CORA Cork Open Research Archive
Cartlann Taighde Oscailte Chorcaí

Title	Predicting risk of postpartum haemorrhage during the intrapartum period in a general obstetric population
Authors	Maher, Gillian M.;McKernan, Joye;O'Byrne, Laura;Corcoran, Paul;Greene, Richard A.;Khashan, Ali S.;McCarthy, Fergus P.
Publication date	2022-09-01
Original Citation	Maher, G. M., McKernan, J., O'Byrne, L., Corcoran, P., Greene, R. A., Khashan, A. S. and McCarthy, F. P. (2022) 'Predicting risk of postpartum haemorrhage during the intrapartum period in a general obstetric population', European Journal of Obstetrics & Gynecology and Reproductive Biology, 276, pp. 168-173. doi: 10.1016/j.ejogrb.2022.07.024
Type of publication	Article (peer-reviewed)
Link to publisher's version	10.1016/j.ejogrb.2022.07.024
Rights	© 2022 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/). - https://creativecommons.org/licenses/by/4.0/
Download date	2026-11-07 03:08:07
Item downloaded from	https://hdl.handle.net/10468/13801

UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

European Journal of Obstetrics and Gynecology 276 (2022) 168–173

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.journals.elsevier.com/european-journal-of-obstetrics-and-gynecology-and-reproductive-biology

Predicting risk of postpartum haemorrhage during the intrapartum period in a general obstetric population

Gillian M. Maher [a,b,*], Joye McKernan [c], Laura O'Byrne [a,d], Paul Corcoran [c], Richard A. Greene [c], Ali S. Khashan [a,b], Fergus P. McCarthy [a,d]

[a] INFANT Research Centre, Cork, Ireland
[b] School of Public Health, University College Cork, Cork, Ireland
[c] National Perinatal Epidemiology Centre, Department of Obstetrics and Gynaecology, University College Cork, Cork, Ireland
[d] Department of Obstetrics and Gynaecology, University College Cork, Cork, Ireland

ARTICLE INFO

Keywords:
Postpartum haemorrhage
Prediction model
Internal validation
External validation

ABSTRACT

Objective: To develop and validate (both internally and externally) a prediction model examining a combination of risk factors in order to predict postpartum haemorrhage (PPH) in a general obstetric Irish population of singleton pregnancies.

Study design: We used data from the National Maternal and Newborn Clinical Management System (MN-CMS), including all singleton deliveries at Cork University Maternity Hospital (CUMH), Ireland during 2019. We defined PPH as an estimated blood loss of $\geq$ 1000 ml following the birth of the baby. Multivariable logistic regression with backward stepwise selection was used to develop the prediction model. Candidate predictors included maternal age, maternal body mass index, parity, previous caesarean section, assisted fertility, gestational age, fetal macrosomia, mode of delivery and history of PPH. Discrimination was assessed using the area under the receiver operating characteristic curve (ROC) C-statistic. We used bootstrapping for internal validation to assess overfitting, and conducted a temporal external validation using data from all singleton deliveries at CUMH during 2020.

Results: Out of 6,077 women, 5,807 with complete data were included in the analyses, and there were 270 (4.65%) cases of PPH. Four variables were considered the best combined predictors of PPH, including parity (specifically nulliparous), macrosomia, mode of delivery (specifically operative vaginal delivery, emergency caesarean section and prelabour caesarean section), and history of PPH. These predictors were used to develop a nomogram to provide individualised risk assessment for PPH. The original apparent C-statistic was 0.751 (95% CI: 0.721, 0.779) suggesting good discriminative performance. There was minimal optimism adjustment to the C-statistic after bootstrapping, indicating good internal performance (optimism adjusted C-statistic: 0.748). Results of external validation were comparable with the development model suggesting good reproducibility.

Conclusions: Four routinely collected variables (parity, fetal macrosomia, mode of delivery and history of PPH) were identified when predicting PPH in a general obstetric Irish population of singleton pregnancies. Use of our nomogram could potentially assist with individualised risk assessment of PPH and inform clinical decision-making allowing those at highest risk of PPH be actively managed.

