

# Predicting risk of postpartum haemorrhage: a systematic review

Charlotte Neary<sup>1</sup>, David McLernon<sup>2</sup>, Sanobar Naheed<sup>3</sup>, and Mairead Black<sup>3</sup>

<sup>1</sup>Royal Hospital for Children Glasgow

<sup>2</sup>Sch Med

<sup>3</sup>Aberdeen Maternity Hospital

May 5, 2020

## Abstract

**Background:** Postpartum haemorrhage (PPH) rates are increasing in developed countries. A reliable prognostic tool for PPH has potential to aid prevention efforts. **Objective:** To systematically identify and appraise prognostic modelling studies for prediction of PPH. **Search strategy:** MEDLINE, Embase, CINAHL and the Cochrane Library were searched using a combination of terms and synonyms including ‘prediction tool’, ‘risk score’ and ‘postpartum haemorrhage’. **Selection criteria:** Any observational or experimental study developing a prognostic model for women’s risk of PPH. English language publications. **Data collection and analysis:** Predesigned data extraction form to record: data source; participant criteria; outcome; candidate predictors; actual predictors; sample size; missing data; model development; model performance; model evaluation; interpretation. **Main Results:** Of 1723 citations screened, 10 studies were eligible for inclusion. An additional paper was published and identified following completion of the search. Studies addressed populations of women who experienced; placenta praevia; vaginal births; caesarean birth; and the general obstetric population. Primary study authors deemed four models to be confirmatory. There was a high risk of bias across all studies due to a combination of retrospective selection of women, low sample size, no internal validation, suboptimal external validation and no reporting of missing data. **Conclusion:** Of eleven prognostic models for PPH risk, one developed for women undergoing caesarean section is deemed suitable for external validation. Future research requires robust internal and external validation of existing tools and development of a model that can be used to predict PPH in the general obstetric population. Protocol registration number: PROSPERO 95587

## Title:

Charlotte Neary, NHS Greater Glasgow and Clyde, Paediatric Surgery, Royal Hospital for Children in Glasgow, 1345 Govan Road Glasgow G51 4TF

Sanobar Naheed, NHS Grampian, Department of Obstetrics and Gynaecology, Aberdeen Maternity hospital, Cornhill Road, Aberdeen, AB252ZD

David J McLernon, Department of Medical Statistics, Institute of Applied Health Sciences, University of Aberdeen, Polwarth Building, Cornhill Road, Aberdeen, AB252ZD

Mairead Black, Aberdeen Centre for Women’s Health Research, University of Aberdeen, Room 4, Second Floor, Aberdeen Maternity hospital, Cornhill Road, Aberdeen, AB252ZD, 01224 438437, Mairead.black@abdn.ac.uk

## Abstract

**Background:** Postpartum haemorrhage (PPH) rates are increasing in developed countries. A reliable prognostic tool for PPH has potential to aid prevention efforts.

**Objective:** To systematically identify and appraise prognostic modelling studies for prediction of PPH.

Search strategy: MEDLINE, Embase, CINAHL and the Cochrane Library were searched using a combination of terms and synonyms including ‘prediction tool’, ‘risk score’ and ‘postpartum haemorrhage’.

Selection criteria: Any observational or experimental study developing a prognostic model for women’s risk of PPH. English language publications.

Data collection and analysis: Predesigned data extraction form to record: data source; participant criteria; outcome; candidate predictors; actual predictors; sample size; missing data; model development; model performance; model evaluation; interpretation.

Main Results: Of 1723 citations screened, 10 studies were eligible for inclusion. An additional paper was published and identified following completion of the search. Studies addressed populations of women who experienced; placenta praevia; vaginal births; caesarean birth; and the general obstetric population. Primary study authors deemed four models to be confirmatory. There was a high risk of bias across all studies due to a combination of retrospective selection of women, low sample size, no internal validation, suboptimal external validation and no reporting of missing data.

Conclusion: Of eleven prognostic models for PPH risk, one developed for women undergoing caesarean section is deemed suitable for external validation. Future research requires robust internal and external validation of existing tools and development of a model that can be used to predict PPH in the general obstetric population.

