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# Reporting errors, incidence and risk factors for postpartum haemorrhage and progression to severe PPH: a prospective observational study

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**Objective** To quantify reporting errors, measure incidence of postpartum haemorrhage (PPH) and define risk factors for PPH ( $\geq 500$  ml) and progression to severe PPH ( $\geq 1500$  ml).

**Design** Prospective observational study.

**Setting** Two UK maternity services.

**Population** Women giving birth between 1 August 2008 and 31 July 2009 ( $n = 10\ 213$ ).

**Methods** Weighted sampling with sequential adjustment by multivariate analysis.

**Main outcome measures** Incidence and risk factors for PPH and progression to severe PPH.

**Results** Errors in transcribing blood volume were frequent (14%) with evidence of threshold preference and avoidance. The incidences of PPH  $\geq 500$ ,  $\geq 1500$  and  $\geq 2500$  ml were 33.7% (95% CI 31.2–36.2), 3.9% (95% CI 3.3–4.6) and 0.8% (95% CI 0.6–1.0). New independent risk factors predicting PPH  $\geq 500$  ml included

Black African ethnicity (adjusted odds ratio [aOR] 1.77, 95% CI 1.31–2.39) and assisted conception (aOR 2.93, 95% CI 1.30–6.59). Modelling demonstrated how prepregnancy- and pregnancy-acquired factors may be mediated through intrapartum events, including caesarean section, elective (aOR 24.4, 95% CI 5.53–108.00) or emergency (aOR 40.5, 95% CI 16.30–101.00), and retained placenta (aOR 21.3, 95% CI 8.31–54.7). New risk factors were identified for progression to severe PPH, including index of multiple deprivation (education, skills and training) (aOR 1.75, 95% CI 1.11–2.74), multiparity without caesarean section (aOR 1.65, 95% CI 1.20–2.28) and administration of steroids for fetal reasons (aOR 2.00, 95% CI 1.24–3.22).

**Conclusions** Sequential, interacting, traditional and new risk factors explain the highest rates of PPH and severe PPH reported to date.

**Keywords** Blood loss, observational study, pregnancy, progression, risk factors, severe adverse maternal morbidity.

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## Introduction

Postpartum haemorrhage (PPH), defined as blood loss  $\geq 500$  ml, is a major cause of maternal mortality and morbidity worldwide.<sup>1</sup> For every death, 20 women live with the consequences of associated morbidities,<sup>2</sup> with the greatest burden in low-income countries.<sup>3</sup> PPH is a common emergency, and readily treatable when appropriate resources are available.<sup>4</sup>

Severe PPH (variously defined from 1000 ml upwards) has been used as a measure of severe morbidity and is an

appropriate adjunct to mortality reports.<sup>4–6</sup> In Europe, one in eight maternal deaths are linked to PPH.<sup>7</sup> In the UK, despite the widespread availability of effective treatments and guidelines, deaths from PPH still occur (9/107 direct deaths in 2006–2008, 0.39/100 000 maternities; 95% CI 0.20–0.75).<sup>5</sup> Additionally, for each death, 15 women undergo hysterectomy.<sup>8</sup>

Despite surgical, medical and training innovations, PPH rates remain high in several high-income countries including the UK<sup>9–11</sup> with an incidence of 13% recently reported, and evidence that both PPH<sup>12</sup> and severe PPH<sup>13</sup> are

increasing. The causes are likely to be multifactorial with shifting demography and health status widely cited, e.g. age, obesity, comorbidity, multiple pregnancy and ethnicity,<sup>14–19</sup> in addition to rising caesarean section rates.<sup>10,17,20</sup> These suppositions require formal evaluation.

The quantification of blood loss remains problematic. Although recognised as unreliable,<sup>21,22</sup> the usual method is visual assessment following minimal training.<sup>23</sup> Accurate estimation is critical because volume thresholds are used to initiate treatment and resuscitation protocols. Despite this, rigorous evaluation of those errors, which may reduce the accuracy of estimated blood loss (EBL), has seldom been attempted.<sup>24–26</sup>

This prospective observational study aimed to: (i) quantify common EBL reporting errors; (ii) measure PPH incidence; (iii) identify chronologically ordered risk factors (pre-existing or acquired) for PPH and progression to severe PPH.

## Methods

This is the quantitative component of the mixed methodology STOP (Surveillance and Treatment of Postpartum haemorrhage) study. PPH management and qualitative results will be reported separately.

A prospective observational study was undertaken in two maternity services incorporating an inner London tertiary referral teaching hospital and a district general hospital in South East England.

### Patients and data collection

The population studied comprised all women giving birth between 1 August 2008 and 31 July 2009 ( $n = 10\,213$ ).

In both centres, maternity data were primarily documented in paper records that remained with the woman throughout her pregnancy and early puerperium. Summary data, transcribed from the notes, were entered onto electronic patient databases immediately following birth. This procedure is widespread in UK maternity units.

For the study, blood loss and minimal demographic/delivery data were imported within 1 week of birth from the hospital clinical electronic databases (Healthware™ and EuroKing™) to a secure, bespoke data management system (MedSciNet<sup>AB</sup>). Preservation of anonymity, data handling and storage were in compliance with the UK Data Protection Act 1988.

### Weighted sample

Detailed review of all maternity records was impractical and limited by resource and time constraints. Therefore a weighted sample design (disproportionate stratified sampling), commonly employed in national statistics, accountability and business surveys, was adopted<sup>27,28</sup> (see

Supporting information, Appendix S1 Supplementary Methods).

