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Why current risk factor-based approaches fall short in predicting stillbirth: a national cohort study of nulliparous women in England

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Abstract

Background Stillbirth is a profound and devastating outcome of pregnancy that has a long-lasting emotional and physiological impact on parents and families. Current risk assessment approaches largely rely on maternal characteristics and clinical history, yet their predictive accuracy remains poor, particularly among nulliparous women (women with no previous birth beyond 24 weeks of gestation). We evaluated the extent to which routinely collected pregnancy risk factors can predict stillbirth and assessed their contribution among singleton births in nulliparous women.

Methods We conducted a population-based retrospective cohort study of 876,279 nulliparous women receiving maternity care across 130 National Health Service (NHS) Trusts in England between 2015 and 2019. Thirty-one maternal and pregnancy factors routinely collected during antenatal care were analysed. We used modified Poisson regressions with generalised estimating equations to account for clustering of women within Trusts to compute risk ratios (RR) and 95% confidence intervals (CI). We calculated adjusted population attributable risks (PARs) for significant factors.

Results Among 876,279 nulliparous women receiving maternity care, 2568 stillbirths occurred. Modifiable maternal characteristics associated with increased risk included elevated body mass index (BMI) (RR 1.22, 95% CI 1.03–1.45 for BMI 35– < 40 kg/m^2; RR 1.70, 95% CI 1.39–2.07 for BMI ≥ 40 kg/m^2, both compared to BMI 18.5– < 25 kg/m^2), smoking at booking (RR 1.34, 95% CI 1.19–1.51), current substance misuse (RR 1.52, 95% CI 1.16–1.98), lack of folic acid consumption before conception (RR 1.28, 95% CI 1.16–1.40) or during pregnancy (RR 1.38, 95% CI 1.18–1.61), and late antenatal booking after 12 weeks of gestation (RR 1.18, 95% CI 1.07–1.30). Fetal growth restriction accounted for the largest population attributable risk for stillbirth (RR 2.96, 95% CI 2.73–3.21).

Conclusions Maternal and clinical risk factors explain only a fraction of stillbirths in nulliparous women and cannot underpin a clinically useful prediction model. These findings demonstrate the limitations of risk-based screening strategies and highlight the need for integrated approaches that combine maternal characteristics with biochemical, biophysical, and system-level factors to achieve meaningful advances in stillbirth prevention.

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Keywords Stillbirth, Nulliparous women, Maternal risk factors

Background

Stillbirth remains one of the most devastating complications of pregnancy, with profound and long-lasting emotional, psychological, and social impacts on families [1]. In the United Kingdom (UK), it remains a significant public health concern, occurring at a rate of 3.65 stillbirths per 1000 total births [2]. Despite overall declines in neonatal mortality, stillbirth rates have plateaued [3], with persistent inequalities by deprivation and ethnicity [2].

Evidence consistently shows that models of care offering midwifery continuity are associated with reductions in fetal loss at all gestations, compared with fragmented models of care [4, 5]. Scaling up such continuity has the potential to prevent a measurable number of stillbirths and neonatal deaths at the population level. However, ongoing maternity workforce shortages often prevent widespread implementation of continuity models, thereby increasing risks, particularly among marginalised or high-risk groups [4]. Integrating personalised risk assessment into maternity pathways could help target continuity resources towards those at greatest risk, ensuring the most effective use of limited workforce capacity. Personalising care with more accurate stillbirth prediction will improve safety and constitutes a key research priority [6].

The National Institute for Health and Care Excellence (NICE) guidance is used to assign risk for complications in pregnancy, such as pre-eclampsia [7]. Saving Babies Lives Care Bundle and the Royal College of Obstetricians and Gynaecologists also recommend risk assessments for small for gestational age babies and placental dysfunction which can be identifiable risk factors for stillbirth [8]. Yet, the prediction of stillbirth remains an unmet challenge. Current preventive strategies include identifying women with known risk factors, such as smoking, obesity, advanced maternal age, and previous miscarriage [3], and detecting fetal growth restriction (FGR) [9, 10], followed by targeted counselling, lifestyle advice, and enhanced antenatal monitoring.

Nulliparity has been reported to be an independent and prevalent risk factor for stillbirth [11]. However, current risk factors are deemed poor predictors for several reasons, including low sensitivity and specificity, which limit their ability to accurately identify women who will experience stillbirth versus those who will not. Additionally, stillbirth often results from a complex interplay of multiple factors, including genetic influences, placental dysfunction, and maternal health conditions [12]. Many established risk factors are static or non-modifiable and may be less informative in nulliparous women with no prior pregnancy history. Furthermore, current models largely rely on clinical and demographic factors and do not incorporate dynamic or novel biomarkers, which could enhance predictive accuracy [13]. Finally, while these risk factors may be associated with stillbirth at the population level, their ability to predict individual outcomes remains limited [14–16].

Despite advances in antenatal care, most stillbirths occur in women without identifiable risk factors, and predictive accuracy for nulliparous women remains particularly poor. Nulliparity is common, accounting for over 40% of births in the UK [17], and this group lacks the historical pregnancy data often used to stratify risk. Therefore, evaluating the utility of routinely collected early and late pregnancy factors in nulliparous women provides an essential test of whether current approaches to risk stratification can realistically be expected to improve stillbirth prediction. This study aimed to identify early and late pregnancy risk factors for stillbirth among nulliparous women and quantify their relative and population-level contributions.