Systematic review registration number: PROSPERO 95587

Tweetable abstract

Current PPH prediction tools need external validation: One for CS; one for placenta praevia. Tools are needed for labouring women.

## Introduction

Postpartum haemorrhage (PPH) remains a leading cause of morbidity and mortality globally, and was the second highest cause of direct maternal death in the UK 2013-2015.

The incidence of PPH is problematic in developing countries but is also noted to be increasing in developed countries. While early diagnosis is essential in the management of PPH, diagnosis of PPH itself presents a challenge due to the reliance upon quantification of the volume of blood loss. For vaginal delivery, cut-offs for haemorrhage are typically over 500ml of blood loss whilst for caesarean section (CS) it is over 1000ml.

Prevention of PPH could arise through identification of women at highest risk, allowing for measures to be taken for active management of third stage of labour, presence of experienced clinicians and immediate access to resources such as oxytocin infusion and tranexamic acid. There are numerous studies identifying individual risk factors for PPH but these don’t reliably identify women at greatest risk by combining multiple risk factors. A combination of risk factors is common in practice but quantifying the associated risk without the aid of a clinical prediction model is challenging. Once a reliable and high performing prediction model is developed this could be converted into a user-friendly tool such as an online risk calculator or embedded within electronic health records.

A review by Kleinroueler et al., 2015 found over 200 prognostic models available in obstetrics, three of which related to PPH. The review found very few models in any area of obstetrics that were being applied to routine clinical practice and the majority of studies had not presented model formulas to allow researchers to conduct independent external validation of the models.

In order to progress efforts to identify women at risk of PPH as early and as accurately as possible, a systematic review of existing prognostic models was considered essential. This would enable assessment of existing models for their suitability for immediate use, or identify those which perform well internally but

require external validation on an independent cohort before being considered for clinical use. This approach has potential to be more efficient than the addition of a new model to aid prevention of PPH.

Since publication of the aforementioned review several attempts at developing prognostic models for PPH have been published. This review aims to systematically identify and appraise studies which develop prognostic models that can predict the chance of PPH in pregnant women.

## Methods

This review adhered to principles outlined in guidance published by PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) and CHARMS (CHECKlist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies). The protocol for this review has been published by PROSPERO and is available online.

A literature search was conducted during May 2018 of the following databases: Medline, Embase, CINAHL and the Cochrane Library. To inform the full search strategy a limited search of Medline was first conducted followed by an extensive search of the literature of the aforementioned databases. A copy of the search strategy for Medline and Embase is available in *Table S1*. The main search terms were ‘predict\$', ‘risk score’ and ‘postpartum haemorrhage’ with the appropriate synonyms adopted.

Inclusion criteria and exclusion criteria for this review are outlined in *Table 1*. Titles and abstracts were independently screened by two reviewers (CN and SN) with any disagreements resolved by a third reviewer (MB).

Data extraction and quality assessment (at study level) were conducted independently in accordance with the CHARMS checklist (*Table S2*) to allow identification of potential bias in primary studies and identify limitations to applicability of the results. Items extracted were as follows: source of data; participants; outcome to be predicted; candidate predictors (or index tests); sample size; missing data; model development; model performance; model evaluation; results and interpretation (including whether authors deemed their model fit for purpose or nature of further research required before using). The findings were tabulated and a narrative synthesis performed. The findings address the baseline characteristics of the studies, the type of models included, evaluation of the models and the applicability of the models to clinical practice.

## Results

The search strategy identified 1723 citations; following removal of duplicates and screening, 52 full text articles were assessed for eligibility (PRISMA Flow Diagram, *Figure 1*). This review included 11 studies with a total of 11 final prediction models identified.

The populations of the included studies are shown in *Tables 2 and 3*. Four studies included only women with placenta praevia, four studies included only vaginal deliveries, two studies had a population consisting of CS (planned and unplanned) and one study had a population encompassing the general obstetric population.