Introduction

Obstetric haemorrhage is a leading cause of maternal mortality worldwide, accounting for nearly-one quarter of all maternal deaths globally [1], while it is also associated with severe maternal morbidity including long-term psychological trauma [2], multi-organ failure and peripartum hysterectomy [3]. Early diagnosis is essential in the effective management of obstetric haemorrhage, and while a consensus on the exact definition is lacking, it typically refers to any kind of excessive pregnancy related bleeding during the antepartum period, childbirth, or

Abbreviations: PPH, postpartum haemorrhage; MN-CMS, National Maternal and Newborn Clinical Management System; CUMH, Cork University Maternity Hospital; ROC, receiver operating characteristic curve; HER, electronic health record; CITL, calibration-in-the-large; C-slope, calibration slope.

* Corresponding author at: INFANT Research Centre, 5th floor, Cork University Maternity Hospital, Cork, Ireland.
E-mail address: gillian.maher@ucc.ie (G.M. Maher).

https://doi.org/10.1016/j.ejogrb.2022.07.024
Received 21 March 2022; Received in revised form 22 June 2022; Accepted 26 July 2022
Available online 29 July 2022
0301-2115/© 2022 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

in the postpartum period [4,5].

The definition of postpartum haemorrhage (PPH) was traditionally defined as a blood loss in excess of 500 ml after vaginal delivery or > 1000 ml after a caesarean delivery [6]. However, the.

American College of Obstetricians and Gynaecologists (ACOG) now define PPH as cumulative blood loss ≥ 1000 ml regardless of route of delivery [7], while the Royal College of Obstetricians and Gynaecologists (RCOG) divide PPH into minor (blood loss 500–1000 ml) or major (blood loss > 1000 ml) [8].

Several studies to date have identified risk factors for PPH such as advanced maternal age, high body mass index (BMI), parity, assisted reproductive technologies, and preeclampsia [3,9–11]. While these are useful to identify and quantify individual factors associated with obstetric haemorrhage, it is likely that a combination of multiple risk factors are at play in practice [4]. A recent systematic review has identified three risk prediction tools for PPH with potential clinical use [4]: one in cases of caesarean section [12], one for the prediction of massive transfusion in caesarean section with known placenta praevia [13], and one for prediction of PPH in women with suspected placenta accreta spectrum disorders who underwent MRI for placenta evaluation ahead of caesarean section [4,14]. However, development and validation of a PPH prediction model for use in a general obstetric population is still warranted. Identifying such risk factors would allow clinicians to recognise those who may be at high risk of PPH and thus inform clinical decision-making and effective planning of care.

Therefore, using data from the National Maternal and Newborn Clinical Management System (MN-CMS), the aim of this study was to develop and validate a prediction model examining a combination of risk factors in order to predict PPH in a general obstetric Irish population of singleton pregnancies.

Materials and methods

Study population

In December 2016, the Republic of Ireland rolled out a national project called The Maternal and Newborn Clinical Management System (MN-CMS) which is the design and implementation of an electronic health record for all women and their babies. With this system, all pregnant women in maternity services in Ireland were switched from paper clinical notes to an electronic health record, allowing all maternal and newborn information to be stored on one record. Cork University Maternity Hospital (CUMH) was the first maternity hospital to implement the electronic health record, therefore CUMH data was used for the current study. Our study population consisted of all singleton deliveries at CUMH during 2019.

Ethical approval was obtained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals (ECM4(v)09/04/2020). The Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) checklist was used as a guideline for reporting the current study (available at https://www.tripod-statement.org).

Predictors and outcome

We considered routinely measured predictors using a combination of expert opinion (comprising obstetricians, epidemiologists and experts on the MN-CMS), a review of existing literature, as well as the distribution of the predictor in the data, (for example, any variables with < 5 exposed cases of PPH were not included) [15]. Predictors included maternal age, maternal BMI, parity, previous caesarean section, assisted fertility, gestational age, fetal macrosomia, mode of delivery and history of PPH.