### Data extraction and analysis

Two researchers reviewed all clinical data from the original handheld records to more accurately evaluate blood loss and identify transcription errors. Additional information was obtained from other electronic sources (blood transfusion, routine haematology and ultrasound). Variation between researchers of the total volume documented was always <5%; and was always resolved by discussion.

Data analysis was performed using STATA, version 11.2 (Stata Corp, College Station, TX, USA). Summaries, estimates and comparisons were calculated using proportional weighting to adjust for the sampling plan.

### Definitions

Study definitions, including the categorisation of PPH by EBL are listed (see Supporting information, Table S1).

### Estimation of errors in reported clinical data

Discrepancies were determined using three approaches: (i) evaluating the frequency and magnitude of transcription errors for EBL between paper and electronic records; these were compared to calculated errors for maternal age, maternal date of birth, mode of delivery, baby date of birth, time of birth, sex and birthweight; (ii) cross-checking the observed discrepancies; this was undertaken by two researchers and decision was deferred to a third when required, and to the study Chief Investigator (CI) if there was persistent disagreement; (iii) independently re-examining every tenth set of notes and related electronic records within the weighted sample.

Precise EBL was not recorded in 61/101 waterbirths (including eight homebirths) but following review of these notes, 57 were categorised within 0–499 ml and four within 500–999 ml.

### Assessment of incidence of PPH

The incidence of PPH and all other analyses was calculated after adjustment of the EBL categories following inspection of the handheld records.

### Determination of potential risk factors for PPH to be assessed

A detailed list of potential risk factors was compiled with the intention of determining which were associated with increased blood loss or increased risk of PPH. This included previously identified and potential risk factors assessed in three sequential groups: (a) pre-pregnancy, (b) during pregnancy, (c) labour and birth. These were further subdivided into pre-defined subgroups arranged, as far as possible, in the order they generally occur (Appendix S1: Supplementary Methods).

The ultimate causes, identified from group (a) may be of public health importance, while intermediate and immediate causes from groups (b) and (c) may have more clinical relevance. The strength of this approach is that appropriately adjusted estimates for both earlier and later predictors are obtained. While earlier factors can possibly be confounders for later events, the reverse does not apply. For example, age influences multiple pregnancy, which is itself believed to be a risk factor for caesarean section and blood loss. Age is therefore a potential confounder of the effect of multiple pregnancy, and multiple pregnancy is a potential confounder of the effect of caesarean section, but not *vice versa*.

Models were designed to investigate three clinically important aspects of blood loss: (i) in all women, absolute blood loss (ml) (linear regression) and (ii) PPH  $\geq 500$  ml (logistic regression); (iii) in women with PPH  $\geq 500$  ml, the risk of progression onto severe PPH  $\geq 1500$  ml (logistic regression). These models address the three questions: 'How much blood is this woman likely to lose?', 'Is this woman at risk of PPH ( $\geq 500$  ml)?' and 'Having lost 500 ml, what is the likelihood of this woman experiencing severe PPH ( $\geq 1500$  ml) requiring major intervention?' (more fully described in Appendix S1: Supplementary Methods).

### Justification of study duration, population and sample size

All births over a complete year were studied to eliminate seasonal fluctuations. Population diversity was increased by inclusion of two centres. As this observational study did not assess the influence of a single risk factor or intervention, a conventional power calculation was not undertaken.

### Comparison with previous and contemporary evidence

To examine time trends, comparison was undertaken with historical data from a prospective population-based case-control study of severe maternal morbidity, involving the same NHS Trusts (1997/98),<sup>16</sup> using present study PPH definitions. Comparison of PPH  $\geq 2500$  ml was made using the Scottish national morbidity audit for the same time frame as the current study.<sup>13</sup>

## Results

### Population and demography

Following selection by weighting, 1897 case notes were examined; two women had no documentation of blood loss. Allowing for weighting, the sample represented 9939 women of whom 9937 (>99.9%) had sufficient data (Figure 1, STROBE diagram).

In the whole group, 60% were  $\geq 30$  and 26% were  $\geq 35$  years old. Almost 60% were White, with Black African the largest minority ethnic group (17%). Over 37% were

overweight or obese, 39% lived in areas of highest deprivation and 12% were cigarette smokers. Table S2 (see Supporting information) shows population demography and outcomes in women with and without PPH.

### Estimated blood loss error in electronic clinical records

Comparison with paper records revealed a 14% error rate in recorded EBL. This compares with error rates of 0.5% maternal age, 0.2% maternal date of birth, 2.0% mode of delivery, 0.0% baby date of birth, 0.4% time of delivery, 0.4% sex and 2.0% birthweight.

Table 1 shows categories of PPH by EBL. Following review of the paper records 207/1895 weighted sample were re-categorised: 1688 (89.1%) were unchanged, 192 (10.2%) were moved to a higher and 15 (0.8%) to a lower EBL category; women with no electronically recorded EBL (131/10213, 1.28%) were assigned to categories 0–499 ml ( $n = 101$ ), 500–999 ml ( $n = 19$ ), 1000–1499 ml ( $n = 6$ ) and  $\geq 1500$  ml ( $n = 5$ ).

There was a preference to record EBLs ending in 0, or as multiples of 5, 10, 50 and 100. In the full cohort ( $n = 10\ 213$ ) disproportionate numbers of women had documented blood loss at exact thresholds; 500 ml (8.4%), 1000 ml (2.1%), 1500 ml (0.8%), 2000 ml (1.5%) and 2500 ml (0.2%). At each threshold, volumes just under (within 50 ml) were favoured over those just above.