Methods

Study design and setting

We conducted a population-based retrospective cohort study including all nulliparous women with singleton pregnancies cared for in 130 NHS Trusts in England between 1 January 2015 and 31 December 2019. We analysed the Maternity Information Systems (MIS) data following approval from (DARS-NIC-430380-F7L4Z-v1.2). Four trusts did not submit complete MIS records to NHS Digital for the relevant years and were therefore excluded. This dataset contains routinely collected, individual-level maternity records for all NHS-funded maternity services in England. Variable definitions and coding were based on the NHS Digital Data Dictionary for the Maternity Services Data Set [18].

Study population

We included all pregnancies and live births (≥ 24 weeks of gestation). Multiparous and primiparous women were not included. Only singleton births from nulliparous women were included due to the higher occurrence of adverse outcomes associated with multiple pregnancy (pregnancies with more than one fetus) [19]. Congenital disorders were excluded as they are associated with an increased risk of stillbirth [20]. We investigated risk

factors associated with fetal development in singleton pregnancies and estimated the magnitude and strength of these factors with the risk of stillbirth in the national population.

Exposure data

A list of all the considered covariates can be found in Additionalfile 1: Table 1. All covariates were defined according to the NHS Digital Data Dictionary specifications [18]. The dataset comprised information regarding maternal characteristics (e.g. body mass index, ethnicity, and age), pregnancy-related characteristics (e.g. number of previous miscarriages, smoking status at booking, and folic acid consumption), social complexities (e.g. index of multiple deprivation quintile and complex social factor indicator [21]), family history (e.g. pregnancy hypertension and diabetes), health status at booking (e.g. diabetes and mental health conditions [included diagnoses of depression, anxiety disorders, bipolar affective disorder, psychosis, and other specified mental health conditions]), obstetric risk factors (e.g. gestational diabetes and pre-eclampsia), as well as baby characteristics (e.g. birthweight and phenotypic sex). Alcohol consumption at booking was categorised as 0 units per week versus 1–14 units per week. Although we initially considered subdividing alcohol intake into smaller categories, there were too few women in the higher intake groups to allow stable regression estimates. Therefore, a single category for 1–14 units was used to preserve statistical robustness. Maternal ethnicity was derived from the raw NHS Digital codes and categorised into nine groups (Table 1) for analysis. The grouping was designed to balance statistical power and clinical relevance. Pakistani women were kept as a separate category due to sufficient sample size and known differences in maternal and perinatal outcomes compared with other South Asian groups [2]. Indian and Bangladeshi women were combined due to smaller numbers and similar risk profiles. Other ethnicities were grouped to ensure adequate numbers for stable estimates while preserving clinically meaningful distinctions. As FGR is associated with an increased risk in stillbirth [9, 10], we used the gestation-related optimal weight standard (GROW) tool to determine gestation age centile [22]. Below the 10th centile was used as the threshold to assess the presence of FGR, as this limit is in line with standard clinical practice [23]. We deliberately separated early (< 13 weeks) and later (> 12 weeks) gestational risk factors to reflect real-world decision-making windows and to test whether timing of factor identification influences predictive potential. Covariates included in multivariable models were selected a priori, informed by existing literature and clinical relevance, rather than based on statistical significance in univariable analyses, to minimise over-fitting and residual confounding.

Outcome data

We defined stillbirth as antepartum or intrapartum fetal death occurring at ≥ 24 weeks of gestation [24].

Statistical analysis

We used Zou's modified Poisson regression to establish the average effect of explanatory variables on stillbirth [25]. Analyses accounted for clustering by NHS Trust, which each serves defined geographical regions within NHS England, by applying the sandwich variance estimator for clustered data [26]. Two models were created, one for pregnancy factors that can be identified early in gestation (< 12 weeks) and another for factors measured in late-term gestation (> 12 weeks) to establish the contribution of each factor as the pregnancy progresses. All regression models were adjusted for maternal sociodemographic, obstetric, and clinical characteristics irrespective of statistical significance in univariable analyses. Covariates included smoking status, ethnicity, socioeconomic status (Index of Multiple Deprivation quintile 2015), maternal age at booking, previous miscarriage, body mass index, substance use, alcohol consumption, folic acid supplementation, complex social factors, late booking, pre-existing hypertension, cardiac disease, gynaecological history, mental health disorders, diabetes, and family history (FH) of diabetes, hypertension, mental health disorders, multifetal pregnancy, pregnancy-related hypertension, congenital disorders, and inherited disorders. The late-term gestation model was also adjusted for severe preeclampsia, eclampsia, gestational diabetes, gestational hypertension, antepartum haemorrhage, FGR, and gestational age category. Results were presented as risk ratios (RR) and 95% confidence intervals (CI). Association strength was interpreted as per Sterne et al. [27].