A description of candidate predictors are as follows: Maternal age in years was recorded at initial prenatal visit. Maternal height (cm) and weight (kg) at initial prenatal visit were used to calculate maternal BMI. BMI was recategorised as underweight < 18.5, normal weight ≥ 18.5 to ≤ 24.9, overweight ≥ 25 to ≤ 29.9 and obese ≥ 30, with underweight and normal weight combined due to small numbers. Parity was recorded as number of previous completed pregnancies and was re-categorised as nulliparous or multiparous. Previous caesarean section was categorised as yes/no. Whether the pregnancy was a result of assisted fertility treatment was categorised as yes/no. Gestational age was recorded as number of completed weeks at delivery, and re-categorised as < 37 weeks', ≥37 to ≤ 39 weeks', and ≥ 40 weeks'. Macrosomia was defined as birthweight > 4000 g. Mode of delivery was recorded as spontaneous vaginal delivery, operative vaginal delivery, emergency caesarean section and prelabour caesarean section. History of PPH was recorded at booking visit and recoded as yes/no.

Outcome: PPH was defined as an estimated blood loss of ≥ 1000 ml following the birth of the baby. Blood loss was estimated by weighing the packs and sponges used to absorb the blood, with 1 ml of blood weighing approximately 1 g).

Statistical analysis

Statistical analysis was performed using Stata MP 14.2. Univariable logistic regression analysis examined associations between candidate predictors and the odds of PPH. Multivariable logistic regression with backward stepwise selection (with a p-value of 0.1 for exclusion) was used to develop the prediction model, where all candidate predictors are included at first and the least useful predictors (i.e. the variable that is the least statistically significant) are subsequently removed one by one.

Sample Size: Sample size calculation was conducted using the *pmsampsize* command. Assuming an outcome event proportion (prevalence) of 0.05, a target shrinkage factor of 0.9, a c-statistic of 0.75, and 13 candidate predictors/categories (i.e. those included in our model), a minimum sample size of 2,717 (with 136 events) would be required to minimise overfitting [16].

Model Performance and Internal Validation: We assessed overall fit, discrimination and calibration to examine model performance. Overall fit was assessed using Brier Score and Cragg & Uhler's (Nagelkerke) R^2. Discrimination (i.e. how well the model differentiates between those patients who experience the outcome and those who do not [15]) was assessed using the area under the receiver operating characteristic curve (ROC) C-statistic. Calibration (i.e. how closely the predictions of the model match the observed outcomes in the data [15]) was assessed using calibration-in-the-large (CITL) and calibration slope (C-slope). Calibration was also assessed graphically across ten risk groups of individuals using a calibration plot (pmcalplot) of observed against expected probabilities (i.e. deciles of risk were used as cut-off points to compare observed and expected probabilities in groups of individuals) [17].

We used bootstrapping (with 1000 repetitions) to assess overfitting and calculate the optimism adjusted C-statistic, CITL and C-slope. A nomogram (graphical representation of prediction model) was developed to provide individualised risk assessment for PPH.

External validation: We conducted a temporal external validation using data from all singleton deliveries at CUMH during 2020. Discrimination was assessed using the C-statistic, and calibration was assessed using the CITL and C-slope.

Results

There were 6,077 singleton deliveries recorded on the electronic health record at CUMH in 2019. The total amount of missing data was < 5 %, and we used complete case analysis when handling missing data [18]. Therefore, a total of 5,807 women were included in the analyses, and there were 270 (4.6 %) cases of PPH (blood loss of ≥ 1000 ml). Characteristics of study participants are outlined in Table 1. Univariable logistic regression analysis examining associations between candidate predictors and PPH are shown in Table A1 in the Appendix. Factors significantly associated with PPH included maternal BMI, parity,

Table 1
Characteristics of study participants.

	Estimated blood loss < 1000 ml N = 5537	Estimated blood loss ≥ 1000 ml N = 270
Maternal age (years)	34.6 (5.1)	35.1 (4.8)
Maternal BMI		
Underweight/normal weight	2752 (49.7)	111 (41.1)
Overweight	1710 (30.9)	94 (34.8)
Obese	1075 (19.4)	65 (24.1)
Parity		
≥1	3416 (61.7)	126 (46.7)
0	2121 (38.3)	144 (53.3)
Previous caesarean section		
No	4490 (81.1)	209 (77.4)
Yes	1047 (18.9)	61 (22.6)
Assisted fertility		
No	5356 (96.7)	252 (93.3)
Yes	181 (3.3)	18 (6.7)
Gestational age		
37–39 weeks'	3005 (54.3)	138 (51.1)
≥40 weeks'	2259 (40.8)	115 (42.6)
<37 weeks'	273 (4.9)	17 (6.306)
Macrosomia (>4000 g)		
No	4832 (87.3)	203 (75.2)
Yes	705 (12.7)	67 (24.8)
Mode of delivery		
SVD	2949 (53.3)	57 (21.1)
Operative vaginal delivery	847 (15.3)	64 (23.7)
Emergency caesarean section	584 (10.5)	65 (24.1)
Prelabour caesarean section	1157 (20.9)	84 (31.1)
History of PPH		
No	5364 (96.9)	221 (81.9)
Yes	173 (3.1)	49 (18.1)