### PPH incidence

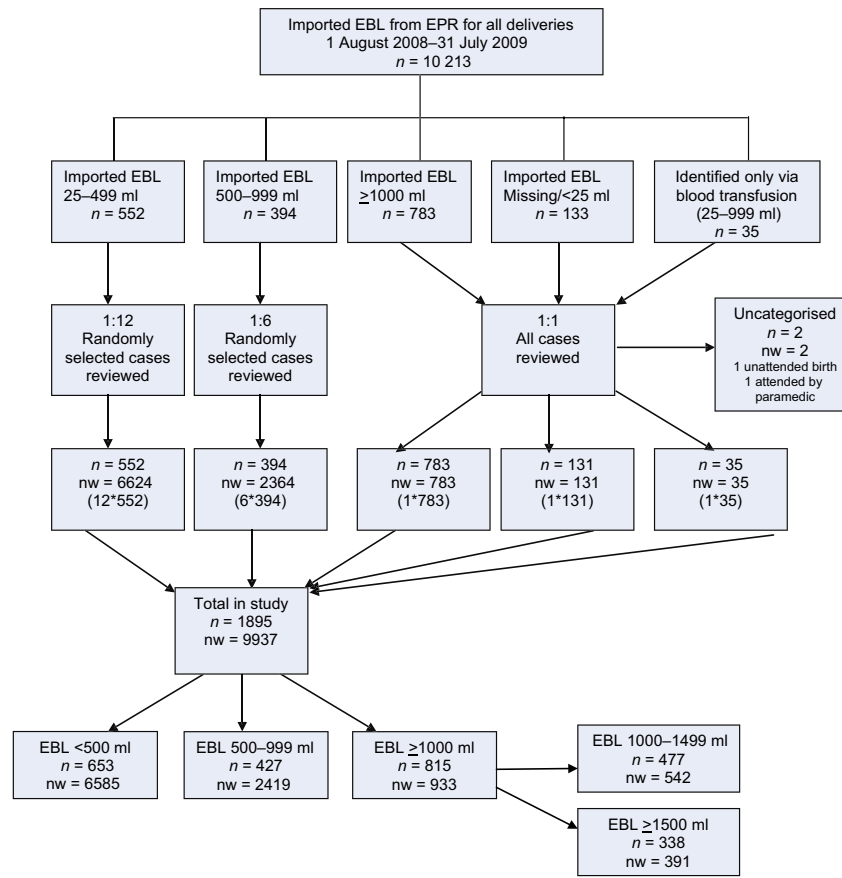
Following adjustment for transcription errors, 33.7% had a PPH  $\geq 500$  ml, 3.9%  $\geq 1500$  ml and 0.82%  $\geq 2500$  ml (Table 1).

### Determination of risk factors for PPH and progression to severe PPH

Unadjusted results for all 211 variables are given in the Supporting information, Table S3, including tests for changes in blood loss, PPH  $\geq 500$  ml and progression onto severe PPH ( $\geq 1500$  ml). Fifty predictors of PPH  $\geq 500$  ml (ten prepregnancy, 15 during pregnancy and 25 intrapartum) selected on the basis of unadjusted significance were entered into the next stage of the PPH model. A different 50 predictors of progression to PPH  $\geq 1500$  ml (11 prepregnancy, 15 during pregnancy and 24 intrapartum) were similarly entered into the progression model.

### Modelling according to chronological sequence

Table 2 summarises the prediction of PPH. It uses only predictors significant before adjustment. Each column shows the adjusted odds ratios from a single model. Column 1 deals with prepregnancy factors only (appropriate at first antenatal appointment). Column 2 includes risk factors arising during pregnancy (appropriate prelabour).



Key: EPR; Electronic patient record. nw; number of women represented by the reviewed notes allowing for the weighted sampling.

**Figure 1.** STROBE diagram. Identification and classification of cases according to imported electronic patient records, recategorisation by blood loss documented in handheld maternity notes and sample weighting.

**Table 1.** Estimated rates of blood loss as % in each category in study population (allowing for weighted sampling)

Category	Blood loss (ml)	All (%)	95% CI
No PPH	<500	66.3	63.8–68.8
PPH – All	≥500	33.7	31.2–36.2
PPH – Minor	500–999	24.3	22.0–26.6
PPH – Moderate	1000–1499	5.5	4.8–6.1
PPH – Severe	1500–1999	2.0	1.6–2.4
	2000–2499	1.1	0.74–1.5
	≥1500	3.9	3.3–4.6
	≥2500	0.82	0.63–1.0

Column 3 includes risk factors linked to labour and birth (appropriate postpartum).

Only 15 factors remained significant postpartum. Black African ethnicity, previous PPH, placenta praevia (anterior and major), maximum birthweight, temperature per degree >37°C, chorioamnionitis, instrumental delivery, elective

caesarean, emergency caesarean, retained placenta, interval to suturing (time taken and unrecorded) increased risk. Intramuscular Syntometrine® and Syntocinon® 40/50 IU infusion were protective.

Eight variables significant in columns 1 or 2 are not significant in column 3 (age, body mass index [BMI], assisted conception, multiple pregnancy, 'warning' antepartum haemorrhage, pre-eclampsia, antibiotics and multiparity without previous caesarean). Their effects may be mediated through the 15 significant factors (see Methods).

Table 3 deals similarly with risk factors for progression to severe PPH (≥1500 ml) and Figure 2A,B show all significant variables diagrammatically.

### Incidence of severe PPH in historical comparison

Numbers of births increased from 8329 to 10 213 (19.7% rise) between 1997/98<sup>16</sup> and 2008/09. Over this 11-year period, there was a 3.4 (95% CI 2.7–4.3) risk ratio for PPH ≥ 1500 ml ( $n = 93$  versus  $n = 391$ ) and an 8.3 (95% CI 4.0–17.1) risk ratio for PPH ≥ 2500 ml ( $n = 8$  versus  $n = 81$ ).