We estimated the adjusted population attributable risk (PAR) for each risk factor that was associated with an increased risk of stillbirth ($p < 0.05$) in the multivariable regression models. Adjusted relative risks (RRs) were obtained from these models, and the prevalence of each risk factor was derived from the study dataset. PARs were then calculated using the standard formula:

$$\text{Population attributable risk} = [\text{prevalence} * (\text{RR} - 1)]/[1 + \text{prevalence} * (\text{RR} - 1)]$$

Calculations were performed using the *AF* package in RStudio (version 4.5.1). PARs quantify the proportion of stillbirths in the population that could theoretically be prevented if the exposure were eliminated, assuming a causal relationship. We restricted PAR estimation to risk

Table 1 Baseline characteristics of study population included in the analysis and incidence rates. Complex social factors are defined in NICE CG110 and recorded in the dataset. Maternal ethnicity was derived from the raw NHS Digital codes and categorised into nine groups. The grouping was designed to balance statistical power and clinical relevance. Pakistani women were kept as a separate category due to sufficient sample size and known differences in maternal and perinatal outcomes compared with other South Asian groups. Indian and Bangladeshi women were combined due to smaller numbers and similar risk profiles. Other ethnicities were grouped to ensure adequate numbers for stable estimates while preserving clinically meaningful distinctions. No additional reclassification has been made

Pregnancy outcome	Overall, *N* = 876,629 *N* (%)	Stillbirth, *N* = 2568 *N* (%)	Rate per 1000 births
Maternal characteristics			
Ethnicity			
White British	492,931 (66.4%)	1321 (60.1%)	2.68
White other	93,462 (12.6%)	239 (10.9%)	2.56
Asian—Indian or Bangladeshi	36,557 (4.9%)	141 (6.4%)	3.86
Asian—other	16,225 (2.2%)	55 (2.5%)	3.39
Asian—Pakistani	27,027 (3.6%)	136 (6.2%)	5.03
Black African	17,598 (2.4%)	107 (4.9%)	6.08
Black other	11,609 (1.6%)	64 (2.9%)	5.51
Mixed ethnicity	13,766 (1.9%)	45 (2.0%)	3.27
Other ethnicity	32,924 (4.4%)	89 (4.1%)	2.70
Unknown	134,530	371	
Age of woman at booking (years)			
< 20	54,019 (6.2%)	178 (6.9%)	3.30
20–24	163,883 (18.7%)	517 (20.1%)	3.15
25–29	267,116 (30.5%)	732 (28.5%)	2.74
30–34	254,733 (29.1%)	679 (26.4%)	2.67
35–39	113,829 (13.0%)	371 (14.4%)	3.26
≥ 40	23,049 (2.6%)	91 (3.5%)	3.95
Body mass index at booking			
Underweight (< 18.5)	41,375 (6.0%)	90 (4.4%)	2.18
Normal weight (18.5 to < 25)	338,368 (49.2%)	933 (45.5%)	2.76
Overweight (25 to < 30)	180,156 (26.2%)	561 (27.3%)	3.11
Obesity class I (30 to < 35)	79,332 (11.5%)	261 (12.7%)	3.29
Obesity class II (35 to < 40)	31,795 (4.6%)	121 (5.9%)	3.81
Obesity class III (≥ 40)	16,819 (2.4%)	86 (4.2%)	5.11
Unknown	188,784	516	
Pregnancy related characteristics			
Smoking status at booking			
Current	82,894 (11.2%)	349 (16.1%)	4.21
Ex smoker -after conception	57,327 (7.7%)	150 (6.9%)	2.62
Ex smoker -more than 1y before conception	47,826 (6.5%)	129 (6.0%)	2.70
Ex smoker -within 1y before conception	27,449 (3.7%)	60 (2.8%)	2.19
Never smoked	422,733 (57.1%)	1192 (55.1%)	2.82
Non-smoker (history unknown)	102,350 (13.8%)	284 (13.1%)	2.77
Unknown	136,050	404	
Antenatal booking after 12 weeks			
Yes	142,853 (16.3%)	523 (20.4%)	3.66
No	733,776 (83.7%)	2045 (79.6%)	2.79
Social complexities			
Complex Social Factors			
Yes	77,324 (11.5%)	294 (14.7%)	3.80

Table 1 (continued)

Pregnancy outcome	Overall, *N* = 876,629 *N* (%)	Stillbirth, *N* = 2568 *N* (%)	Rate per 1000 births
No	596,639 (88.5%)	1703 (85.3%)	2.85
Unknown	202,666	571	
Index of multiple deprivation (quintiles)			
1—Most deprived	220,924 (25.7%)	787 (31.4%)	3.56
2	195,288 (22.7%)	611 (24.4%)	3.13
3	165,242 (19.2%)	461 (18.4%)	2.79
4	150,080 (17.4%)	359 (14.3%)	2.39
5—Least deprived	128,761 (15.0%)	288 (11.5%)	2.24
Unknown	16,334	62	
Health status at booking			
Hypertension			
No	870,940 (99.4%)	2556 (99.5%)	2.93
Yes	5689 (0.6%)	12 (0.5%)	2.11
Mental health conditions			
No	819,749 (93.5%)	2376 (92.5%)	2.90
Yes	56,880 (6.5%)	192 (7.5%)	3.38
Pre-existing diabetes			
No	869,370 (99.2%)	2,518 (98.1%)	2.90
Yes	7259 (0.8%)	50 (1.9%)	6.89
Baby characteristics			
Fetal growth restriction (< 10th percentile)			
No	466,641 (87.3%)	875 (55.7%)	1.88
Yes	67,995 (12.7%)	696 (44.3%)	10.24
Unknown	341,993	997	

factors associated with increased stillbirth risk (RR > 1), as negative PAR values derived from protective associations (RR < 1) are not meaningful in this context.

Missing data were imputed using multiple imputation by chained equations under the missing at random assumption [28]. We created 44 complete data sets, pooling results using Rubin's rules [29]. As a sensitivity analysis, we performed a univariable complete case analysis to compare to the imputed results. Comparisons were made using chi-squared tests (Additional file 2: Table 2). The analyses were done using statistical package R studio version 4.5.1.

