD	LOW
Feerasta	7.67 (6.2-9.0) [gestational diabetes]	aOR	332	VD	Not reported	HIGH

Lutomski	1.28 (1.14-1.42) [diabetes]	aRR	649,019	VD, CD	ICD	LOW
Anemia						
Feerasta	0.93 (0.53-1.64) [Hgb<11g/dl]	uOR	332	VD	Not reported	HIGH
Grotegut	1.15 (1.01-1.35) [per 1-unit decrease in admission Hct]	aOR	108	VD, CD	ICD	LOW
Wetta	2.46 (0.92-6.56) [Hgb<9]	aOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Obesity						
Driessen	Ref: BMI 18-25 ≤18: 1.10 (0.78-1.55) >25-30: 0.85 (0.67-1.08) >30: 0.89 (0.63-1.24)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Grotegut	1.03 (0.96-1.12) [per 1-unit decrease BMI]	aOR	108	VD, CD	ICD	LOW
Mehrabadi	Ref: BMI <30 ≥30: 1.00 (0.99-1.00)	aOR	371,193	VD, CD	ICD	MOD
Regalia	Ref: <30 >40: 0.66 (0.29-1.49)	uOR	10,756	VD	Clinical diagnosis	HIGH
Tran	Ref: BMI <40 ≥40: 1.334 (0.562-3.163)	aOR	490	CD	Need for additional intervention to manage blood loss (uterotonic, surgical)	LOW
Wetta	Ref: BMI <25 BMI 25-30: 1.48 (0.92-2.38) BMI ≥30: 2.25 (1.41-3.62)	aOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Fibroids						
Bateman	1.84 (1.28-2.64)	uOR	876,641	VD, CD	ICD	LOW
Driessen	0.74 (0.29-1.98)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Regalia	0.52 (0.16-1.64)	uOR	10,756	VD	Clinical diagnosis	HIGH
Liver disease						
Joseph	1.25 (0.84-1.86)	arr	138,704	VD, CD	ICD	MOD
Thrombocytopenia						
Joseph	1.31 (0.94-1.83)	arr	138,704	VD, CD	ICD	MOD
Asthma						
Joseph	0.99 (0.83-1.17)	arr	138,704	VD, CD	ICD	MOD

Elevated Uric Acid						
Kovacheva	1.53 (1.17-1.99)	aOR	345	CD	Administration of second line uterotonic	MOD
Alcohol use disorder						
Joseph	0.97 (0.42-2.23)	arr	138,704	VD, CD	ICD	MOD
Smoking						
Mehrabadi	0.83 (0.79-0.88)	aOR	371,193	VD, CD	ICD	MOD
PREGNANCY-RELATED RISK FACTORS						
	Effect Size	Statistic	Number of Patients	Mode of Delivery	Atony Definition	Risk of Bias
Polyhydramnios						
Bateman	1.9 (1.2-3.1)	aOR	876,641	VD, CD	ICD	LOW
Driessen	0.94 (0.42-2.11)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Joseph	5.00 (0.31-80.0)	urr	138,704	VD, CD	ICD	MOD
Lutomski	1.46 (1.19-1.78)	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	0.95 (0.77-1.16)	aOR	371,193	VD, CD	ICD	MOD
Regalia	1.21 (0.71-2.05)	uOR	10,756	VD	Clinical diagnosis	HIGH
Tran	0.995 (0.110-9.005)	aOR	490	CD	Need for additional intervention to manage blood loss (uterotonic, surgical)	LOW
Wetta	1.75 (0.65-4.69)	aOR	1,798	VD	Diagnosis made “based on the discretion of the treating obstetrical team”	HIGH
Multiple Gestation						
Bateman	2.8 (2.2-3.6)	aOR	876,641	VD, CD	ICD	LOW
Bekabil	9.43 (2.64-33.33) [Twins]	uRR	432	VD, CD	Clinical diagnosis	HIGH
Driessen	1.17 (0.70-1.96)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Joseph	1.86 (1.43-2.41)	urr	138,704	VD, CD	ICD	MOD
Lutomski	1.94 (1.77-2.13)	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	3.55 (3.20-3.94)	aOR	371,193	VD, CD	ICD	MOD
Tran	1.237 (0.141-8.72)	aOR	490	CD	Need for additional intervention to manage blood loss (uterotonic, surgical)	LOW

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Wetta	2.64 (0.54-12.9) [Twins]	aOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Malpresentation						
Mehrabadi	0.84 (0.74-0.95) [Breech] 1.41 (1.03-1.93) [Transverse]	aOR	371,193	VD, CD	ICD	MOD
Macrosomia						
Driessen	Ref: 2501-3999 grams ≤2500: 0.97 (0.56-1.69) ≥4000: 1.21 (0.95-1.58)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Feerasta	Ref: ≤3000 grams >3000: 2.02 (1.22-3.35	uOR	332	VD	Not reported	HIGH
Kovacheva	Ref: not reported 1.00 (0.99-1.00)	aOR	345	CD	Administration of second line uterotonic	HIGH
Lutomski	Ref: ≤4000 grams >4000: 1.44 (1.25-1.67)	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	Ref: 2500-3999 <1500: 0.58 (0.40-0.85) 1500-2499: 0.71 (0.64-0.78) 4000-4499: 1.49 (1.43-1.56) ≥4500: 1.95 (1.79-2.13)	aOR	371,193	VD, CD	ICD	MOD
Regalia	Ref: 2500-4000 <2500: 0.23 (0.08-0.85) >4000: 2.03 (1.47-2.79)	aOR	10,756	VD	Clinical diagnosis	HIGH
Tran	Ref: ≤4500 grams >4500: 1.224 (0.241-6.216)	aOR	490	CD	Need for additional intervention to manage blood loss (uterotonic, surgical)	LOW
Wetta	Ref: 2500-3999 <2500: 0.8 (0.4-1.5) ≥4000: 1.1 (0.5-2.3)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Placental Disorders						
Bateman	4.1 (3.1-5.5) [Retained placenta]	aOR	876,641	VD, CD	ICD	LOW
Joseph	1.48 (1.27-1.74) [Placenta previa, abruption]	urr	138,704	VD, CD	ICD	MOD
Lutomski	3.55 (3.22-3.90) [Placenta previa, vasa previa, abruption]	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	3.91 (3.32-4.61) [Placenta previa]	aOR	371,193	VD, CD	ICD	MOD