**Table 2.** Risk pathways for PPH  $\geq$  500 ml according to chronological variables grouped as prepregnancy, during pregnancy, labour and birth

Risk factors included in final model	Pre-Pregnancy Variable subgroups 1–4 (1895 women included) OR (95% CI), p	During Pregnancy Variable subgroups 1–10 (1868 women included; 27 excluded due to 1 missing data and 26 perfectly predicted) OR (95% CI), p	Labour and Birth Variable subgroups 1–16 (1724 women included; 171 excluded due to 135 missing data, 36 perfectly predicted) OR (95% CI), p
<b>(1) Sociodemographic</b>			
Age, for each 10 years	1.45 (1.19–1.76), 0.000	1.44 (1.18–1.75), 0.000	0.93 (0.73–1.19), 0.57
Black African	1.77 (1.31–2.39), 0.000	1.77 (1.30–2.41), 0.000	1.94 (1.35–2.79), 0.000
<b>(2) Local Deprivation: index of multiple deprivation, most deprived UK quintile (%)</b>			
Barriers – housing and services	1.06 (0.87–1.33), 0.61	1.05 (0.83–1.32), 0.69	1.04 (0.79–1.36), 0.80
Education, skills and training	0.93 (0.64–1.36), 0.72	0.93 (0.64–1.36), 0.71	1.03 (0.57–1.62), 0.89
<b>(3) General and medical risk factors</b>			
Current smoker	0.76 (0.54–1.09), 0.14	0.77 (0.53–1.10), 0.15	0.82 (0.53–1.28), 0.38
BMI (kg/m <sup>2</sup> ) per unit	1.03 (1.01–1.05), 0.006	1.03 (1.00–1.05), 0.016	1.01 (0.99–1.04), 0.32
Assisted conception	2.93 (1.30–6.59), 0.010	2.28 (0.99–5.29), 0.054	2.10 (0.83–5.33), 0.19
<b>(4) Previous obstetric history</b>			
Previous PPH	2.34 (1.33–4.12), 0.003	2.45 (1.38–4.35), 0.002	2.75 (1.40–5.44), 0.003
Multiparous previous caesarean	1.32 (0.93–1.87), 0.19	1.30 (0.91–1.86), 0.14	0.96 (0.61–1.51), 0.86
Multiparous no previous caesarean	0.33 (0.26–0.42), 0.000	0.33 (0.25–0.42), 0.000	0.79 (0.56–1.11), 0.18
<b>(5) Current pregnancy</b>			
Multiple pregnancy		2.27 (1.04–4.96), 0.039	2.02 (0.82–5.00), 0.13
Admissions >24 weeks		0.82 (0.57–1.18), 0.28	0.82 (0.53–1.29), 0.39
<b>(6) Antenatal day unit (ADU) attendances</b>			
Any ADU attendance		1.06 (0.84–1.34), 0.62	0.95 (0.72–1.26), 0.74
Pre-eclampsia screen		1.06 (0.65–1.75), 0.81	1.04 (0.57–1.91), 0.89
Generally unwell		1.22 (0.68–2.18), 0.50	1.33 (0.69–2.60), 0.40
<b>(7) Placenta praevia: All 26 women with major or anterior placenta praevia PPH &gt; 500 ml</b>			
<b>(8) Antepartum haemorrhage (APH) and urinary tract infection</b>			
APH		1.11 (0.62–1.99), 0.74	1.27 (0.65–2.51), 0.48
'Warning APH'		8.95 (1.02–78.7), 0.048	1.92 (0.19–19.3), 0.58
<b>(9) Pre-eclampsia (PET) and anaemia</b>			
Gestational hypertension		1.83 (0.83–4.03), 0.13	2.22 (0.87–5.63), 0.093
Pre-eclampsia		3.16 (1.12–8.93), 0.030	3.21 (0.94–10.90), 0.062
<b>(10) Medications in pregnancy pre-birth</b>			
Antibiotics		1.35 (1.01–1.80), 0.043	1.14 (0.77–1.66), 0.52
Antihypertensives (including for PET)		0.75 (0.44–1.29), 0.30	0.66 (0.33–1.32), 0.24
Diabetic Rx		1.89 (0.79–4.56), 0.15	1.20 (0.43–3.37), 0.73
Steroids for fetal reasons		0.90 (0.57–1.43), 0.65	1.23 (0.69–2.18), 0.49
<b>(11) Gestation at birth</b>			
Gestation at delivery (weeks)			0.98 (0.90–1.08), 0.70
<b>(12) Birthweight</b>			
Maximum birthweight (kg)			2.19 (1.62–2.99), 0.000
<b>(13) Onset of labour</b>			
No labour onset			1.51 (0.47–4.90), 0.49
Induction			0.75 (0.39–1.46), 0.40
Augmentation			0.83 (0.42–1.64), 0.59
ROM > 2 hours before onset			0.95 (0.64–1.41), 0.79
ROM > 6 hours before onset			1.35 (0.90–2.02), 0.14
ROM not recorded			1.03 (0.60–1.77), 0.91
<b>(14) Intrapartum: all ten women with evidence of chorioamnionitis PPH &gt; 500 ml</b>			
Prostin			1.04 (0.53–2.02), 0.91
Syntocinon <sup>®</sup>			1.44 (0.95–2.16), 0.085

Table 2. (Continued)