Ethical approval

Data were anonymised prior to analysis, and individual patient consent was not required.

Sample size and power

Across the study period, 876,279 nulliparous women met inclusion criteria, with 2568 stillbirths observed (2.93 per 1000). With this event rate, the study had > 90% power at a two-sided α of 0.05 to detect risk ratios as small as 1.2 for exposures with prevalence ≥ 10%. For less common exposures (e.g. substance misuse, prevalence < 2%), the study retained > 80% power to detect risk ratios ≥ 1.5. This ensured adequate statistical power to evaluate both common and less frequent maternal risk factors.

Results

A flow diagram of the study sample is shown in Fig. 1. During the study period, 1,656,870 births were recorded, including 1,651,242 live births and 5628 stillbirths (3.40 per 1000 births). After excluding 780,241 births due to parity, congenital disorders, or multiple pregnancy, the study sample comprised 876,629 live births and 2,568 stillbirths (2.93 per 1000 births) from 130 of 134 NHS Trusts. The dataset covers the majority of all total births in England, and the data is of high quality [17]. Baseline characteristics are presented in Table 1, with the full stratified dataset available in Additional file: Table 1. Characteristics of the imputed dataset were comparable to the pre-imputation data (Additional file: Table 2).

Early gestation (~ < 13 weeks)

The results of the Poisson regression model for early gestation (~ < 13 weeks) pregnancy factors with stillbirth are displayed in Fig. 2.

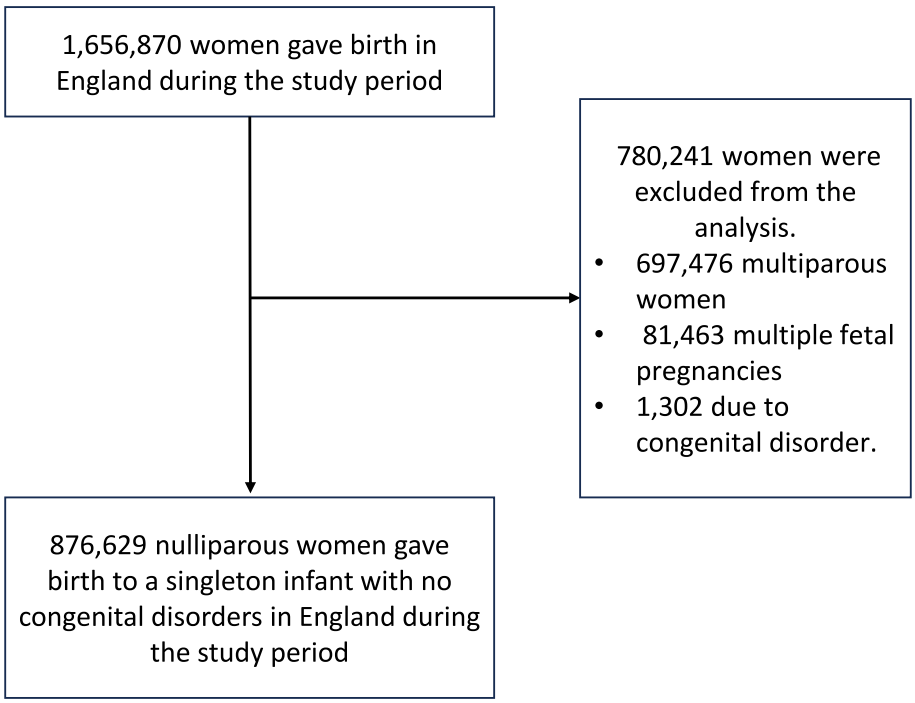

Fig. 1 Study sample

Modifiable risk factors

Increasing body-mass index (BMI) was associated with a higher risk of stillbirth, particularly for BMI ≥ 40 kg/m^2 compared with 18.5– < 25 kg/m^2 (RR 1.70, 95% CI 1.39–2.07). Women who were current smokers or reported substance use at their booking appointment had increased risk relative to women who had never smoked (RR 1.34, 95% CI 1.19–1.51) or used substances (RR 1.52, 95% CI 1.16–1.98). Not taking folic acid supplements before conception (RR 1.28, 95% CI 1.16–1.40) or during early pregnancy (RR 1.38, 95% CI 1.18–1.61) was also associated with higher risk. Booking appointments after 12 weeks of gestation were linked with greater stillbirth risk than earlier booking (RR 1.18, 95% CI 1.07–1.30). These early modifiable factors represent potential targets for preconception or early pregnancy interventions.

Non-modifiable risk factors

Women from Asian (Indian or Bangladeshi) (RR 1.39, 95% CI 1.18–1.64), Asian (Pakistani) (RR 1.57, 95% CI 1.32–1.88), Black (African) (RR 1.76, 95% CI 1.45–2.15), and Black (other) (RR 1.67, 95% CI 1.32–2.13) had higher stillbirth risk compared with white British women. Maternal age ≥ 35 years was associated with increased risk relative to 30–34 years (RR 1.22, 95% CI 1.08–1.39) with risk further elevated at ≥ 40 years (RR 1.44, 95% CI 1.16–1.79). A family history of multiple pregnancies (RR 1.23, 95% CI 1.04–1.46) and pre-existing diabetes (RR 2.05, 95% CI 1.55–2.72) were also associated with higher risk. Living in the most deprived areas was linked with increased stillbirth risk (IMD1: RR 1.26, 95% CI 1.10–1.45; IMD2: RR 1.20, 95% CI 1.04–1.38).