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	1.62 (1.41-1.86) [Abruption]					
Antepartum hemorrhage						
Bateman	3.8 (3.0-4.8)	aOR	876,641	VD, CD	ICD	LOW
Stillbirth						
Bateman	2.09 (1.39-3.16)	uOR	876,641	VD, CD	ICD	LOW
LABOR-RELATED RISK FACTORS						
	Effect Size	Statistic	Number of Patients	Mode of Delivery	Atony Definition	Risk of Bias
Chorioamnionitis						
Bateman	2.5 (1.9-3.3)	aOR	876,641	VD, CD	ICD	LOW
Grotegut	4.38 (0.42-58.5)	aOR	108	VD, CD	ICD	LOW
Joseph	1.59 (1.41-1.80)	urr	138,704	VD, CD	ICD	MOD
Lutomski	2.77 (2.09-3.69)	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	1.63 (1.46-1.82)	aOR	371,193	VD, CD	ICD	MOD
Tran	1.078 (0.450-2.587)	aOR	490	CD	Need for additional intervention to manage blood loss (uterotonic, surgical)	LOW
Wetta	2.42 (1.35-4.34)	aOR	1,798	VD	Diagnosis made “based on the discretion of the treating obstetrical team”	HIGH
Uterine rupture						
Joseph	1.97 (1.09-3.59)	urr	138,704	VD, CD	ICD	MOD
Mehrabadi	2.59 (1.67-4.02)	aOR	371,193	VD, CD	ICD	MOD
Pre-delivery oxytocin exposure						
Driessen	1.04 (0.85-1.28)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Feerasta	1.08 (0.66-1.75)	uOR	332	VD	Not reported	HIGH
Foley	1.94 (1.19-3.15)	aOR	402	CD	High rate postpartum oxytocin infusion	LOW
Grotegut	1.58 (1.05-2.57) [per 5000-mU increase oxytocin area under the curve]	aOR	108	VD, CD	ICD	LOW
Kovacheva	1.04 (1.00-1.08) [duration of oxytocin in hours]	aOR	345	CD	Administration of second line uterotonic	HIGH
Mehrabadi	1.09 (1.04-1.14)	aOR	371,193	VD, CD	ICD	MOD
Regalia	1.42 (1.11-1.83)	aOR	10,756	VD	Clinical diagnosis	HIGH

Tran	0.997 (0.959-1.036) [recovery interval, per 10min] 1.004 (1.001-1.008) [oxytocin augmentation, per 100mU]	aOR	490	CD	Need for additional intervention to manage blood loss (uterotonic, surgical)	LOW
Wetta	1.08 (0.56-2.08)	aOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Induction of labor						
Bateman	1.12 (0.99-1.28)	uOR	876,641	VD, CD	ICD	LOW
Callaghan	Ref: CD no IOL VD IOL: 2.1 (1.9-2.2) VD no IOL: 1.6 (1.5-1.7) CD IOL: 2.0 (1.8-2.2)	aOR	10,481,197	VD, CD	ICD	MOD
Driessen	1.20 (0.93-1.55) 1.45 (1.13-1.85) [cervical ripening]	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Feerasta	1.01 (0.61-1.67)	uOR	332	VD	Not reported	HIGH
Grotegut	1.16 (0.34-3.78)	aOR	108	VD, CD	ICD	LOW
Joseph	1.54 (1.43-1.65)	urr	138,704	VD, CD	ICD	MOD
Lutomski	Ref: VD no IOL VD IOL: 1.17 (1.11-1.25)	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	1.16 (1.12-1.20)	aOR	371,193	VD, CD	ICD	MOD
Regalia	2.61 (1.68-4.04) [oxytocin IOL] 1.46 (1.14-1.88) [prostaglandin IOL]	aOR uOR	10,756	VD	Clinical diagnosis	HIGH
Tran	1.288 (0.764-2.173) [oxytocin IOL]	aOR	490	CD	Need for additional intervention to manage blood loss (uterotonic, surgical)	LOW
Wetta	1.60 (0.80-3.18)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Prolonged labor						
Bateman	1.98 (1.37-2.86) [prolonged labor]	uOR	876,641	VD, CD	ICD	LOW
Driessen	1.27 (1.06-1.53) [prolonged labor] 0.97 (0.77-1.24) [prolonged expulsive efforts]	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Feerasta	4.06 (3.1-5.0) [prolonged 2nd stage in multiparous]	aOR	332	VD	Not reported	HIGH
Joseph	1.73 (1.49-2.02)	urr	138,704	VD, CD	ICD	MOD
Looft	Ref: 2nd stage <1h 1-<2h: 1.12 (1.01-1.25) 2-<3h: 1.18 (1.05-1.32) 3-<4h: 1.35 (1.19-1.53)	aRR	57,267	VD	ICD	MOD