The key findings of the studies are detailed in *Table 2* including whether the study is to be interpreted as exploratory (requiring more research) or confirmatory (of use in clinical practice) as judged by the primary study authors. All candidate predictors and the predictors included in the final published models is listed in *Table 3*. The setting of the included studies were hospitals across the following countries; Italy, China, France, United States, United Kingdom, South Korea, Netherlands, Spain, Zimbabwe, Denmark and Egypt. The study designs included were eight cohort studies of which one used whole population registry data, and three case-control, of which one was nested within a population cohort. The number of participants included in each study ranged from 110 in a prospective cohort study to 56,967 in a retrospective cohort.

Despite the attempt to predict PPH across all studies, the chosen outcomes differed. Five studies listed PPH or massive haemorrhage as an outcome, three studies listed blood transfusion or massive blood transfusion as an outcome, two studies reported postpartum blood loss, and one study had a combined outcome of peripartum complications encompassing perioperative blood transfusion or uterine artery embolization or caesarean hysterectomy. There is also variation in the definition and method of measurement of each outcome as shown in *Table 2*.

The quality of studies, assessed using the CHARMS checklist to assess risk of bias, is summarised in *Table 4*. Overall there was a high risk of bias across the studies. The source of data was deemed of low/moderate risk of bias in eight studies due to the use of a retrospective design for measurement of predictor and outcome. Two studies

were at high risk of bias due to a lack of definition or method of measurement of the outcome to be predicted. There was a high risk of bias for the candidate predictors in three studies due to a lack of definition or predictors requiring subjective interpretation. Regarding sample size, six studies were of high risk of bias for sample size as a result of a low number of events per variable (EPV). Risk of bias for missing data was uncertain for all papers because none reported any missing data.

From the 11 studies there was a total of 97 unique variables selected as candidate predictors (range 5-23 per study) and 56 variables selected as predictors (range 5-15 per study) in the final models. The following predictors were found to be predictive in two or more studies: (parity n=4 studies), low antenatal haemoglobin (n=3), antepartum haemorrhage/bleed (n=3), maternal age [?]35 years old (n=4), high neonatal weight (n=2), multiple pregnancy (n=2), BMI [?]25 (n=2), previous CS (n=3), anterior placenta (n=2) and retained placenta (n=2).

The predictive ability of the statistical models evaluated using measures of calibration (concerned with agreement between the predicted probabilities of the outcome and the observed proportions of the outcome) and discrimination (how well the model can differentiate between patients with high and low risk) was evident in four and six

out of 11 studies respectively. Of the four studies to report calibration, two used the Hosmer-Lemeshow (H-L) test with Kim et al., reporting good calibration with a result of  $p=0.44$  and Rubio-Alvarez et al., failing to report a result. However, Hosmer-Lemeshow test is not recommended for calibration assessment due to poor interpretation as it does not provide a direction or magnitude of the miscalibration and has limited power in small samples. Biguzzi presented a calibration plot demonstrating overall good performance, however, there was inadequate information relating to curve development. Ahmadzia et al., report calibration plots and association between predicted probability of transfusion and observed incidence in deciles of the risk score distribution. However, the authors have not reported, at the very least, a Hosmer-Lemeshow test nor demonstrated a suitable calibration plot.<sup>14</sup> The calibration plots are described as curves but only display a point for each decile with no 95% confidence intervals. Ideally the calibration slope should be reported along with a calibration curve demonstrating the non-parametric relationship between observed outcome and predicted risk.<sup>28</sup> Discrimination was reported as the area under the receiver operator curve (AUC) where 1 is perfect discrimination and 0.5 is no better than a coin toss. The AUC ranged from 0.70 to 0.9 across all studies as shown in *Table 2*.

Of 11 studies, four presented validated models deemed by their primary study authors as ready for use in clinical practice.<sup>14,18,19,22</sup> Ahmadzia et al., present an online risk calculator developed in patients who underwent CS and Dunkerton et al., presented a decision tree based on Hothorn et al's non-parametric recursive partitioning algorithm also developed in women who underwent a CS. Kim et al., presented a scoring system developed in women with placenta praevia and Rubio-Alvarez et al., present an Excel risk tool developed in women vaginally delivering singletons. However, Ahmadzia et al and Dunkerton et al did not externally validate their models – an important requirement before use in clinical practice.<sup>29</sup> The discriminatory performance on external validation for Kim et al and for Rubio-Alvarez et al models were good with AUCs of 0.88 and 0.83 respectively.