Risk factors included in final model	Pre-Pregnancy Variable subgroups 1–4 (1895 women included) OR (95% CI), p	During Pregnancy Variable subgroups 1–10 (1868 women included; 27 excluded due to 1 missing data and 26 perfectly predicted) OR (95% CI), p	Labour and Birth Variable subgroups 1–16 (1724 women included; 171 excluded due to 135 missing data, 36 perfectly predicted) OR (95% CI), p
Spinal anaesthesia			0.87 (0.51–1.49), 0.60
Epidural analgesia			1.08 (0.71–1.65), 0.71
Raised temperature (per degree >37.0°C)			2.62 (1.24–5.52), 0.011
Temperature not recorded			0.75 (0.50–1.11), 0.15
<b>(15) Birth</b>			
Instrumental vaginal			3.50 (2.21–5.24), 0.000
Elective caesarean			24.4 (5.53–108.00), 0.000
Emergency caesarean section			40.5 (16.30–101.00), 0.000
<b>(16) Third stage</b>			
Physiological			1.48 (0.80–2.77), 0.22
Syntometrine® intramuscular			0.55 (0.33–0.91), 0.019
Syntocinon® intravenous bolus			0.58 (0.27–1.25), 0.17
Syntocinon® 40/50 IU infusion commenced			0.61 (0.38–0.99), 0.045
Retained placenta			21.3 (8.31–54.70), 0.000
Suture interval after vaginal birth (hours)			2.03 (1.65–2.50), 0.000
Suture interval not recorded			2.2 (1.32–3.69), 0.003

Full regression model; result of three multiple regression models selecting the principal significant variables. In each model, an additional group of predictors is added. Results adjusted for other members of the same group and for previous groups only.

### Incidence of severe PPH in contemporary cohort

The incidence of PPH  $\geq 2500$  ml was 0.82% (95% CI 0.63–1.0,  $n = 81/9937$ ) compared with 0.56% (95% CI 0.49–0.62,  $n = 306/54910$ ) in Scotland during the same period.<sup>13</sup>

## Discussion

### Main findings

The incidences of PPH and severe PPH in the present study are, to our knowledge, the highest reported from any high-income or low-income country.<sup>1,3,9–12</sup> The novel application of weighted sampling highlighted errors between clinical notes and electronic summary data. Established and novel risk factors for both PPH and progression to severe PPH have been quantified. Rigorous and chronological assessment of contributory factors illuminate the complex multifactorial origin of recent rises in PPH.

### Strengths and limitations

Strengths include prospective design and contemporaneous, robust data collection, mitigating ascertainment bias. Weighted sample design maintained statistical power and overcame the limitations of case-control studies. Risk

assessment using chronological categories was preferable to stepwise regression (Appendix S1: Supplementary Methods). Generalisability may be limited by the higher deprivation (39% lowest quintile) and larger proportion of women >30 years in the current cohort compared with contemporaneous maternity data for England and Wales (60% versus 47%),<sup>29</sup> although obesity rates were similar to recent national figures (15.2% versus 15.6%).<sup>30</sup> Comparison with UK maternal ethnic distribution was not feasible because these data are not in the public domain.<sup>31</sup> Historical comparison could have been influenced by different methodologies, changes in local service provision and shifting population. Despite controlling for known confounding variables, associations cannot necessarily be assumed to be causal. Gynaecological history, intended place of birth and degree of perineal trauma were not included.

### Interpretation

#### Reporting errors

This is the first study, to our knowledge, to identify major errors in blood loss reporting in electronic maternity records. As these summary data form the sole source of information regarding hospital admissions, treatment and management,

**Table 3.** Risk pathways for progression of PPH from  $\geq 500$  ml to severe PPH  $\geq 1500$  ml according to chronological variables grouped as prepregnancy, during pregnancy, labour and birth