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	≥4h: 1.62 (1.42-1.85)					
Lutomski	1.30 (1.16-1.46) [prolonged 1st stage] 0.96 (0.90-1.04) [prolonged 2nd stage]	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	1.32 (1.24-1.41) [prolonged 1st stage] 1.39 (1.32-1.46) [prolonged 2nd stage]	aOR	371,193	VD, CD	ICD	MOD
Regalia	1st stage ref: 1-2 cm/h <1: 1.91 (1.50-2.45) >2-4: 0.75 (0.58-0.97) >4: 0.72 (0.53-0.99) 2nd stage ref: 1-15min 16-30: 0.30 (1.00-1.69) 31-45: 1.47 (1.00-2.02) 46-60: 1.66 (1.13-2.44) >60: 1.87 (1.39-2.42)	uOR	10,756	VD	Clinical diagnosis	HIGH
Wetta	1.73 (0.92-3.26) [protracted 2nd stage] 1.9 (0.6-5.4) [prolonged 3rd stage]	aOR uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Epidural						
Feerasta	1.33 (0.48-3.67)	uOR	332	VD	Not reported	HIGH
Driessen	0.53 (0.43-0.67)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Joseph	1.34 (1.25-1.43)	urr	138,704	VD, CD	ICD	MOD
Mehrabadi	1.05 (1.02-1.09)	aOR	371,193	VD, CD	ICD	MOD
Wetta	0.9 (0.5-1.5)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Magnesium exposure						
Grotegut	1.17 (0.27-5.34)	aOR	108	VD, CD	ICD	LOW
Kovacheva	1.35 (0.36-5.02)	aOR	345	CD	Administration of second line uterotonic	HIGH
Wetta	2.8 (1.8-4.4)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Tocolytic exposure						
Feerasta	0.73 (0.15-3.13)	uOR	332	VD	Not reported	HIGH

Joseph	1.03 (0.91-1.17) [beta agonist only]	arr	138,704	VD, CD	ICD	MOD
DELIVERY-RELATED RISK FACTORS						
Gestational Age						
Driessen	Ref: 37-41 <37: 1.14 (0.70-1.85) >41: 1.10 (0.89-1.37)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Kovacheva	Ref: not reported 0.90 (0.73-1.11)	aOR	345	CD	Administration of second line uterotonic	HIGH
Mehrabadi	Ref: 37-42 <28: 0.46 (0.29-0.73) 28-31: 1.16 (0.88-1.53) 32-36: 0.92 (0.86-0.98) ≥42: 1.01 (0.90-1.14)	aOR	371,193	VD, CD	ICD	MOD
Regalia	Ref: 37-41 35-36: 0.36 (0.14-0.88) >41: 1.29 (1.01-1.64)	uOR aOR	10,756	VD	Clinical diagnosis	HIGH
Wetta	Ref: not reported 1.0 (0.9-1.1)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Genital Tract trauma						
Driessen	Ref: SVD no episiotomy SVD with episiotomy: 1.55 (1.27-2.87) Operative with episiotomy: 1.70 (1.33-2.18)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Joseph	2.12 (1.89-2.38) [perineal laceration] 3.70 (2.42-5.66) [cervical laceration] 1.56 (1.36-1.79) [high vaginal laceration]	urr	138,704	VD, CD	ICD	MOD
Lutomski	1.27 (1.20-1.34) [episiotomy] 3.30 (3.05-3.56) [other genital tract trauma including 3rd and 4th degree perineal tears, high vaginal and cervical lacerations]	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	1.82 (1.71-1.93) [3/4th degree perineal tear] 3.07 (2.63-3.58) [high vaginal laceration] 8.37 (7.00-9.99) [cervical laceration]	aOR	371,193	VD, CD	ICD	MOD

Instrumented vaginal delivery						
Driessen	Ref: SVD no episiotomy Instrumented VD with episiotomy: 1.70 (1.33-2.18) Instrumented VD no episiotomy: 1.05 (0.69-1.62)	aOR	146,876	VD	EBL and/or drop in Hgb >2 g/dL, case report form to elucidate etiology	LOW
Feerasta	Ref: SVD Instrumented VD: 4.27 (2.46-7.44)	uOR	332	VD	Not reported	HIGH
Lutomski	Ref: SVD not induced Instrumented not induced: 1.88 (1.77-2.01) Instrumented induced: 2.16 (2.01-2.33)	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	Ref: SVD Forceps: 1.80 (1.69-1.91) Vacuum: 1.23 (1.17-1.29) Forceps and vacuum: 1.69 (1.48-1.92)	aOR	371,193	VD, CD	ICD	MOD
Waheed	Ref: SVD Instrumented VD: 1.62 (0.39-6.72)	uOR	8,713	VD, CD	EBL and/or change in vital signs for PPH, atony "established by abdominal examination eliciting a soft, boggy uterus"	HIGH
Wetta	Ref: SVD Instrumented VD: 1.3 (0.7-2.4)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH
Cesarean Delivery						
Bateman	Ref: VD CD no labor: 1.3 (1.1-1.5) CD with labor: 1.7 (1.5-2.0)	aOR	876,641	VD, CD	ICD	LOW
Callaghan	Ref: CD not induced VD induced: 2.1 (1.9-2.2) VD not induced: 1.6 (1.5-1.7) CD induced: 2.0 (1.8-2.2)	aOR	10,481,197	VD, CD	ICD	MOD
Joseph	Ref: VD CD: 0.78 (0.72-0.84)	urr	138,704	VD, CD	ICD	MOD
Lutomski	Ref: VD not induced CD not induced: 1.88 (1.79-1.98) CD induced: 2.66 (2.48-2.86)	aRR	649,019	VD, CD	ICD	LOW
Mehrabadi	Ref: VD CD: 0.30 (0.29-0.32)	aOR	371,193	VD, CD	ICD	MOD
Vendittelli	Ref: VD	uRR	129,110	VD, CD	EBL for PPH, definition of atony not stated	HIGH

	CD: 1.15 (1.08-1.22)					
Waheed	Ref: VD CD: 2.29 (1.52-3.47)	uOR	8,713	VD, CD	EBL and/or change in vital signs for PPH, atony "established by abdominal examination eliciting a soft, boggy uterus"	HIGH
Cord blood collection						
Guillaume	0.69 (0.50-0.97)	aOR	7,810	VD	EBL + cause "identified by the medical team in charge of the patient"	MOD
Breastfeeding						
Wetta	1.5 (1.0-2.2)	uOR	1,798	VD	Diagnosis made "based on the discretion of the treating obstetrical team"	HIGH