## Discussion

### Main Findings

This review is, to our knowledge, the first to systematically identify published studies attempting to provide risk scoring or prognostic models for the prediction of PPH. Of eleven eligible studies, two have presented externally validated risk tools but neither were developed using recommended methods. Kim et al. (predicting blood transfusion ([?]8u) following CS for placenta praevia) and Rubio-Alvarez et al. (predicting excessive postpartum blood loss in women with singleton pregnancies who underwent vaginal delivery) did not define candidate predictors and both demonstrated very low events per variable. Chi et al., was the only study to have a tool applicable to the general obstetric population but is of high risk of bias; until it has been validated, it cannot be recommended for clinical use. The other eight studies identified are not deemed suitable for use in clinical practice due to a lack of clinical relevance of some study populations, high risk of bias and lack of external validation. Six out of eleven studies featured substantially less than 10 events per potential predictor being tested such that sample size presents a major threat to reliability of findings.

### Strengths and Limitations

A strength of this review is the prospective publication of the protocol in PROSPERO with strict adherence to this. The aim was to find a clinically meaningful formula or tool which could be of use to a clinician in daily practice. Numerous related studies have not published a useable tool or logistic regression model with a formula which a clinician could use in clinical practice – this may reflect poor (or poorer than anticipated) performance of the model. This review benefits from use of broad and general search criteria to maximise identification of relevant studies. Additionally, the results yielded by the search strategy were double-screened by two reviewers (CN and SN). The use of the CHARMS checklist allowed for systematic data extraction and assessment of risk of bias.

A limitation of this review is that three studies were unable to be obtained which may have been appropriate for inclusion. One of these was part of an unpublished PhD thesis and the other two were behind a paywall.

This review highlights shortcomings regarding the risk of bias and reporting of the included studies.

The review included only studies in English language such that this may limit the value of the findings.

### Interpretation

This review suggests that there are no published prediction tools for PPH that are ready for clinical use. Future research to generate prognostic models for use specifically in elective CS or in women aiming for vaginal birth would facilitate advanced planning of personnel to optimise care provided.

The clinical usefulness of models generated by some of the identified studies is limited by the target population. Four studies focus on vaginal births which is not clinically meaningful as this cannot be guaranteed in advance. The circumstances during labour are subject to change with a risk of CS present until the fetal head is delivered. Therefore, despite one of these studies, Rubio-Alvarez et al., providing an externally validated user-friendly risk prediction tool in Excel, its validity in practice is extremely limited as it is not possible to know which women will give birth vaginally and thus for whom the model is valid. Only one study produced a scoring tool aimed at use in the general obstetric population but the study design was unclear and attempts to contact the author were not successful. The study included 923 women in Beijing, China, of whom almost half had a PPH, and it did not assess predictive performance via internal or external

validation. Therefore, despite the presentation of an equation to predict PPH with AUC of 0.86, its lack of performance assessment means it cannot be recommended for use in clinical practice.

Most studies were retrospective, meaning that some predictors may not have been measured, but the vast majority of relevant risk factors for PPH can be assessed retrospectively such that this is not considered to be a major problem.

Some studies' prediction models or tools are clinically unhelpful in regard to the final predictors included due to some not being known at time of birth. Both Biguzzi et al., and Rubio-Alvarez et al., included neonatal birthweight as a predictor, which suggests that the intended time for the nomogram and risk tool use is after weighing of the baby, most likely once the highest risk of PPH has passed. These models are therefore of limited value for preparation of resources prior to birth. Estimated birthweight may be a more appropriate measure but this has not been included as a predictor in any model.

Use of intrapartum factors can aid risk assessment in a dynamic scenario. Two studies have included these: duration of the first and second stage of delivery; non-use of uterotonics and cord traction. Intrapartum risk scoring may be facilitated by use of electronic health records, where the tool could be embedded within the system, but otherwise may present logistical difficulties if it requires ongoing computer access as per Rubio-Alvarez et al's proposed risk tool.