Population-level missed opportunities

Table 2 shows the population attributable risk (PAR) for each factor. The PAR for living in the most deprived areas (IMD1) was 6%, while initiating folic acid only after pregnancy confirmation had a PAR of 15%.

Late gestation risk factors

The results of the Poisson regression model for late gestation (> 12 weeks) pregnancy factors with stillbirth are displayed in Fig. 3.

Non-modifiable risk factors

Women diagnosed during pregnancy with severe pre-eclampsia (RR 0.18, 95% CI 0.06–0.56) or gestational diabetes (RR 0.34, 95% CI 0.20–0.60) had lower risk compared with those not diagnosed, reflecting increased monitoring and early delivery in affected pregnancies. Gestation < 37 weeks (RR 24.49, 95% CI 22.06–27.19) and FGR (RR 2.96, 95% CI 2.73–3.21) were strongly associated with increased risk.

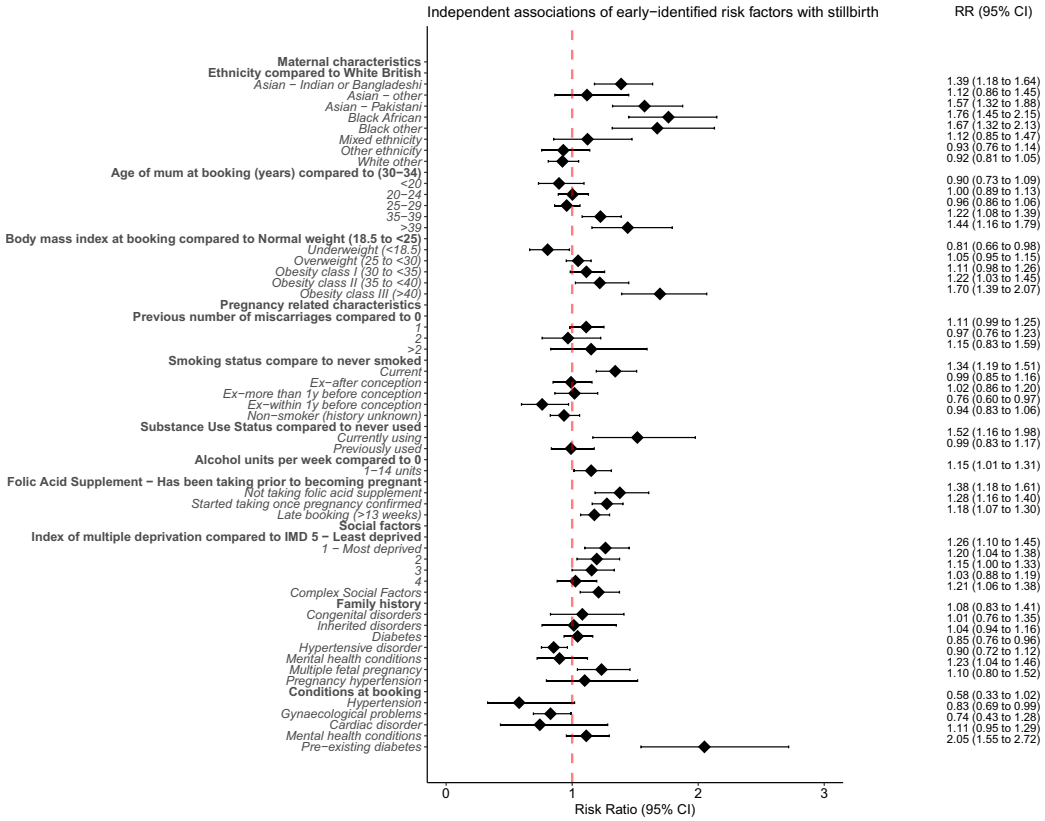

Fig. 2 Risk factors for stillbirth that can be identified during early gestation (< 13 weeks). The early pregnancy (< 13 weeks) regression model was adjusted for maternal sociodemographic, obstetric, and clinical characteristics, including smoking status, ethnicity, socioeconomic status (Index of Multiple Deprivation quintile 2015), maternal age at booking, previous miscarriage, body mass index, substance use, alcohol consumption, folic acid supplementation, complex social factors, late booking, pre-existing hypertension, cardiac disease, gynaecological history, mental health disorders, diabetes, as well as family history of diabetes, hypertension, mental health disorders, multifetal pregnancy, pregnancy-related hypertension, congenital disorders, and inherited disorders

Population-level missed opportunities

Table 3 presents PARs for significant late gestation factors. FGR had the highest PAR at 22%, highlighting its substantial population-level impact.

Sensitivity analysis

Univariable analysis restricted to complete cases yielded findings consistent with the imputed dataset (Additional file: Table 3), supporting the robustness of our results.

Discussion

Main findings

To our knowledge, this is the largest analysis to date of stillbirth risk factors, using routinely collected data from 130 NHS Trusts in England between 2015 and 2019. We identified a broad range of maternal and pregnancy risk factors associated with stillbirth. Despite this, the application of population attributable risk and regression models could not reliably identify women at risk of stillbirth and is therefore unlikely to have clinical utility.