Unless otherwise stated, all statistics are in reference to lack of risk factor

Abbreviations: ref-reference, aOR-adjusted odds ratio, uOR-unadjusted odds ratio, aRR-adjusted relative risk, uRR-unadjusted relative risk, arr-adjusted rate ratio, urr-unadjusted rate ratio, PPH-postpartum hemorrhage, VD-vaginal delivery, CD-cesarean delivery, ICD-International Classification of Diseases, EBL-estimated blood loss, Hgb-hemoglobin, Hct-hematocrit, BMI-body mass index, , IOL-induction of labor, SVD-spontaneous vaginal delivery

Appendix 3. Narrative Summary of Risk Factors With Results of Qualitative and Quantitative Synthesis

Below is a narrative summary of all risk factors identified in this systematic review, including those related to maternal history or demographics, maternal comorbidities, pregnancy, labor, and delivery. For each risk factor, the narrative summary is followed by the results of a qualitative synthesis (based on definitions presented in Box 1) and meta-analysis (where applicable). Additional information relating to each risk factor and the studies evaluating it can be found in Appendix 2. Numeric ranges in parentheses represent 95% confidence intervals, unless otherwise specified. All reference numbers refer to the reference list in the manuscript document.

Maternal History and Demographics

Age

Seven studies assessed the association between age and atonic PPH. Age <20y was associated with atony in one study,[1] with an aOR 1.8 compared to reference age 20-34y. Advanced age (≥40y) showed elevated risk in two of seven studies, with aOR 1.13 and 1.7, respectively.[1,19] Of note, the studies supporting age as a risk factor included more subjects (n=876,641 and n=371,193) than did all the negative studies combined.[20-24]

Qualitative synthesis: Unclear risk factor (majority of studies negative but at least one low or moderate risk of bias study positive)

Meta-analysis: Not implemented due to heterogeneity in cut-off ages and reference ranges

Hispanic

The relationship of Hispanic ethnicity to atonic PPH was assessed in four studies, three of which found a significant association (aOR estimates ranged from 1.21 to 2.26) compared to the reference of white or Black women.[23,25,26] The one study that failed to find this association was smaller (n=108) than the positive studies (n=1,798 to 2,488,974) but was assessed as low risk of bias.[27]

Qualitative synthesis: Likely risk factor (majority low and moderate risk of bias studies positive (2-4 studies))

Meta-analysis: Combined OR for Hispanic compared to Caucasian race 1.23 (1.20-1.25)

Asian

Asian race was associated with atony in all three studies with aOR 1.31 to 1.45 and uOR 1.41.[25,28,29]

Qualitative synthesis: Definite risk factor (all low and moderate risk of bias studies positive (≥3 studies))

Meta-analysis: Combined OR for Asian compared to Caucasian race 1.39 (1.33-1.46)

Native American

In a single high risk of bias study that evaluated American Indian race, an association with atony was reported with an uOR 2.0.[30]

Qualitative synthesis: Not a risk factor (no low or moderate risk of bias studies positive)

Meta-analysis: Not implemented (no low or moderate risk of bias studies)

Black or African American

Three studies assessing the association of atony with the Black or African American race showed mixed results. One study found an increased risk with uOR 1.14 (1.10-1.18).[26] Another study showed an equivocal risk of atony (aOR 0.88) but an increased risk of blood transfusion (aOR 1.18).[25] A third study showed no increased risk compared to White women and potentially lower risk compared to Hispanics.[23]

Qualitative synthesis: Unclear risk factor (low and moderate risk of bias studies show mixed or conflicting results)

Meta-analysis: Combined OR for Black compared to Caucasian race 1.00 (0.78-1.29)

Nulliparity

Data on parity were conflicting; however, most studies favored nulliparity as a risk factor for atony. Three of six studies evaluating parity showed a statistically significant association between nulliparity and atony (aOR 1.29 to 1.88)[19,20,22]. A fourth study reported an uOR 1.4 with the lower bound of CI just reaching 1.0.[23] Equivocal results were found in a fifth study, which was smaller (n=332) than the positive studies (n=1,798 to 371,193) and demonstrated a high risk of bias.[31] The final study found nulliparity to be protective, with uOR 0.41.[26]

Qualitative synthesis: Likely risk factor (majority low and moderate risk of bias studies positive (2-4 studies))

Meta-analysis: Not implemented due to heterogeneity in risk factor definitions and reference ranges

Prior Atony or PPH

Four studies evaluated the association between prior atony or PPH and recurrent atony. Three of the largest and low/moderate risk of bias studies found a significant association, with aOR 1.47 to 6.35 and aRR 3.3.[20,22,32] One small (n=332), high risk of bias study found no association between prior PPH and risk of subsequent atonic PPH.[31]

Qualitative synthesis: Definite risk factor (all low and moderate risk of bias studies positive (≥3))

Meta-analysis: Combined OR for all-cause prior PPH 2.25 (1.02-4.96)

Prior Cesarean Delivery

Five studies evaluated prior CD as a risk factor for atonic PPH. Two large studies of patients having either vaginal birth after cesarean (VBAC) or repeat CD found no increased risk.[1,19] The remaining three studies included only patients undergoing VBAC: two high risk of bias studies showed no increased risk,[22,23] while one large, low risk of bias study showed aOR 1.66 (1.15-2.41).[20]

Qualitative synthesis: Unclear risk factor (majority of studies negative, but at least one low or moderate risk of bias study positive)

Meta-analysis: Combined OR for ≥ 1 prior CD 1.12 (0.96-1.32)

Other Demographics/History

Blood group O was assessed as a possible risk factor for atonic PPH in one study but did not show significant association.[33] Multiple studies have examined the effect of medication exposure on the risk of atonic PPH. Bateman et al. found no association with calcium channel blocker prescription during pregnancy and atonic PPH (aOR 0.93).[34] Joseph et al. investigated multiple drug exposures, including antidepressants, aspirin, nonsteroidal anti-inflammatory medications, and doxylamine, and found only antidepressants to be positively associated with atonic PPH (arr 1.40).[35]