N (%) for categorical variables, mean (SD) for continuous variables. Abbreviations: SD, standard deviation; BMI, body mass index; SVD, spontaneous vaginal delivery; PPH, postpartum haemorrhage.

assisted fertility, macrosomia, mode of delivery, and history of PPH.

Risk prediction model

Multivariable logistic regression with backward stepwise selection identified four variables that were considered the best combined predictors of PPH. These included parity (specifically nulliparous), macrosomia, mode of delivery (specifically operative vaginal delivery, emergency caesarean section and prelabour caesarean section) and history of PPH (Table 2).

These predictors were used to develop a nomogram to provide individualised risk assessment for PPH (Fig. 1). For example, a history of PPH (score 10.00), multiparous (score 0), fetal macrosomia (score 3.50), and prelabour caesarean section (score 7.20), the total score is 20.7 corresponding to a ~50 % risk of PPH.

Model performance and internal validation

Brier Score and Cragg & Uhler's (Nagelkerke) R^2 were 0.041 and 0.136 respectively indicating good overall performance. The calibration plot suggested that average model predictions match average observed outcomes for the ten groups of patients, indicating good calibration. Most of the deciles are clustered at the bottom left, indicating most individuals have low risk of PPH. The lowess smoother shows that there is little miscalibration at the individual level in the higher risk individuals, though there is little data at the higher risk probabilities as suggested by the spike plot at the bottom of the graph (Fig. A1 in the Appendix).

The original apparent C-statistic was 0.751 (95 % CI: 0.721, 0.779)

Table 2
Best combined predictors of postpartum haemorrhage.

Characteristic	Coefficient (95 % CI)	N (%)	OR (95 % CI)
Parity			
≥1	–	3542 (61.0)	ref
0	0.431 (0.129, 0.732)	2265 (39.0)	1.53 (1.13, 2.07)
Macrosomia			
No	–	5035 (86.7)	ref
Yes	0.720 (0.416, 1.025)	772 (13.3)	2.05 (1.51, 2.78)
Mode of delivery			
SVD	–	3006 (51.8)	ref
Operative vaginal delivery	1.211 (0.808, 1.614)	911 (15.7)	3.35 (2.24, 5.02)
Emergency caesarean section	1.743 (1.335, 2.150)	649 (11.2)	5.71 (3.80, 8.59)
Prelabour caesarean section	1.463 (1.103, 1.822)	1241 (21.4)	4.31 (3.01, 6.19)
History of PPH			
No	–	5585 (96.2)	ref
Yes	2.159 (1.782, 2.535)	222 (3.8)	8.66 (5.94, 12.62)
Intercept	−5.290 (-6.291, −4.289)	–	–

Abbreviations: OR, odds ratio; 95 % CI, 95 % confidence interval; ref, reference category; SVD, spontaneous vaginal delivery; PPH, postpartum haemorrhage.

suggesting good discriminative performance of the model. There was minimal optimism adjustment to the C-statistic after bootstrapping, indicating good internal performance in terms of discrimination (optimism adjusted C-statistic: 0.748). The miscalibration in CITL and C-slope were small suggesting that overfitting was unlikely to be an issue. (Table 3).

External validation: This analysis included 6,691 women with data on all predictors and there were 255 (3.8 %) cases of PPH (blood loss of ≥ 1000 ml). The C-statistic was 0.694 (95 % CI: 0.661, 0.725), while the CITL and C-slope were very close to 0 and 1 respectively, suggesting the overall (average) calibration of the model was good.