Placental dysfunction is reported to contribute to the largest proportion of stillbirth cases [11, 30, 31]. In our analysis, FGR, commonly resulting from placental dysfunction, was associated with the highest population attributable risk. However, it is currently identified too late for effective early screening. This highlights the importance of improving detection of growth restriction to enhance prediction and care planning, consistent with previous reports [10, 32, 33].

Importantly, several early pregnancy and sociodemographic factors also contributed substantially to overall stillbirth risk. For example, initiating folic acid supplementation only after pregnancy confirmation accounted for an estimated 15% of the population attributable risk [34], while living in the most deprived areas contributed 6%. These findings underscore that prevention efforts should address both early modifiable factors and wider social determinants, alongside improving late-pregnancy detection of placental dysfunction.

Table 2 Adjusted population attributable risk (PAR) of risk factors that met our p-value threshold (< 0.05) in the early gestation analysis

Risk factor	Adjusted relative risk (95% CI)	*p*-value	Population attributable risk (%)
Ethnicity			
White British	Reference		
White other	0.92 (0.81–1.05)	0.227	-
Asian—Indian or Bangladeshi	1.39 (1.18–1.64)	< 0.001	1.89
Asian—Pakistani	1.57 (1.32–1.88)	< 0.001	2.04
Asian—other	1.12 (0.86–1.45)	0.402	-
Black African	1.76 (1.45–2.15)	< 0.001	1.81
Black other	1.67 (1.32–2.13)	< 0.001	1.06
Mixed ethnicity	1.12 (0.85–1.47)	0.411	-
Other ethnicity	0.93 (0.76–1.14)	0.483	-
Age			
< 20	0.90 (0.73–1.09)	0.280	-
20–24	1.00 (0.89–1.13)	0.972	-
25–29	0.96 (0.86–1.06)	0.404	-
30–34	Reference		-
35–39	1.22 (1.08–1.39)	< 0.001	2.83
≥ 40	1.44 (1.16–1.79)	< 0.001	1.15
Body mass index			
Underweight (< 18.5)	0.81 (0.66–0.98)	0.029	-
Normal weight (18.5 to < 25)	Reference		-
Overweight (25 to < 30)	1.05 (0.95–1.15)	0.339	-
Obesity class II (35 to < 40)	1.22 (1.03–1.45)	0.025	1.00
Obesity class III (≥ 40)	1.70 (1.39–2.07)	< 0.001	1.67
Smoking status			
Current	1.34 (1.19–1.51)	< 0.001	3.71
Ex smoker -after conception	0.99 (0.85–1.16)	0.906	-
Ex smoker -more than 1y before conception	1.02 (0.86–1.20)	0.829	-
Ex smoker -within 1y before conception	0.76 (0.60–0.97)	0.028	-
Never smoked	Reference		-
Non-smoker (history unknown)	0.94 (0.83–1.06)	0.290	-
Substance misuse			
Current	1.52 (1.16–1.98)	0.002	0.63
Never used	Reference		-
Previously used	0.99 (0.83–1.17)	(0.912)	-
Alcohol units			
1–14 units	1.15 (1.01–1.31)	0.034	1.32
Folic acid supplementation			
Has been taking prior to becoming pregnant	Reference		-
Not taking folic acid	1.38 (1.18–1.61)	< 0.001	2.76
Started taking when pregnancy occurred	1.28 (1.16–1.40)	< 0.001	14.62
Late booking (≥ 13 weeks)	1.18 (1.07–1.30)	0.001	2.79
Index of multiple deprivation			
IMD1	1.26 (1.10–1.45)	< 0.001	6.34
IMD2	1.20 (1.04–1.38)	0.013	4.24
IMD3	1.15 (1.00–1.33)	0.052	-
IMD4	1.03 (0.88–1.19)	0.740	-
IMD5	Reference		-
Complex social factors	1.21 (1.06–1.38)	0.004	2.79

Table 2 (continued)

Risk factor	Adjusted relative risk (95% CI)	*p*-value	Population attributable risk (%)
Pre-existing diabetes	2.05 (1.55–2.72)	< 0.001	0.86
Family history of multifetal pregnancy	1.23 (1.04–1.46)	0.015	1.17