Qualitative synthesis (antidepressant exposure): Unclear risk factor (all low and moderate risk of bias studies positive (one study))

Meta-analysis (antidepressant exposure): Not implemented (only one available study)

Maternal Comorbidities

Hypertensive Disorders

The association between atonic PPH and hypertensive disorders was evaluated in nine studies, most of which (7/9 studies) showed a significant association. Of the two negative studies, both were small (<500 subjects), and one had a high risk of bias.[31,36] Among the seven positive studies, one reported aRR 1.44 for all-cause hypertension,[21] while the remaining studies evaluated hypertensive disorders of pregnancy specifically and demonstrated aOR that ranged from 1.81 to 3.01,[1,19,22,23] uOR 4.9,[27] and urr 1.63.[35]

Qualitative synthesis: Definite risk factor (majority low and moderate risk of bias studies positive (≥5 studies))

Meta-analysis: Combined OR of all-cause hypertensive disorders 1.84 (1.45-2.33)

Diabetes Mellitus

Diabetes and gestational diabetes were found to be associated with atonic PPH in all three studies that evaluated it as a risk factor. One small, high risk of bias study showed a significant association with aOR 7.67,[31] while two larger, low risk of bias studies showed a more moderate association – uOR 1.11 and aRR 1.28.[1,21]

Qualitative synthesis: Definite risk factor (all low and moderate risk of bias studies positive (≥3 studies))

Meta-analysis: Combined OR for chronic or gestational diabetes 1.22 (1.08-1.39)

Anemia

Of three studies evaluating anemia as a risk factor for atonic PPH, only one demonstrated a positive association with aOR 1.15 (1.01-1.35) per 1-point decrease in admission hematocrit.[27] While this study demonstrated a low risk of bias, it included only 108 subjects. The two negative studies on anemia were also relatively small (n=332 and 1,798), and both showed a high risk of bias.[23,31]

Qualitative synthesis: Unclear risk factor (all low and moderate risk of bias studies positive (one study))

Meta-analysis: Not implemented (only one low or moderate risk of bias study)

Obesity

Six studies evaluated the association between maternal body mass index (BMI) and atonic PPH, with only one study showing a positive correlation – namely, an aOR 2.25 (1.41-3.62) for BMI ≥30 compared to normal or underweight parturients;[23] however, this study suffered from a high risk of bias. Of the studies failing to demonstrate an association, three were deemed low risk of bias, with one including nearly 150,000 subjects.

Qualitative synthesis: Not a risk factor (no low or moderate risk of bias studies positive)

Meta-analysis: Not implemented due to heterogeneity in risk factor definitions and reference ranges

Fibroids

Three large studies evaluated fibroids as a risk factor for atonic PPH and found mixed results. One low risk of bias study demonstrated an association with uOR 1.84 (1.28-2.64),[1] while another low-risk study demonstrated no association with aOR 0.74 (0.29-1.98).[20] A third high risk of bias study also showed no association.[22]

Qualitative synthesis: Unclear risk factor (low and moderate risk of bias studies show mixed or conflicting results)

Meta-analysis: Combined OR for the presence of fibroids 1.31 (0.55-3.10)

Other Maternal Comorbidities

Multiple other maternal comorbidities were evaluated in only one study and were not shown to be associated with atonic PPH: liver disease arr 1.25 (0.84-1.86), thrombocytopenia arr 1.31 (0.94-1.83), asthma arr 0.99 (0.83-1.17), and alcohol use disorder arr 0.97 (0.42-2.23).[35] Elevated uric acid was independently associated with atony in one study, with an aOR 1.53 (1.17-1.99).[37] Smoking was similarly assessed in a single study and found to be protective with aOR 0.83 (0.79-0.88).[19]

Pregnancy-Related

Polyhydramnios

Results were mixed for the association between polyhydramnios and atonic PPH. Eight studies evaluated this risk factor: four assessed as low risk of bias, two moderate risk of bias, and two high risk of bias. All moderate and high risk of bias studies showed no association.[19,22,23,35] Of the low risk of bias studies, one small study (n=490) and one larger

study (n=146,876) found no association (aOR 0.995 and 0.94 respectively);[20,36] while two other large studies (n=876,641 and n=649,019) showed a positive association with aOR 1.9 (1.2-3.1) and aRR 1.46 (1.19-1.78).[1,21]

Qualitative synthesis: Unclear risk factor (majority of studies negative but at least one low or moderate risk of bias study positive)

Meta-analysis: Combined OR for the presence of polyhydramnios 1.29 (0.94-1.76)

Multiple Gestation

Multiple gestation was assessed as a risk factor in eight studies, with five of eight showing a positive association (2 low risk, 2 moderate risk, and 1 high risk of bias studies).[1,19,21,35,38] Effect sizes in the positive studies ranged from 1.86 (1.43-2.41) to 9.43 (2.64-33.33). The three negative studies were judged to be low (2) or high (1) risk of bias.

Qualitative synthesis: Likely risk factor (majority low and moderate risk of bias studies positive (2-4 studies))

Meta-analysis: Combined OR for multiple gestation 2.16 (1.53-3.06)

Malpresentation

The association between malpresentation and atonic PPH was assessed in only one moderate risk of bias study. The transverse presentation showed a positive association with aOR 1.41 (1.03-1.93), while the breech presentation showed a protective effect with aOR 0.84 (0.74-0.95).[19]

Qualitative synthesis: Unclear risk factor (all low and moderate risk of bias studies positive (one study))

Meta-analysis: Not implemented (only one available study)

Macrosomia

Eight studies evaluated macrosomia as a risk factor for atonic PPH; however, the studies showed significant heterogeneity in defining fetal birth weight cut-offs. Of the eight studies, three were determined to be low risk of bias. Of these, one small study (n=490) showed no association but a large confidence interval – aOR 1.224 (0.241-6.216).[36] One larger study (n=146,876) showed aOR 1.21 (0.95-1.58) for birth weight ≥4000 g.[1] The third study (n=649,019) showed aRR 1.44 (1.25-1.67) for atonic PPH "with a large fetus" .[21]