Discussion

Prediction of adverse maternal events is critical to allow services allocate appropriate resources to those most at risk. This study developed and validated a prediction model for PPH in a general obstetric Irish population of singleton pregnancies. We identified four routinely collected variables when predicting PPH in this population. These included parity (specifically nulliparous), fetal macrosomia, mode of delivery (specifically operative vaginal delivery, emergency caesarean section and prelabour caesarean section), and history of PPH. The latter three of these predictors, in particular, are in line with the four basic processes of PPH, namely tone, trauma, tissue and thrombin. For example, macrosomia is a risk factor for overdistension of the uterus associated with poor 'tone'; lacerations of the cervix, vagina or perineum during operative delivery or lacerations during caesarean section may relate to 'trauma'; while a history of previous PPH may be more closely related to 'thrombin' [19].

Internal validation indicated good overall performance and calibration, while our model showed good discriminative performance, with an optimism adjusted C-statistic of 0.748. Finally, results of our external validation were comparable with our development model suggesting good reproducibility.

While several prediction models for PPH have been developed with an AUC ranging from 0.7 to 0.9, many have been deemed to be at high risk of bias due to small sample sizes, few events per variable, and no

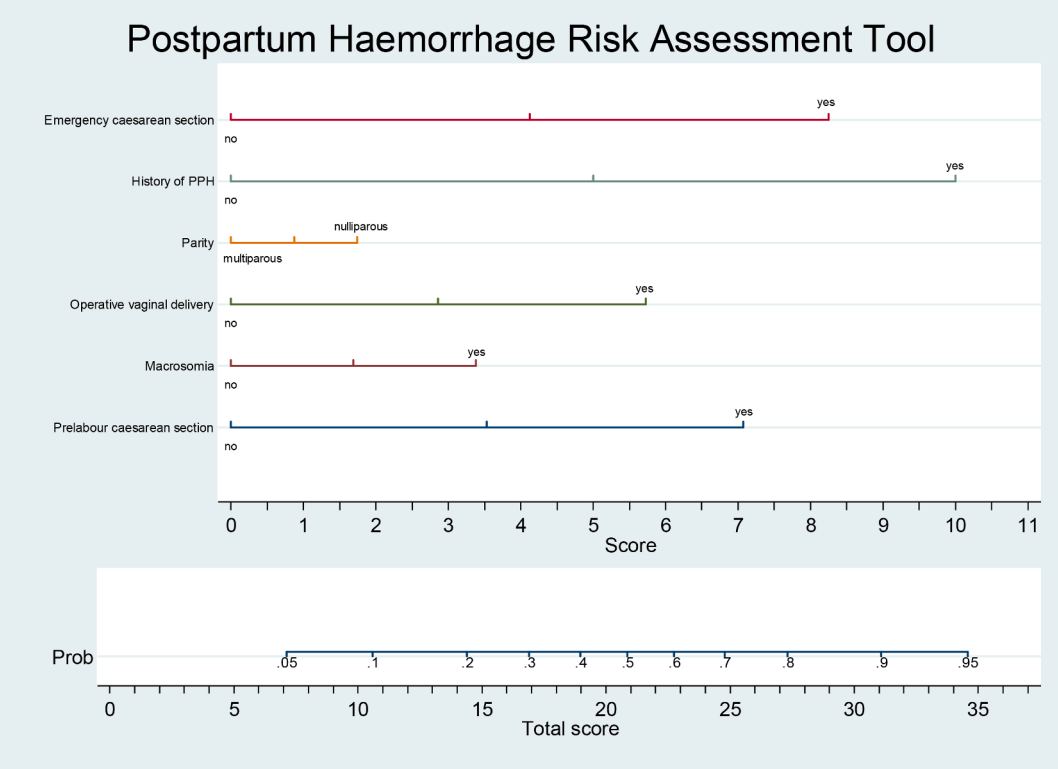


Fig. 1. Nomogram providing individualised risk assessment for postpartum haemorrhage. For example, a history of PPH (score 10.00), multiparous (score 0), fetal macrosomia (score 3.50), and prelabour caesarean section (score 7.20), the total score is 20.7 corresponding to a ~50 % risk of PPH.

Table 3
Assessment of model performance.