Robust external validation was absent from all prediction models identified, suggesting that this is poorly understood and undervalued. Of the two models externally validated both utilised Hosmer-Lemeshow testing which is not recommended, and only one provided validation results. Internal validation is a reasonable alternative as this assesses how well the model performs in the underlying population from which the model was developed, but only five studies did this and only one is considered appropriate for prospective use (in placenta praevia population) and thus this would benefit from future external validation.

The prediction models identified were at high risk of bias overall, with lack of detail of candidate predictors, small sample size and suboptimal statistical analysis being common, and missing data not reported in any study. Without missing data information it is not possible to fully assess the related risk of bias.<sup>39</sup>

The need for adequately powered studies is clear. Half the included studies have shown a low EPV (<10) with only one conducting any shrinkage methods to overcome problems arising from overfitting of the model (and risk of optimistic predictions) when there is a low number of events. Despite this, several authors recommended use of affected models without external validation.<sup>19,20,22</sup> As a result of heterogeneity and low EPV, it was not possible to conduct a meta-analysis of the results. However, there is potential for synthesis of findings for predicting PPH in a population of women with placenta praevia, where individual participant data (IPD) meta-analysis could be used.

## Conclusion

This review has identified two PPH risk prediction tools with potential for clinical use pending robust external validation, one for use in cases of CS (Leicester PPH predict score) and the other for predicting massive transfusion ( $\geq 8$ u packed red cells) in cases of CS with known placenta praevia. There is a need for the development of a model applicable to the wider obstetric population which can be used when planning birth.

Contribution to authorship

CN drafted the manuscript and performed the first literature search, data extraction and analysis.

SN performed the second screening of the titles, abstracts and full papers and approved the final draft of the manuscript.

DM commented on all versions of the manuscript and provided methodological advice throughout the study.

MB designed the study, supervised all steps and commented on all drafts of the manuscript. MB is corresponding author.

Conflicts of interest

The authors have no conflicts of interest to declare.

Funding

This study received no external or specific source of funding.

## References

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Observational studies	Studies which aim only to
Experimental studies	Studies only describing to
Pregnant women over the age of 16	Studies investigating a si
Development &/or validation of a prognostic multivariable tool or model to predict risk of PPH	Case-reports
Published since 1946	Non-English language pu

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study				
Study Author	Study Design	<b>Study Population</b>	Exclusion Criteria	Outcome with Definition and Method of Measurement	Candidate Predictors,	Participants (events)	Events per Variable	Modelling Method in	Predictor Final Model, <i>n</i>	Calibration	Discrimination	Validation	Presence of final prediction model or tool

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study
Ahmadzi et al., 2018 <sup>14</sup>	Retrospective Cohort	Patients who underwent caesarean section for delivery	Vaginal delivery and incomplete data for intrapartum and postpartum blood transfusion	Intraoperative and postoperative blood transfusion	Model 1: 16 Model 2: 23	56,967 (1488)	Model 1: 93 Model 2: 64.7	Logistic	14	Association between predicted probability of transfusion and observed incidence in deciles of the risk score distribution' Calibration graph provided.	Model 1: AUC (95% CI 0.75-0.78) Model 2: AUC (95% CI 0.81-0.84)	Internal validation by random split of data	Online Risk Calculation

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study
Baba et al., 2014 <sup>15</sup>	Retrospective Cohort	All women with placenta praevia who underwent a caesarean section	None	Blood Transfusion: haemoglobin <6.0g/dL or systolic BP <70mmHg or estimated blood loss reached >2500ml	9	205 (20)	2.22	Logistic	5	None	AUC 0.844 (95% CI 0.731-0.958)	None	Equa

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study
Biguzzi et al., 2011 <sup>16</sup>	Unclear	All women who underwent vaginal delivery	Age <18 years, Caesarean section, Delivery before the 37th week of gestation, Twin pregnancy, No comprehension of the Italian language, Refusal to sign a written informed consent. Deliveries that occurred on Friday afternoon	Postpartum haemorrhage (blood loss of [?]500ml) measured by visual estimation using graduated basin	16	6011 (1435)	89.69	Logistic	5	Graph plotting predicted probabilities against observed outcomes – inadequate information on how curve was developed	AUC 0.70	Internal Validation with bootstrap sampling	Nominal