One moderate risk of bias study demonstrated a significant association with aOR 1.49 (1.43-1.56) for fetal weight 4000-4499 g and aOR 1.95 (1.79-2.13) for fetal weight ≥4500 g compared to reference 2500-3999 g.[19] This same study demonstrated a protective effect of low birth weight (aOR 0.58 <1500g, aOR 0.71 1500-2499 g). Of the remaining four high risk of bias studies, two found a positive association between fetal birth weight and risk of atonic PPH,[22,31] while two did not.[23,37]

Qualitative synthesis: Unclear risk factor (low and moderate risk of bias studies show mixed or conflicting results)

Meta-analysis: Combined OR for weight >4000 g 1.46 (1.35-1.57)

Placental Disorders

Placental disorders, encompassing a variety of placental pathologies, were strongly associated with increased risk of atonic PPH in all studies that evaluated them. Bateman et al. showed aOR 4.1 (3.1-5.5) for retained placenta, while Mehrabadi et al. demonstrated aOR 3.91 (3.32-4.61) for placenta previa and aOR 1.62 (1.41-1.86) for abruption.[1,19] Joseph et al. found an urr 1.48 (1.27-1.74) for previa/abruption combined.[35] A final study by Lutomski et al. showed aRR 3.55 (3.22-3.90) for a composite of all placental disorders.[21]

Qualitative synthesis: Definite risk factor (all low and moderate risk of bias studies positive (≥3 studies))

Meta-analysis: Combined OR for previa/abruption 2.74 (1.57-4.79)

Antepartum Hemorrhage

A single study reported on antepartum hemorrhage as a risk factor for atonic PPH, with aOR 3.8 (3.0-4.8).[1]

Qualitative synthesis: Unclear risk factor (all low and moderate risk of bias studies positive (one study))

Meta-analysis: Not implemented (only one available study)

Stillbirth

Only one study assessed the relationship between stillbirth and atonic PPH.[1] This large study (n=876,641) of both vaginal and cesarean deliveries reported an uOR 2.09 (1.39-3.16).

Qualitative synthesis: Unclear risk factor (all low and moderate risk of bias studies positive (one study))

Meta-analysis: Not implemented (only one available study)

Labor-Related

Chorioamnionitis

Chorioamnionitis was significantly associated with an increased risk of atonic PPH in five out of seven studies that evaluated it. The positive studies included two low risk, two moderate risk, and one high risk of bias, and effect sizes ranged from aOR 1.63 to 2.5, aRR 2.77, and urr 1.59.[1,19,21,23,35] Sample size in the positive studies ranged from 1,798 to 876,641 subjects. Among negative studies, one demonstrated a low risk of bias; however, it included few subjects (n=108) and reported a large confidence interval – aOR 4.38 (0.42-58.5).[27] The other was also relatively small (n=490) and low risk of bias, with aOR 1.078 (0.450-2.587).[36]

Qualitative synthesis: Likely risk factor (majority low and moderate risk of bias studies positive (2-4 studies))

Meta-analysis: Combined OR for chorioamnionitis 1.93 (1.56-2.39)

Uterine Rupture

Only two moderate risk of bias studies evaluated uterine rupture as a risk factor for atonic PPH; however, both showed a significant association with moderate effect size. Joseph et al. demonstrated an urr of 1.97 (1.09-3.59), while Mehrabadi et al. showed an aOR 2.59 (1.67-4.02).[19,35]

Qualitative synthesis: Likely risk factor (all low and moderate risk of bias studies positive (two studies))

Meta-analysis: Combined OR for uterine rupture 2.35 (1.65-3.35)

Pre-Delivery Oxytocin Exposure

While nine studies assessed the relationship between pre-delivery oxytocin exposure and atonic PPH, the definitions of this exposure varied widely from specific oxytocin doses to recovery intervals to the presence or absence of oxytocin augmentation. Of the six studies evaluating oxytocin augmentation in reference to spontaneous, un-augmented labor, three showed association with atonic PPH (one low risk, one moderate risk, one high risk of bias), with aOR ranging from 1.09 (1.04-1.14) to 1.94 (1.19-3.15).[19,22,39] The remaining three studies (one low risk, two high risk of bias) did not show an effect, with aOR ranging from 1.04 (0.85-1.28) to 1.08 (0.56-2.08).[20,23,31] Two additional low risk of bias studies evaluated the cumulative dose of oxytocin exposure, with both showing a significant association to the risk of atonic PPH. Grotegut et al. demonstrated an aOR 1.58 (1.05-2.57) per 5000-mU increase in oxytocin area under the curve, while Tran et al. demonstrated aOR 1.004 (1.001-1.008) per 100mU oxytocin exposure.[27,36] A final study by Kovacheva et al. showed aOR 1.04 (1.00-1.08) for the administration of second-line uterotonic medication per hour of oxytocin exposure before cesarean delivery.[37]

Qualitative synthesis: Likely risk factor (majority low and moderate risk of bias studies positive (2-4 studies))

Meta-analysis: Combined OR for any oxytocin exposure 1.15 (0.95-1.40)

Induction of Labor

In addition to oxytocin exposure, multiple studies also evaluated the effect of induction of labor compared to the spontaneous onset of labor on the risk of atonic PPH. Eleven studies evaluated this risk factor, with seven large studies (n=10,756 to 10,481,197; three low risk, two moderate risk, two high risk of bias) demonstrating a positive effect. Of those studies, four included patients undergoing both vaginal and cesarean delivery, and effect sizes varied from aOR 1.16 to 2.1, uOR 1.12, and urr 1.54.[1,19,35,40] The three remaining studies included only vaginal deliveries. Induction of labor was associated with atonic PPH in these studies with aOR 1.20 to 2.61 and aRR 1.17.[20-22] Two of these studies evaluated induced cervical ripening with prostaglandins separately, with aOR 1.45 to 1.46.[20,22] Four additional small studies (n=108 to 1,798; two low risk, two high risk of bias) showed no significant association between induction of labor and atonic PPH.[23,27,31,36]