Risk factors included in final model (1230 women included; 70 excluded due to missing data in addition to all women with EBL<500 ml)	Prepregnancy Variable subgroups 1–4 OR (95% CI), P	During pregnancy Variable subgroups 1–10 OR (95% CI), P	Labour and birth Variable subgroups 1–16 OR (95% CI), P
<b>(1) Sociodemographic</b>			
Age, for each 10 years	0.85 (0.67–1.07), 0.16	0.90 (0.68–1.09), 0.20	0.99 (0.77–1.29), 0.96
Black African	0.86 (0.62–1.19), 0.36	0.84 (0.61–1.17), 0.31	0.91 (0.64–1.30), 0.61
<b>(2) Local Deprivation: index of multiple deprivation, most deprived UK quintile (%)</b>			
Barriers to housing and services	0.79 (0.60–1.03), 0.076	0.78 (0.59–1.02), 0.069	0.75 (0.56–1.01), 0.055
Education, skills and training	1.75 (1.11–2.74), 0.015	1.84 (1.16–2.92), 0.009	1.82 (1.10–3.00), 0.019
<b>(3) General and medical risk factors</b>			
Current smoker	0.59 (0.36–0.97), 0.039	0.56 (0.33–0.93), 0.026	0.67 (0.38–1.17), 0.16
BMI (kg/m <sup>2</sup> ) per unit	1.03 (1.00–1.05), 0.022	1.03 (1.00–1.05), 0.023	1.04 (1.01–1.06), 0.008
Assisted conception	1.41 (0.79–2.50), 0.25	1.02 (0.53–1.93), 0.096	1.18 (0.60–2.35), 0.64
<b>(4) Previous obstetric history</b>			
Previous PPH	1.79 (1.06–3.02), 0.030	1.93 (1.13–3.31), 0.016	2.39 (1.33–4.28), 0.003
Multiparous previous caesarean	0.70 (0.49–1.01), 0.055	0.63 (0.43–0.92), 0.018	0.84 (0.54–1.30), 0.43
Multiparous no previous caesarean	1.65 (1.20–2.28), 0.002	1.55 (1.12–2.16), 0.009	1.17 (0.80–1.74), 0.42
<b>(5) Current pregnancy</b>			
Multiple pregnancy		2.00 (1.05–3.82), 0.035	2.60 (1.27–5.38), 0.009
Admissions >24 weeks		0.67 (0.44–1.02), 0.062	0.83 (0.53–1.32), 0.43
<b>(6) Antenatal day unit (ADU) attendances</b>			
Any ADU attendance		1.17 (0.89–1.56), 0.26	1.05 (0.77–1.43), 0.75
Pre-eclampsia screen		0.93 (0.55–1.57), 0.80	1.15 (0.66–2.01), 0.62
Generally unwell		1.49 (0.82–2.70), 0.19	1.69 (0.90–3.20), 0.11
<b>(7) Placenta praevia</b>			
Anterior		3.37 (0.86–13.30), 0.082	5.55 (1.29–23.9), 0.022
Major		0.72 (0.17–3.05), 0.660	0.97 (0.22–4.25), 0.97
<b>(8) Antepartum haemorrhage (APH) and urinary tract infection</b>			
APH		1.26 (0.67–2.37), 0.48	1.25 (0.62–2.52), 0.53
‘Warning APH’		1.70 (0.56–5.20), 0.35	1.99 (0.58–6.81), 0.27
<b>(9) Pre-eclampsia (PET) and anaemia</b>			
Gestational hypertension		1.00 (0.47–2.16), 0.99	0.98 (0.43–2.22), 0.97
Pre-eclampsia (PET)		1.03 (0.43–2.50), 0.95	0.87 (0.32–2.13), 0.69
<b>(10) Medications in pregnancy prebirth</b>			
Antibiotics		1.02 (0.74–1.40), 0.91	0.95 (0.65–1.39), 0.79
Antihypertensives (including for PET)		0.99 (0.56–1.78), 0.92	0.91 (0.49–1.70), 0.77
Diabetic Rx		0.98 (0.44–2.18), 0.96	1.23 (0.52–2.91), 0.64
Steroids for fetal reasons		2.00 (1.24–3.22), 0.004	2.00 (1.17–3.41), 0.011
<b>(11) Gestation at birth</b>			
Gestation at delivery (weeks)			0.95 (0.86–1.04), 0.25
<b>(12) Birthweight</b>			
Maximum birthweight (kg)			1.17 (0.87–1.59), 0.30
<b>(13) Onset of labour</b>			
No labour onset			1.28 (0.54–3.03), 0.58
Induction			1.07 (0.56–2.04), 0.83
Augmentation			1.37 (0.73–2.58), 0.33
ROM >2 hours before onset			1.01 (0.60–1.70), 0.96
ROM >6 hours before onset			1.16 (0.73–1.85), 0.52
ROM unknown			0.95 (0.52–1.73), 0.86
<b>(14) Intrapartum</b>			
Prostin			1.12 (0.60–2.11), 0.73
Syntocinon®			0.75 (0.49–1.13), 0.17
Spinal anaesthesia			0.73 (0.45–1.18), 0.20
Epidural analgesia			1.20 (0.78–1.85), 0.41



**Table 3.** (Continued)

<b>Risk factors included in final model (1230 women included; 70 excluded due to missing data in addition to all women with EBL&lt;500 ml)</b>	<b>Prepregnancy Variable subgroups 1–4 OR (95% CI), <i>P</i></b>	<b>During pregnancy Variable subgroups 1–10 OR (95% CI), <i>P</i></b>	<b>Labour and birth Variable subgroups 1–16 OR (95% CI), <i>P</i></b>
Raised temperature (per degree >37.0°C)			1.21 (0.75–1.94), 0.44
Temperature not recorded			1.40 (0.86–2.27), 0.17
Chorioamnionitis			2.70 (0.70–10.5), 0.15
<b>(15) Birth</b>			
Instrumental vaginal			0.79 (0.49–1.29), 0.36
Elective caesarean			0.14 (0.04–0.46), 0.001
Emergency caesarean section			0.34 (0.15–0.80), 0.013
<b>(16) Third stage</b>			
Physiological			3.74 (1.72–8.10), 0.001
Syntometrine® intramuscular			1.12 (0.66–1.91), 0.68
Syntocinon® intravenous bolus			1.35 (0.63–2.87), 0.44
Syntocinon® 40/50 IU infusion commenced			0.97 (0.65–1.44), 0.87
Retained placenta			1.40 (0.77–2.54), 0.27
Suture interval after vaginal birth (hours)			1.16 (0.99–1.35), 0.058
Suture interval not recorded			0.44 (0.25–0.79), 0.006

Full regression model: result of three multiple regression models selecting the principal significant variables. In each model, a new additional group of predictors is used. Results are adjusted for other members of the same group and for previous groups only. Women with EBL <500 ml are excluded.

errors have implications for individual healthcare and policy. Commonest errors were incorrect addition and failure to include documented blood loss in totals, both in paper notes and electronic records. The only relevant study, from 1994, considered electronic data accurate, despite error rates of 5–19%.<sup>32</sup> Threshold avoidance and preference biases, although identified for blood pressure<sup>33</sup> and birthweight,<sup>34</sup> have not been previously reported for blood loss. Underestimation is widespread for all birth modes,<sup>35</sup> partly caused by visual assessment<sup>23,36</sup> although one study reports overestimation following caesarean section.<sup>37</sup> Our data confirm that under-reporting remains unresolved.