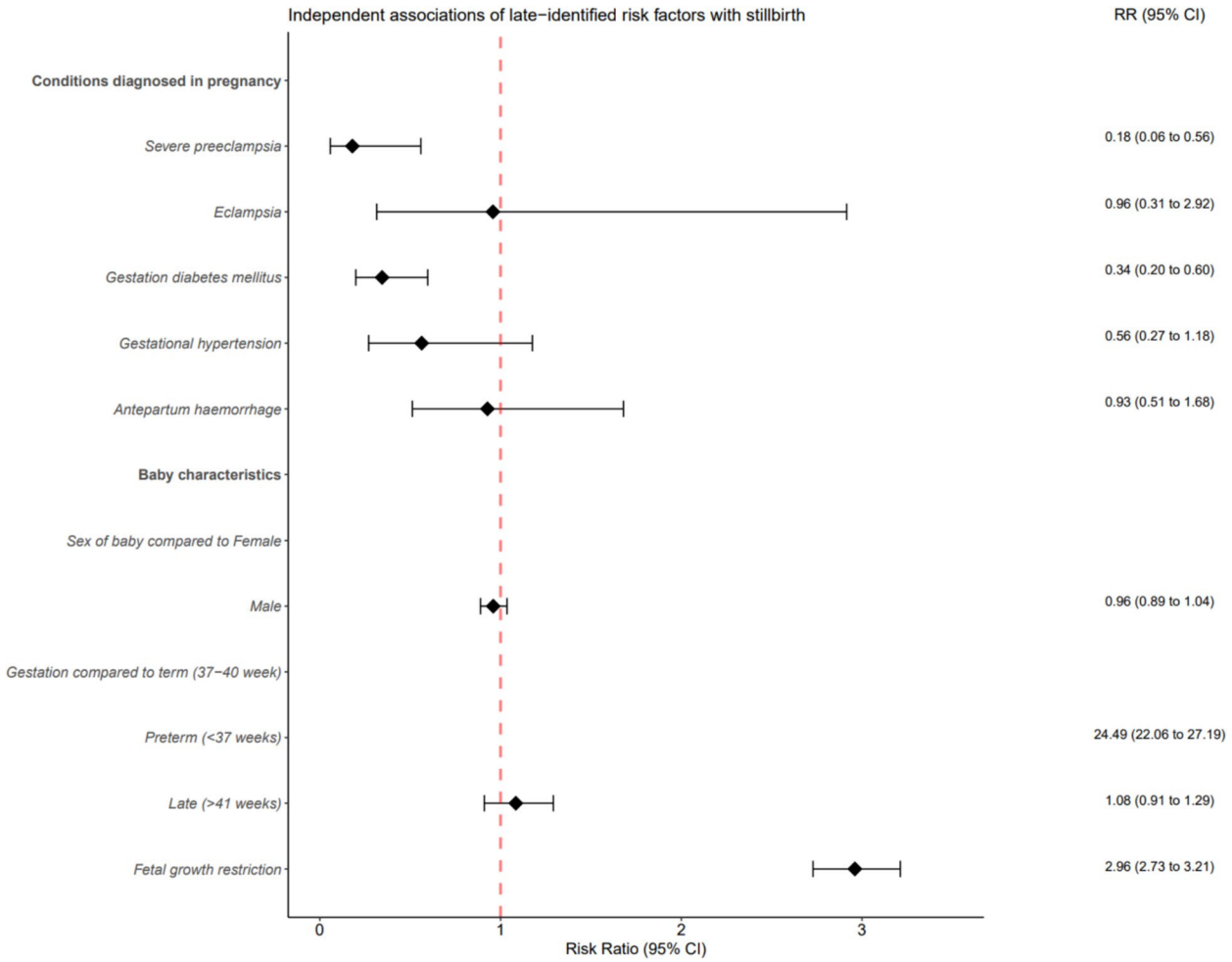

Fig. 3 Risk factors for stillbirth that can be identified during late pregnancy. The late pregnancy (> 12 weeks of gestation) regression models were adjusted for maternal sociodemographic, obstetric, and clinical characteristics, including smoking status, ethnicity, socioeconomic status (Index of Multiple Deprivation quintile 2015), maternal age at booking, previous miscarriage, body mass index, substance use, alcohol consumption, folic acid supplementation, complex social factors, late booking, severe preeclampsia, eclampsia, gestational diabetes, gestational hypertension, antepartum haemorrhage, pre-existing hypertension, cardiac disease, gynaecological history, mental health disorders, diabetes, fetal growth restriction, and gestational age category, as well as family history (FH) of diabetes, hypertension, mental health disorders, multifetal pregnancy, pregnancy-related hypertension, congenital disorders, and inherited disorders

Clinical implications

Our results underscore that risk factor-based screening strategies, which are central to current NICE and Royal College guidelines, have limited capacity to prevent stillbirth at the population level. The findings are consistent with a recent systematic review, which reported none of the three published stillbirth predictive models, using maternal-clinical characteristics, can be applied to clinical practice [15]. However, it is important to recognise that such risk factors are not designed to predict stillbirth directly, but rather to triage women who are deemed high risk. RCOG recommends that maternal risk factors

Table 3 Adjusted population attributable risk of risk factors that met our p-value threshold (< 0.05) in the late-term gestation analysis

Risk factor	Adjusted relative risk (95% CI)	*p*-value	Population attributable risk (%)
Fetal growth restriction	2.96 (2.73–3.21)	< 0.001	22.15

inform referral for ultrasound, and serial growth scans or doppler studies for those at higher risk [35]. Our findings support the rationale behind this risk-stratified approach but suggest that reliance on static maternal characteristics alone is insufficient [36]. Many women who experience stillbirth do not exhibit these predefined risk factors, while others classified as high-risk have healthy outcomes [11]. This limits both the sensitivity and specificity of current triage models.

A clinically useful tool could support personalised risk stratification and targeted interventions for stillbirth prevention. Evidence suggests that models incorporating biochemical markers and ultrasound findings have greater predictive performance [13]. As stillbirth is a heterogeneous outcome, developing a single prediction model for all cases appears unattainable. Future approaches could focus on developing individualised models that incorporate biochemical markers, ultrasound findings, and personalised risk factors, including sociodemographic and intersectionality aspects, for women at increased risk due to specific pathophysiological pathways such as placental dysfunction [37]. Policymakers should reconsider the emphasis on static maternal risk profiles and instead invest in scalable approaches that combine integrating maternal characteristics with biochemical and biophysical markers, similar to first-trimester preeclampsia or Down syndrome screening [38].