Qualitative synthesis: Likely risk factor (majority low and moderate risk of bias studies positive (2-4 studies))

Meta-analysis: Combined OR for induction of labor 1.23 (1.10-1.39)

Prolonged Labor

Prolonged labor was evaluated as a risk factor for atonic PPH in nine studies and showed a positive association in eight studies, including all of those rated as low or moderate risk of bias. Two studies reported "long or prolonged labor" generally, with uOR 1.98 and urr 1.73.[1,35] Four studies examined the length of the first stage of labor as a risk factor, with all showing a positive association. Driessen et al. reported aOR 1.27 (1.06-1.53), Mehrabadi et al. reported aOR 1.32 (1.24-1.41), while Lutomski et al. reported aRR 1.30 (1.16-1.46).[19-21] The fourth study, by Regalia et al., showed that compared to the first stage of labor 1-2 cm/h, parturients with first stage <1 cm/h had aOR 1.91 (1.50-2.45).[22] Seven studies additionally evaluated the length of the second stage of labor, with four of seven demonstrating a positive association. Two of these studies reported a "prolonged second stage" generally, with aOR 1.39 (1.32-1.46) and 4.06 (3.1-5.0),[19,31] while the remaining two looked at defined time windows. Looft et al. found that compared to second stage lasting <1 hour, second stage of 1-2, 2-3, 3-4, and ≥4 hours were associated with the following aRR respectively: 1.12 (1.01-1.25), 1.18 (1.05-1.32), 1.35 (1.19-1.53), 1.62 (1.42-1.85).[41] Regalia et al. found that compared to reference 1-15 min, the second stage of 16-30, 31-45, 46-60, and >60 min were associated with the following uOR respectively: 1.30 (1.00-1.69), 1.47 (1.00-2.02), 1.66 (1.13-2.44), 1.87 (1.39-2.42).[22]

Qualitative synthesis: Definite risk factor (majority low and moderate risk of bias studies positive (≥5 studies)

Meta-analysis: Combined OR for prolonged labor 1.76 (1.53-2.03), combined OR for prolonged 1st stage 1.31 (1.24-1.38), combined OR for prolonged 2nd stage 1.10 (0.82-1.48)

Epidural Analgesia

Five studies evaluated epidural analgesia as a potential risk factor for atonic PPH. Two studies (both moderate risk of bias) found a significant association with aOR 1.05 (1.02-1.09) and urr 1.34 (1.25-1.43).[19,35] Conversely, one low risk of bias study found epidural analgesia to be negatively associated with atonic PPH, with aOR 0.53 (0.43-0.67).[20] The remaining two studies (both high risk of bias) found no association.[23,31]

Qualitative synthesis: Unclear risk factor (low and moderate risk of bias studies show mixed or conflicting results)

Meta-analysis: Combined OR for the use of epidural analgesia 0.94 (0.72-1.23)

Magnesium Exposure

Three relatively small studies evaluated the relationship between magnesium exposure and risk of atonic PPH. One study with a high risk of bias found an association with uOR 2.8 (1.8-4.4),[23] while two other studies (one low, one high risk of bias) found no relationship.[27,37]

Qualitative synthesis: Not a risk factor (no low or moderate risk of bias studies positive)

Meta-analysis: Not implemented (only one available low or moderate risk of bias study)

Tocolytic Exposure

Tocolytic exposure was evaluated in two studies (one moderate, one high risk of bias), with neither showing any significant effect.[31,35]

Qualitative synthesis: Not a risk factor (no low or moderate risk of bias studies positive)

Meta-analysis: Not implemented (only one available low or moderate risk of bias study)

Delivery-Related

Gestational Age

Five studies evaluated the association between gestational age at delivery and atonic PPH risk. While no studies demonstrated increased risk at higher gestational age, one moderate risk of bias study found a potential protective effect of lower gestational age with aOR for <28 weeks 0.46 (0.29-0.73) and 32-36 weeks 0.92 (0.86-0.98) compared to reference 37-42 weeks.[19]

Qualitative synthesis: Not a risk factor (no low or moderate risk of bias studies positive)

Meta-analysis: Not implemented due to heterogeneity in gestational age cut-offs and reference ranges

Genital tract or Perineal Trauma

Perineal trauma, either spontaneous or iatrogenic, was associated with an increased risk of atonic PPH in the four studies that evaluated it, all of which were low or moderate risk of bias. Two studies evaluated episiotomy; Driessen et al. found that compared with spontaneous vaginal delivery (SVD) without episiotomy, SVD with episiotomy had an aOR 1.55 (1.27-2.87), while operative delivery with episiotomy had an aOR 1.70 (1.33-2.18).[20] Similarly, Lutomski et al. found that episiotomy was associated with aRR 1.27 (1.20-

1.34).[21] Other types of genital tract trauma also showed a significant association with atonic PPH: high vaginal laceration aOR 3.07 (2.63-3.58)/urr 1.56 (1.36-1.79), perineal laceration aOR 1.82 (1.71-1.93)/urr 2.12 (1.89-2.38), and cervical laceration aOR 8.37 (7.00-9.99)/urr 3.70 (2.42-5.66).[19,35]

Qualitative synthesis: Definite risk factor (all low and moderate risk of bias studies positive (≥3 studies)

Meta-analysis: Combined OR for perineal laceration 1.67 (1.28-2.18), combined OR for high vaginal laceration 2.19 (1.13-4.24), combined OR for cervical laceration 5.70 (2.56-12.67)

Instrumented Vaginal Delivery

In six studies evaluating the risk of atonic PPH associated with instrumented vaginal delivery, three found a significant association (one low, one moderate, and one high risk of bias). In contrast, three others found no association (one low, two high risk of bias). Of the positive studies, two assessed all instrumented deliveries collectively, with uOR 4.27 and aRR 1.88.[21,31] The third study assessed forceps (aOR 1.80 [1.69-1.91]) and vacuum (aOR 1.23 [1.17-1.29]) separately.[19]