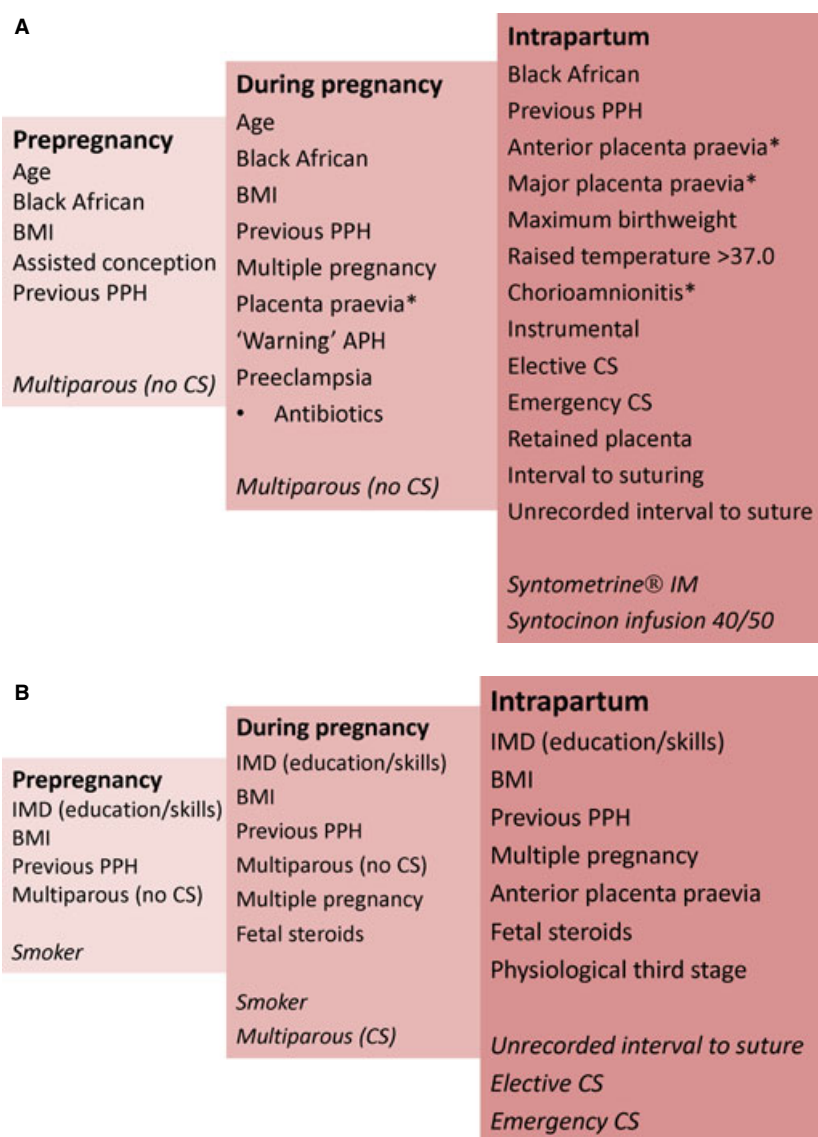
#### Incidence

These PPH rates are higher than previous reports at every threshold. Recent reports of rising rates,<sup>10,17,24,38</sup> up to 13% in high-income countries<sup>12</sup> may be underestimates, because most studies use routinely collected, retrospective and 'coded' electronic data.<sup>10,12,17,24,38–40</sup> The incidence of severe PPH  $\geq 2500$  ml is slightly higher than the contemporaneous Scottish audit,<sup>13</sup> suggesting that they are real underlying trends.

#### Risk factors for PPH, progression to severe PPH and risk pathway modelling according to chronological sequence

Our approach differs from previous studies by highlighting the need to consider underlying interlinked contributing factors, which lead to PPH and contribute to the progression onto severe PPH.

Prepregnancy factors for PPH include age, ethnicity, BMI, previous PPH and assisted conception. The association with age is variably reported<sup>11,41–44</sup> although older women have more medical<sup>45</sup> and obstetric<sup>46</sup> comorbidities and poorer uterine contractility.<sup>47</sup> No previous study has specifically identified Black African ethnicity as an independent predictor,<sup>16–19,48</sup> possibly because of lack of adjustment for potential confounding variables.<sup>49–52</sup> The independent relationship between BMI and PPH concurs with prospective cohort studies,<sup>14,53</sup> although retrospective and routine data reports are equivocal.<sup>54–56</sup> The 4% increase per BMI unit becomes substantial in higher obesity categories. The new association with assisted conception could reflect multiple pregnancy or abnormal placentation.<sup>57</sup> The impact of previous PPH<sup>24,38</sup> was confirmed, and quantified, unlike previous caesarean section.<sup>58</sup> Established risk factors for severe PPH in the general population included age, BMI, multiple pregnancy and previous caesarean.<sup>14–16,54,55,59,60</sup> However, our data did not highlight any association with age, previous caesarean and severe PPH. Although grand multiparity has been associated with PPH,<sup>24</sup> our data reveal multiparity as protective.<sup>38</sup> The unexpected findings that multiparity without caesarean section and index of multiple deprivation (education, skills and training) were risk factors for progression to severe PPH require validation. Despite known associations with placental abruption,<sup>61</sup> the finding that smoking protects against PPH progression may be associated with poor uteroplacental blood flow.<sup>62</sup>



**Figure 2.** Diagram of multiple logistic and chronological regression analysis showing (A) predictors of PPH  $\geq 500$  ml (protective factors in italics; asterisks indicate perfect predictors, i.e. all women had PPH) and (B) predictors of PPH  $\geq 500$  ml onto severe PPH  $\geq 1500$  ml (protective factors in italics).