	Original apparent	Optimism	Optimism adjusted
Discrimination			
C-statistic	0.751 (0.721, 0.779)	0.003	0.748
Calibration			
CITL	0 (-0.126, 0.126)	0.001	−0.001
C-slope	1 (0.871, 1.128)	0.014	0.986

Abbreviations: CITL, calibration-in-the-large; C-slope, calibration slope.

internal or external validation [4]. Furthermore, few models, with limited clinical use, have been developed for a general obstetric population [4,20]. For example, Chi and colleagues developed a prediction model for PPH aimed at a general obstetric population, however, did not provide a definition of the outcome. The authors identified 15 out of 21 predictors for use in their final model and not unlike our findings, macrosomia and a history of pregnancy bleeding remained in the final model. Conversely, mode of delivery was not present in the final model, and parity was not considered as a candidate predictor. Additionally, the authors did not internally or externally validate their model, nor adjust for overfitting [20].

PPH prediction models with potential for clinical use, pending external validation, have also been developed [4,12–14], however, the populations used in these studies included women who underwent caesarean delivery only, therefore findings are most likely limited by the target population on which they were developed [4,12–14]. Finally, a more recent study conducted in the United States used both machine learning and statistical methods to develop a prediction model for PPH. The most important factors predicting PPH included pre-pregnancy maternal weight, admission maternal weight, prenatal diagnosis of fetal macrosomia, admission temperature, attempted trial of labour on admission, pre-pregnancy maternal BMI, admission systolic blood pressure, multiple gestation, anaemia diagnosis during pregnancy, and spontaneous labour on admission [21]. While both machine learning and statistical methods were shown to accurately predict PPH, machine learning models performed the best. However, such advanced methods come with the potential cost of increased complexity, with minimal improvements in clinical significance; factors that should be considered in future prediction models [21].

Clinical implications

Accurate risk prediction models can provide an individualised risk assessment and assist clinical decision-making and effective planning of care. For example, pretransfusion testing has previously been suggested for women who may be deemed as high risk of peripartum haemorrhage by their healthcare provider [22]. Therefore, integration of a risk prediction model into an electronic health record may support timely clinical decisions such as the need for pretransfusion testing. However, the additional benefit of applying a prediction model above current practice should first be considered and trialled in a real time clinical environment. Thus, before applying a risk prediction model in clinical practice, its clinical usefulness must first be determined through an impact study [15,23]. This can be achieved using net benefit and decision curve analyses, and ideally through cluster randomised trials [15,23,24].

Strengths and limitations

This study contained several strengths. First, our sample size was sufficiently large with a high number of events in order to minimise overfitting. Second, our predictors are routinely collected, and internal validation of our model indicated good overall performance and calibration. Third, we conducted a temporal external validation to assess reproducibility of our model. Fourth, the study is designed using data routinely collected in most maternity units worldwide, making it highly relevant and applicable. Finally, we used a nomogram to graphically

display our prediction model allowing the user to quickly and easily estimate the probability of PPH for an individual woman.

However, there are also limitations that should be noted. First, some relevant predictors may not have been measured and were therefore unavailable for inclusion in the model. For example, we did not have access to quality data on preeclampsia or slow progress of labour, which may have further improved the accuracy of our model. However, while including more candidate predictors may improve prediction of PPH, this decision should be considered in terms of feasibility and the risk of delaying intervention [21]. Second, estimated blood loss has been shown to be inaccurate [25] and often underestimated [21,26], with large variation between blood loss and clinical signs, thus making it difficult to establish cut-off points for initiating clinical intervention [27]. However, the definition used in this study (blood loss $\geq$ 1000 ml) would prompt initiation of major PPH treatment protocol and is therefore less likely to be misclassified [28,29]. Third, the goal of our risk prediction model is to allow for prompt implementation of appropriate therapeutic measures should PPH occur. Using macrosomia as a predictor of PPH can be limiting as fetal weight > 4000 g may only become apparent after birth. Furthermore, use of customised birthweight centiles, adjusting for such factors as fetal sex, parity and maternal weight, height and ethnicity may allow for a more accurate diagnosis of macrosomia. As a result, performing fetal size estimation (in particular, among those with a history of PPH for example) while taking account of fetal sex and maternal characteristics, may be more appropriate to allow the nomogram to be applied prior to delivery [4,30]. Fourth, while we have conducted a temporal external validation of our model, geographical external validation is necessary to assess its generalisability. However, it is recommended that external validation should be carried out by an independent research team to evaluate performance objectively [31]. Therefore, we have included the values to calculate the linear predictor of our model to allow researchers to conduct an independent external validation. Fifth, missing data may have introduced bias. However, as the total amount of missing data in the current study was < 5 %, this may not have a large impact on results [18]. Finally, we did not include multiple pregnancies in our study as they carry a higher inherent risk of PPH [32], therefore the prediction model should not be generalised to this group.