Qualitative synthesis: Likely risk factor (Majority low and moderate risk of bias studies positive (2-4 studies))

Meta-analysis: Combined OR for instrumental vaginal delivery 1.67 (1.40-2.00)

Cesarean Delivery

The relationship between mode of delivery and atonic PPH varied among studies assessed. Four studies (two low, two high risk of bias) showed increased risk associated with cesarean compared to vaginal delivery with a range of effect sizes: aOR 1.3 (1.1-1.5) [CD without labor], aOR 1.7 (1.5-2.0) [CD with labor], aRR 1.88 (1.79-1.98) [CD, not induced], aRR 2.66 (2.48-2.86) [CD, induced], uOR 2.29 (1.52-3.47) [all CD], and uRR 1.15 (1.08-1.22) [all CD].[1,21,42,43] Three other studies (two moderate risk, one high risk of bias) demonstrated a negative association between CD and risk of atonic PPH. When compared to VD, Mehrabadi et al. reported aOR 0.30 (0.29-0.32) for CD, while Joseph et al. reported an urr of 0.78 (0.72-0.84) for CD.[19,35]. Callaghan et al. utilized CD not induced as the reference point and demonstrated aOR 2.1 (1.9-2.2) for VD induced and 1.6 (1.5-1.7) for VD, not induced.[40] Only one study with a high risk of bias found no association between atonic PPH and mode of delivery.[23]

Qualitative synthesis: Unclear risk factor (majority of studies negative but at least one low or moderate risk of bias study positive)

Meta-analysis: Not implemented due to heterogeneity in risk factor definitions and reference ranges

Cord Blood Collection

One small study of 7,810 vaginal deliveries showed a negative association between cord blood collection at the time of delivery and atonic PPH with aOR 0.69 (0.50-0.97).[44]

Qualitative synthesis: Not a risk factor (no low or moderate risk of bias studies positive)

Meta-analysis: Not implemented (only one available study)

Breastfeeding

One high risk of bias study of 1,798 vaginal deliveries found no association between breastfeeding and atonic PPH with uOR 1.5 (1.0-2.2).[23]

Qualitative synthesis: Not a risk factor (no low or moderate risk of bias studies positive)

Meta-analysis: Not implemented (only one available study)

Appendix 4. Additional Information on Studies Reporting Data on Race or Ethnicity

Study	Race or Ethnicity Assessed	Who Classified Race or Ethnicity?	Classifications Used	Options Defined by Investigator or Participant?	Reason Race or Ethnicity Assessed Was Assessed	Missing data	Race or Ethnicity Classified in "Other" category
Bryant	Hispanic Asian Black	Patient self-reported (Source: National Inpatient Sample*, documented in hospital discharge abstracts)	White Black Hispanic Asian or Pacific Islander	Study investigators	Race included (by some states) in National Inpatient Sample database, accessed by these investigators to determine association with risk of postpartum hemorrhage	891,597 missing race or ethnicity data (not included in study, some bias possible given certain states systematically do not report this variable)	151,367 coded as category other than Caucasian, African American, Hispanic, or Asian/Pacific Islander (not included in study)
Chalouhi	Native American	Patient self-reported (Source: retrospective medical chart review)	Native American White – European ancestry White – Middle Eastern ancestry African American Hispanic	Study investigators	Race included as part of medical record, accessed by these investigators to determine association with risk of postpartum hemorrhage	None	None
Grotegut	Hispanic	Patient self-reported (Source: retrospective medical chart review)	Caucasian African American Hispanic Asian Other	Study investigators	Race included as part of medical record, accessed by these investigators to determine association with risk of postpartum hemorrhage	0 atony patients, 2 control patients missing race or ethnicity data	2 atony patients (3.7%), 0 control patients classified as other
Harvey	Native Hawaiian and Other Pacific Islander Asian	Patient self-reported (Source: Hawaii Health Information Corporation inpatient data set)	Native Hawaiian and Other Pacific Islander Asian (including Japanese, Filipino, Chinese, and other Asian) White	Study investigators	Race included as part of medical record, accessed by these investigators to determine association with risk of postpartum hemorrhage	41,292 missing race or ethnicity data OR with race-ethnicity other than NHOPI, Asian, or White	41,292 missing race or ethnicity data OR with race-ethnicity other than NHOPI, Asian, or White
Marshall	Hispanic African American	Patient self-reported	White Black Hispanic	Study investigators	Race included (by some states) in National Inpatient Sample database, accessed by these	117,680 (8%) missing at least one variable of interest and excluded (no	4,272 (13.5%) atonic postpartum hemorrhage patients

		(Source: National Inpatient Sample*, documented in hospital discharge abstracts)	Other		investigators to determine association with risk of postpartum hemorrhage	specific number for those missing race or ethnicity)	146,829 (11.2%) non-postpartum hemorrhage patients
Siddiqui	Asian	Patient self-reported (Source: National Inpatient Sample*, documented in hospital discharge abstracts)	Caucasian Asian or Pacific Islander	Study investigators	Race included (by some states) in National Inpatient Sample database, accessed by these investigators to determine association with risk of postpartum hemorrhage	19.64% of admissions missing race or ethnicity data (utilized three validated approaches to account for missing data)	Any race or ethnicity coded as category other than Caucasian or Asian or Pacific Islander was not included in study (this included the "other" category)
Wetta	Hispanic African American	Patient self-reported (Source: retrospective medical chart review)	Hispanic White Black Other	Study investigators	Race included as part of medical record, accessed by these investigators to determine association with risk of postpartum hemorrhage	None	410 patients (23% of sample) classified as "White and other"

*In the National Inpatient Sample, race and ethnicity are combined into a single variable, with ethnicity taking precedence over race if both are reported. Available options include White, Black, Hispanic, Asian or Pacific Islander, Native American, Other, Missing, Invalid, or Unavailable