Confirmed pregnancy-acquired risk factors for PPH include multiple pregnancy,<sup>9</sup> placenta praevia,<sup>17</sup> pre-eclampsia<sup>63</sup> and macrosomia.<sup>64,65</sup> The novel association with prelabour antibiotic use could reflect chorioamnionitis. Similarly, multiple pregnancy<sup>17</sup> and anterior placenta praevia were confirmed as predictors of progression to severe PPH  $\geq 1500$  ml.<sup>16,17,66,67</sup> The novel association with administration of steroids for fetal reasons could be explained by multiple pregnancy and threatened preterm birth although gestation of delivery showed no effect. Over 62% of women with haemoglobin  $<8.5$  g/l had PPH, 26% of whom progressed to severe PPH, concurring with NICE

guidelines identifying this as a threshold for concern.<sup>68</sup> Associations with third trimester anaemia using higher thresholds were not confirmed.<sup>69,70</sup>

Confirmed intrapartum risk factors for PPH were temperature,<sup>69</sup> chorioamnionitis,<sup>64</sup> instrumental and caesarean births<sup>71,72</sup> and retained placenta.<sup>65</sup> We found no association with induction and augmentation, agreeing with an earlier report<sup>73</sup> but at variance with others.<sup>12,47</sup> Although previously reported, the influence of caesarean<sup>59</sup> and retained placenta<sup>69,74</sup> (adjusted odds ratio [aOR] 21.3) were notable. Severe PPH is related to emergency caesarean<sup>75,76</sup> and the Royal College of Obstetricians and

Gynaecologists state that it is less likely following elective caesarean.<sup>76,77</sup> We observed that both are strongly associated with PPH (aORs 24.4 and 40.5) but apparently protect against progression (aORs 0.14 and 0.34); however, this is probably the result of prompt surgical and anaesthetic interventions. Prophylactic Syntometrine<sup>®</sup> and high-dose Syntocinon<sup>®</sup> infusion were protective against PPH, reinforcing concerns<sup>78</sup> about current recommendations for intramuscular Syntocinon<sup>®</sup>.<sup>79</sup> Although not associated with PPH, physiological third stage was a risk factor for progression, possibly related to delays in recognition or treatment, although others report <0.5% maternal postnatal transfers.<sup>80</sup> Time to complete genital tract repair was confirmed as a risk for PPH.<sup>81</sup>

## Conclusion

Identifying risk pathways is important as predisposing risk can underlie factors that appear, accumulate and dominate later events, including subsequent pregnancies.

These findings have implications for 'red flags', training and emergency management. Currently, clinical tools are only designed for PPH  $\geq 500$  ml.<sup>70</sup> Clinicians must remain vigilant, identify and respond to women's accumulating risks, recognise abnormal bleeding, summon assistance and ensure prompt treatment and transfer. Staff must eschew threshold preference and avoidance when assessing blood loss, and keep scrupulous records of cumulative loss. Prompt examination for genital tract trauma and expedient suturing must be ensured. Although current practice requires duplication of data entry,<sup>82</sup> health professionals should ensure accurate and complete transcription from paper to electronic records.

Policy and research should tackle the potentially modifiable risk factors. Public health interventions addressing the ageing reproductive population and obesity should be encouraged. Commissioners must consider instrumental and primary caesarean rates,<sup>38</sup> which may depend on informed decisions about staffing models<sup>83,84</sup> and facilities regarding planned place of birth.<sup>85</sup> PPH is identified as a key metric for quality of care<sup>86-88</sup> yet this study emphasises abundant flaws in measurement and reporting. Standard procedures, including auditing the incidence of PPH and accuracy of recorded EBL, must be improved, otherwise reliance on EBL may be inappropriate.

Research should focus on the transferability of trauma care innovations<sup>89,90</sup> and implementation of clinical improvements, such as cumulative blood loss recording, training and reminders for staff.<sup>23,91,92</sup> Weighted sampling is an underused methodology that reduces data entry burden and could be extrapolated to research, audit and monitor other morbidities. Progression predictors and attenuators might inform the design of an emergency strat-

egy to ameliorate severe PPH which otherwise looks set to continue rising.

## Disclosure of interests

All authors have completed the Unified Competing Interest form available on request from the corresponding author and declare the following: AB, HB, PTS and SB had financial support from Guy's and St Thomas' Charity for the submitted work; AB, LP and PTS received separate financial support from Tommy's Charity (Registered charity no. 1060508 and SC039280); AB also received support from KHP BRC; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

## Contributions to authorship

The authors were involved as follows: AB, SB conception; AB, SB, PTS, GT, MW design; AB, HB, GT, MW data acquisition; AB, SB, PTS analysis and interpretation; AB, SB, PTS, JS, LP and RMT input into drafting article; AB, PTS, HB, GT, MW, LP, JS, RMT, SB were responsible for revision and final approval of manuscript.

## Details of ethics approval

The South East Multicentre Research Ethics Committee (07/H1102/79) approved the study.

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## Data sharing

The authors will be pleased to consider requests for data sharing following publication of the manuscript.

## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Appendix S1.** Supplementary Methods.

**Table S1.** Definitions.

**Table S2.** Characteristics of the study population by PPH (estimated blood loss >500 ml) or no PPH, following correction of errors, categorisation and weighting.

**Table S3.** Changes in estimated blood loss (according to groups and sub-groups of risk factors as appropriate to pre-pregnancy, during pregnancy, labour and birth), principal predictors of postpartum haemorrhage (PPH) >500 ml and conditional predictors of progression to severe PPH >1500 ml; unadjusted associations ■

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