Conclusion

Four routinely collected variables (parity, fetal macrosomia, mode of delivery and history of PPH) were identified when predicting PPH in a general obstetric Irish population of singleton pregnancies. Use of our nomogram could potentially assist with individualised risk assessment of PPH and inform clinical decision-making allowing those at highest risk of PPH be actively managed.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was supported by the Health Research Board (HRB), Ireland [grant number SDAP2019/6359].

Author agreement

All authors agreed with the content and gave explicit consent to submit manuscript for publication.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2022.07.024.

References

[1] Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Global health 2014;2(6):e323–33.
[2] Sentilhes L, Gromez A, Clavier E, Resch B, Descamps P, Marpeau L. Long-term psychological impact of severe postpartum hemorrhage. Acta Obstet Gynecol Scand 2011;90(6):615–20.
[3] Sebghati M, Chandraharan E. An update on the risk factors for and management of obstetric haemorrhage. Womens Health (Lond) 2017;13(2):34–40.
[4] Neary C, Naheed S, McLernon D, Black M. Predicting risk of postpartum haemorrhage: a systematic review. BJOG: Int J Obstet Gynaecol 2021;128(1):46–53.
[5] Trikha A, Singh PM. Management of major obstetric haemorrhage. Indian J Anaesth 2018;62(9):698–703.
[6] Wormer KC, Jamil RT, Bryant SB. Acute Postpartum Hemorrhage StatPearls [Internet]: StatPearls Publishing; 2021 [updated 26th July 2021; cited 2021 30th September]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499988/.
[7] American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 183: Postpartum Hemorrhage. Obstetrics and gynecology. 2017;130(4):e168-e86.
[8] Mavrides E, Allard S, Chandraharan E, Collins P, Green L, Hunt B, et al. Prevention and Management of Postpartum Haemorrhage. BJOG: Int J Obstet Gynaecol 2017;124(5):e106–49.
[9] Sheldon WR, Blum J, Vogel JP, Souza JP, Gülmezoglu AM, Winikoff B. Postpartum haemorrhage management, risks, and maternal outcomes: findings from the World Health Organization Multicountry Survey on Maternal and Newborn Health. BJOG: Int J Obstet Gynaecol 2014;121(Suppl 1):5–13.
[10] Nyfløt LT, Sandven I, Stray-Pedersen B, Pettersen S, Al-Zirqi I, Rosenberg M, et al. Risk factors for severe postpartum hemorrhage: a case-control study. BMC Pregnancy Childbirth 2017;17(1).
[11] Butwick AJ, Ramachandran B, Hegde P, Riley ET, El-Sayed YY, Nelson LM. Risk Factors for Severe Postpartum Hemorrhage After Cesarean Delivery: Case-Control Studies. Anesth Analg 2017;125(2):523–32.
[12] Dunkerton SE, Jeve YB, Walkinshaw N, Breslin E, Singhal T. Predicting Postpartum Hemorrhage (PPH) during Cesarean Delivery Using the Leicester PPH Predict Tool: A Retrospective Cohort Study. Am J Perinatol 2018;35(2):163–9.
[13] Kim J-W, Lee Y-K, Chin J-H, Kim S-O, Lee M-Y, Won H-S, et al. Development of a scoring system to predict massive postpartum transfusion in placenta previa totalis. J Anesthesia 2017;31(4):593–600.
[14] Wu Q, Yao K, Liu Z, Li L, Zhao X, Wang S, et al. Radiomics analysis of placenta on T2WI facilitates prediction of postpartum haemorrhage: A multicentre study. EBioMedicine 2019;50:355–65.
[15] Grant SW, Collins GS, Nashef SAM. Statistical Primer: developing and validating a risk prediction model. Eur J Cardio-thoracic Surg 2018;54(2):203–8.
[16] Riley RD, Van Calster B, Collins GS. A note on estimating the Cox-Snell R(2) from a reported C statistic (AUROC) to inform sample size calculations for developing a prediction model with a binary outcome. Stat Med 2021;40(4):859–64.
[17] Joie Ensor, Kym IE Snell, Martin EC. PMCALPLOT: Stata module to produce calibration plot of prediction model performance," Statistical Software Components: Boston College Department of Economics; 2018 [updated 04 Jan 2020. Available from: https://ideas.repec.org/c/boc/bocode/s458486.html.
[18] Harrell FE. Missing Data. Regression Modeling Strategies. Springer Series in Statistics. 2nd ed. New York: Springer; 2015.
[19] Royal College of Obstetricians and Gynaecologists. Prevention and Management of Postpartum Haemorrhage. BJOG: Int J Obstet Gynaecol 2017;124(5):e106–e49.
[20] Chi Z, Zhang S, Wang Y, Yang L, Yang Y, Li X. Research of the assessable method of postpartum hemorrhage. Technol Health Care 2016;24(Suppl 2):S465–9.
[21] Venkatesh KK, Strauss RA, Grotegut CA, Heine RP, Chescheir NC, Stringer JSA, et al. Machine Learning and Statistical Models to Predict Postpartum Hemorrhage. Obstet Gynecol 2020;135(4):935–44.
[22] Dilla AJ, Waters JH, Yazer MH. Clinical validation of risk stratification criteria for peripartum hemorrhage. Obstet Gynecol 2013;122(1):120–6.
[23] Moons KGM, Altman DG, Vergouwe Y, Royston P. Prognosis and prognostic research: application and impact of prognostic models in clinical practice. BMJ (Clin Res Ed) 2009;338(jun04 2):b606.
[24] Vickers AJ, Van Calster B, Steyerberg EW. Net benefit approaches to the evaluation of prediction models, molecular markers, and diagnostic tests. BMJ (Clin Res Ed) 2016;352:i6.
[25] Duthie SJ, Ven D, Yung GL, Guang DZ, Chan SY, Ma HK. Discrepancy between laboratory determination and visual estimation of blood loss during normal delivery. Eur J Obstet Gynecol Reprod Biol 1991;38(2):119–24.
[26] Patel A, Goudar SS, Geller SE, Kodkany BS, Edlavitch SA, Wagh K, et al. Drape estimation vs. visual assessment for estimating postpartum hemorrhage. Int J Gynecol Obstet 2006;93(3):220–4.
[27] Pacagnella RC, Souza JP, Durocher J, Perel P, Blum J, Winikoff B, et al. A systematic review of the relationship between blood loss and clinical signs. PLoS ONE 2013;8(3):e57594.