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study
Chi et al., 2016 <sup>17</sup>	Retrospective Case-control	Pavurien patients with complete prenatal examination data	None	Postpartum haemorrhage	21	923 (447)	21.29	Logistic	15	None	None	None	Score assign
Dunkerton et al., 2018 <sup>18</sup>	Retrospective cohort	All caesareans at a single university hospital trust in U.K	None	Postpartum haemorrhage (estimated blood loss of [?] 1000ml, annual staff training with pictorial reference cards)	17	24,230 (2997)	176.29	Hothorn et al's non-parametric recursive partitioning algorithm	9	None	None	Internal validation by data splitting	Decision tree

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study
Kim et al., 2017 <sup>19</sup>	Registry data	Patients with placenta praevia who underwent caesarean section	Coagulopathy and incomplete data	Massive transfusion (transfusion of [?]8 units pRBC within 24h after delivery)	12	238 (31)	2.58	Logistic	5	Hosmer-Lemeshow test (p=0.44)	Internal validation AUC (0.84)	Internal validation by bootstrapping and External validation AUC (0.88)	External validation of score model

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study			
Lee et al., 2018 <sup>20</sup>	Retrospective Cohort	Pregnant women with placenta praevia	Multiple pregnancies, Maternal obstetrical or medical problems other than placenta praevia and Fetal anomalies	Massive haemorrhage defined as blood loss [?] 2000ml during surgery, post-partum transfusion of four pints of packed red blood cells, caesarean hysterectomy or uterine arterial embolization triggered by post-partum bleeding.	16	560 (73)	4.56	Logistic	7	None	AUC (0.856)	None	Sum score

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study
Prata et al., 2011 <sup>21</sup>	Prospective Cohort	Women anticipating a singleton vaginal delivery of gestational age >36 weeks	Delivery by caesarean section, missing information on delivery type	Postpartum haemorrhage defined as blood loss greater than 500ml during the first 4 hours after delivery (measured by calibrated drapes)	20	2510 (93)	4.65	Logistic	8	None	None	None	Cumulative number of risk factors vs ri

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study
Rubio-Alvarez et al., 2018 <sup>22</sup>	Retrospective cohort	Women with single-tons pregnancies who had vaginal birth	Antenatal fetal demise, Multiple pregnancies and Gestations <35 weeks	Excessive post-partum blood loss defined as a reduction in haemoglobin (Hb) levels greater than 3.5g/dL and a final Hb <8g/dL between onset of birth and 24 hours after it	14	2336 (43)	3.07	Logistic	6	Hosmer-Lemeshow test (no result reported)	AUC (0.85-0.93)	Internal Validation by random-split of data	Risk Tool for Exce

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study
Tsu 1994 23	Case-control	Women with singleton vertex deliveries and spontaneous onset of labour	None	Postpartum blood loss of at least 600ml after a normal, unassisted vaginal delivery	5	653 (151)	30.2	Logistic	5	None	only ROC no AUC	None	Equa

Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study	Table 2: Key components of each study
Yoon et al., 2014 <sup>24</sup>	Prospective Cohort	Singleton pregnancy women with placenta praevia delivered by caesarean section	None	Occurrence of peripartum complications: Perioperative blood transfusion (determined by attending anaesthesiologist during CS when clinical evidence of inadequate oxygen-carrying capacity or ongoing profuse blood loss) or uterine artery emboliza-	12	110 (38)	2.89	Logistic	6	None	None	None	Score: mod

Table 2: Key components of each study													
---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------	---------------------------------------

Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors
Study Author	Study Population	Candidate Predictors	Predictors in Final Model
Ahmadzia et al., 2018 <sup>14</sup>	Intraoperative and postoperative blood transfusion	Maternal age (extremes <21 or >36), BMI at delivery, Number of previous term deliveries, Gestational age >37 weeks, total years of schooling, African American ethnicity, insurance status for prenatal care, white blood cell count, platelet count, haematocrit, previous cesarean delivery, asthma, heart disease, connective tissue disorder, hypertensive disorder (gestational hypertension/preeclampsia/HELLP), abruption, non-elective caesarean delivery, use of general anaesthesia, failure to progress, preeclampsia/eclampsia or HELLP, abnormal placentation, intrapartum antibiotic use (including treatment for chorioamnionitis or prophylaxis for GBS/caesarean delivery)	Model 1 & 2: Maternal Age, Body Mass Index (BMI, kg/m <sup>2</sup> ), Platelets x10 <sup>3</sup> , Haematocrit (%), Gestational hypertension or Preeclampsia, HELLP, History of asthma, Suspected Abruption, African American, Insurance, Gestational age <37 weeks, 3 or more previous term deliveries, Heart disease, Number prior caesarean deliveries Model 2 also contained: non-elective repeat caesarean delivery, use of general anaesthesia, preeclampsia/eclampsia or HELLP, abnormal placentation, intrapartum antibiotic use

Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors
Chi et al., 2016 <sup>17</sup>	Parturient patients with complete prenatal examination data	Age, BMI, Multiplets, Hypertension family history, Adverse maternal history, History of abdominal operation, Hypertensive disorder complicating pregnancy, Gestational diabetes mellitus, Giant baby, Amniotic fluid, Myoma of uterus, Placenta praevia, Placental abruption, Retained placenta, Adherent placenta, Threatened premature labour, Abnormal pelvic canal, Haemoglobin, Platelet count, Caesarean delivery, Placenta factor	Multiplets, Hypertension family history, Adverse maternal history, History of abdominal operation, Hypertensive disorder complicating pregnancy, Giant baby, Amniotic fluid, Myoma of uterus, Abnormal pelvic canal, Threatened premature labour, Haemoglobin [?] 100, Platelet Count < 100x10 <sup>9</sup> , Age [?] 35, BMI [?] 25, Pregnancy bleeding history
Dunkerton et al., 2018 <sup>18</sup>	All caesareans at a single university hospital trust in U.K	Previous Caesarean, antepartum/intrapartum haemorrhage, emergency caesarean, age [?]40y, maternal sepsis, suspected scar dehiscence, second-stage section, polyhydramnios, macrosomia, fibroids, preeclampsia/pregnancy induced hypertension, multiple pregnancies, previous three caesarean sections, Asian ethnicity, grandmultiparity, placenta praevia, suspected abruption	Placenta praevia, previous caesarean, antepartum haemorrhage, BMI >35, Emergency caesarean section, Asian ethnicity, Multiple Pregnancy, grandmultiparity, pregnancy induced hypertension/Pre-eclampsia

Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors
Kim et al., 2017 <sup>19</sup>	Patients with placenta praevia who underwent caesarean section	Maternal age, BMI, parity, Gestational age, previous caesarean, placental abruption, previous uterine surgery, twin pregnancy, artificial abortion, anterior placenta, cervical vascularity, Suspicion of placental adhesion	Gestational age, previous caesarean, anterior placenta, cervical vascularity, suspicion of placental adhesion

Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors
Lee et al., 2018 <sup>20</sup>	Pregnant women with placenta praevia	Maternal age at delivery, Parity, BMI, Number of previous uterine curettages, Previous uterine surgery (caesarean or myomectomy), Presence of uterine myoma, Cervical length within a week before delivery, Gestational age at first episode of AP bleed (after 20 weeks), Number of incidences of antepartum bleeding (after 20w), Need for emergency CS, Fetal presentation, Placental type (complete or incomplete), Location (anterior or posterior), Multiple lacunae ([?]4 defined as an irregular area of low echogenicity larger than 1x1cm in placental parenchyma), Lack of translucent zone (clear zone defined as the line of low echogenicity between myometrium and placenta), Uteroplacental hypervascularity evident on colour doppler imaging	Maternal age [?]35 years, Antepartum bleeding, fetal non-cephalic presentation, complete placenta praevia, anterior placenta, Multiple lacunae [?]4, Uteroplacental hypervascularity

Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors
Prata et al., 2011 <sup>21</sup>	Women anticipating a singleton vaginal delivery of gestational age >36 weeks	Maternal age, Education, Nulliparity, Previous antenatal care, PPH in previous pregnancy, History of obstetric complications, Intact membranes, Anaemia (measured by blood collected after enrolment and defined as antepartum Hb at or below 11mg/dl), cervical dilatation, Vaginal delivery with instruments, Episiotomy, Labour augmentation, Retained placenta, Vaginal tears, Fetal macrosomia (>3500g), Length of 1st and 2nd stage, Absence of AMTSL (a protocol), Use of uterotonics, Cord clamping, Cord traction, Uterine massage	Elevated number of antenatal care visits, history of PPH, anaemia, labour augmentation, retained placenta, length of 1st and 2nd stage, non-use of uterotonics in the 3rd stage and cord traction
Rubio-Alvarez et al., 2018 <sup>22</sup>	Women with singleton pregnancies who had vaginal birth	Age, BMI, Antepartum haemoglobin, Previous caesarean, Primiparity, Instrumental birth, Duration of first stage, duration of second stage of labour (hours), Use of regional analgesia, Active management (5IU intraoperative oxytocin and consequent controlled umbilical cord traction), Manual removal of placenta, Episiotomy or vaginal tear, Gestational age (weeks)and Neonatal birthweight(g)	Primiparity, Maternal age, Duration of first stage, Duration of second stage, Neonatal birthweight and Antepartum haemorrhage

Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors	Table 3: Study population of included studies alongside predictors
Tsu 1994 <sup>23</sup>	Women with singleton vertex deliveries and spontaneous onset of labour	Advanced maternal age (>35), Low parity (0,1), Poor obstetric outcome in preceding pregnancy, Anaemia during current pregnancy (antenatal haemoglobin <12g/dL) and Admission to hospital for any pregnancy related problem before onset of labour	Combination 1: Poor obstetric outcome in last pregnancy or antenatal admission to hospital for a pregnancy related problem Combination 2: Poor obstetric outcome in last pregnancy or antenatal admission to hospital for a pregnancy related problem or low haemoglobin Combination 3: any 2 or more risk factors (as listed under ‘Candidate Predictors’) Combination 4: any 1 or more risk factors (as listed under ‘Candidate Predictors’)
Yoon et al., 2014 <sup>24</sup>	Singleton pregnancy women with placenta praevia delivered by caesarean section	Type of praevia: partialis and totalis, Location of praevia (posterior, lateral and anterior), Lacunae (classified into 4 grades (0-3)), Echolucent area (intact or absent) Hypervascularity (normal, moderately increased intraplacental vascularity and severe uteroplacental hypervascularity), Bladder-uterine interface (intact or interrupted) Maternal age ([?] 35), Multiparity, Prior caesarean section, Prior praevia, Prior abortion, Antepartum bleeding	Type of placenta praevia, Lacunae, Hypervascularity, Multiparity, Prior praevia, Prior caesarean section

Table 4: Summary table of risk of bias	Table 4: Summary table of risk of bias	Table 4: Summary table of risk of bias
Study Author	Source of Data	Outcomes to be Predicted
Ahmadzia et al., 2018 <sup>14</sup>	+/-	-

**Table 4: Summary table of risk of bias**    **Table 4: Summary table of risk of bias**    **Table 4: Summary table of risk of bias**

Baba et al., 2014 <sup>15</sup>	+/-	+
Biguzzi et al., 2011 <sup>16</sup>	?	+
Chi et al., 2016 <sup>17</sup>	+/-	-
Dunkerton et al., 2018 <sup>18</sup>	+/-	+
Kim et al., 2017 <sup>19</sup>	+/-	+
Lee et al., 2018 <sup>20</sup>	+/-	+
Prata et al., 2011 <sup>21</sup>	+	+
Rubio-Alvarez et al., 2018 <sup>22</sup>	+/-	+
Tsu 1994 <sup>23</sup>	+/-	-
Yoon et al., 2014 <sup>24</sup>	+	+

Green boxes (+) indicate low risk of bias, yellow boxes (+/-) indicate low/moderate risk of bias, red boxes (-) indicate high risk of bias and orange boxes (?) indicate unclear risk of bias.

Figure 1: PRISMA Flow Diagram