[28] Dahlke JD, Mendez-Figueroa H, Maggio L, Hauspurg AK, Sperling JD, Chauhan SP, et al. Prevention and management of postpartum hemorrhage: a comparison of 4 national guidelines. Am J Obstet Gynecol 2015;213(1):76.e1–76.e10.
[29] Institute of Obstetricians and Gynaecologists; Royal College of Physicians of Ireland and Directorate of Strategy and Clinical Programmes Health Service Executive. Clinical Practice Guideline: Prevention and Management of Primary Postpartum Haemorrhage 2014 [Available from: https://www.hse.ie/eng/about/who/acute-hospitals-division/woman-infants/clinical-guidelines/prevention-and-management-of-primary-postpartum-haemorrhage.pdf].
[30] Unterscheider J, Geary MP, Daly S, McAuliffe FM, Kennelly MM, Dornan J, et al. The customized fetal growth potential: a standard for Ireland. Eur J Obstet Gynecol Reprod Biol 2013;166(1):14–7.
[31] Collins GS, Altman DG. An independent and external validation of QRISK2 cardiovascular disease risk score: a prospective open cohort study. BMJ 2010;340 (may13 2):c2442.
[32] Sosa CG, Althabe F, Belizán JM, Buekens P. Risk factors for postpartum hemorrhage in vaginal deliveries in a Latin-American population. Obstet Gynecol 2009;113(6):1313–9.