In addition, there needs to be increased emphasis on addressing health-system and social determinants, such as delayed booking and continuity of care, particularly for disadvantaged groups. The findings from this study are consistent with growing evidence that structural determinants contribute to stillbirth risk [39]. Our findings align with prior research from the UK, Europe and North America showing that women from ethnic minority groups and women living in the most deprived areas experience the highest stillbirth rates [40, 41]. Moreover, our observation that living in the most deprived quintile and delayed antenatal booking contributed a substantial proportion of the population-attributable risk underscores that sociodemographic inequalities cannot be explained by individual-level risk factors alone but are also reflective of systemic and service-level differences [39, 42]. Addressing these disparities therefore requires improving early engagement, booking and continuity of maternity care services while concurrently reducing socioeconomic disadvantage and strengthening trust and access to high-quality maternity services in underserved communities.

Research implications

Future research on stillbirth prediction should explore combinations of clinical, biochemical, and biophysical markers. While placental biomarkers alone lack sufficient utility [43], research targeted at women at higher risk of stillbirth, such as those with evidence of placental dysfunction or reduced fetal movements, may help refine predictive strategies. Additional research is also required to determine the pathways through which sociodemographic inequalities contribute to stillbirth risk to decipher if these factors interact with biological mechanisms such as placental dysfunction [44]. Studies that combine routinely collected clinical data with social and contextual information could help identify modifiable mediators and inform interventions that address both biological and structural contributors to stillbirth. The findings from this study provide a benchmark, demonstrating the limited added value of maternal risk factors alone and setting a foundation for more integrated predictive tools.

Global relevance

Although based in England, these findings are relevant to other high-income settings where stillbirth rates remain higher than desired despite advanced healthcare systems [11, 45, 46]. More broadly, they illustrate a common challenge in global health: over-reliance on maternal demographic factors, which rarely offer sufficient predictive power [11]. Future progress will require investment in integrated prediction tools and system-level interventions that can be adapted internationally.

Strengths and limitations

Major strengths of our analysis included the large sample size accessed from 130 of the 134 NHS Trusts in England, utilising data that is representative of a whole population with the potential for generalizability for the perinatal population in England. In addition, we utilised readily available and routinely collected risk factors. To the best of our knowledge, this is the largest and most comprehensive investigation of risk factors in nulliparous women in relation to stillbirth.

This study is not without limitations. Our analysis utilises observational data and therefore causal inferences cannot be drawn. Associations were identified between ethnicity and stillbirth, and between socioeconomic status (IMD) and stillbirth; however, we did not stratify

ethnicity by IMD, so intersectional effects cannot be directly inferred from these analyses. An additional limitation is the potential for selection bias within the dataset if it is not representative. Certain groups may be underrepresented, including undocumented migrants, women experiencing homelessness, and those who do not engage with maternity care or deliver privately. These groups likely experience systematically different risk profiles and care pathways, which could bias the observed associations and lead to underestimation of true inequalities [47]. A further limitation to this analysis is the potential for measurement error as we used self-reported measurements for several variables, (e.g. alcohol consumption, substance misuse, smoking). Such behaviours are often underreported due to social desirability bias, particularly in maternity care contexts [48]. This misclassification would likely bias associations toward the null, leading to conservative estimates of effect sizes. An important limitation of this study relates to differential missingness in some routinely collected variables. In particular, the prevalence of pre-existing diabetes and reported alcohol consumption was substantially higher among women with missing booking data compared with those with complete records, indicating that missingness for these variables was unlikely to be at random. Although multiple imputation was used to minimise bias associated with missing data, residual bias may persist for variables where the missing at random assumption is violated. Consequently, effect estimates and population attributable risks for diabetes and alcohol consumption should be interpreted with caution. Importantly, these limitations do not affect the overall conclusions regarding the limited predictive utility of maternal risk factors for stillbirth at a population level. Additionally, although FGR contributed substantially to the risk of stillbirth, our results reflect postnatal identification rather than the effectiveness of antenatal detection or surveillance. This limitation highlights the need for integrated datasets capturing both maternal risk factors and antenatal growth monitoring to evaluate predictive strategies for stillbirth. Furthermore, the timing of antenatal booking is influenced by both healthcare system factors and personal circumstances. Consequently, any observed association with stillbirth risk may be underestimated if booking dates are delayed or misreported. Finally, the potential for a treatment paradox should be acknowledged. Women identified as high risk, such as those with gestational diabetes, may receive additional monitoring or interventions which can reduce the apparent association between the risk factor and stillbirth. Consequently, the observed relative risks for some high-risk groups may be underestimated, and the predictive utility of maternal characteristics alone could appear lower than their true biological effect.

Conclusions

This national study shows that routinely collected maternal and clinical characteristics, even when assessed comprehensively, cannot provide a clinically useful prediction model for stillbirth in nulliparous women. This calls for a paradigm shift, from reliance on static risk profiles to integrated, biomarker-informed, and systems-based approaches to prevention. Furthermore, future research should consider intersectional maternal characteristics, including ethnicity and socioeconomic status. Only such approaches are likely to deliver meaningful advances in stillbirth prevention.

Abbreviations

NHS	National Health Service
RR	Risk ratios
CI	Confidence intervals
PARs	Population attributable risks
BMI	Body mass index
UK	United Kingdom
NICE	National Institute for Health and Care Excellence
RCOG	Royal College of Obstetricians and Gynaecologist
IMD	Index of Multiple Deprivation
GROW	Gestation Related Optimal Weight
FGR	Fetal growth restriction

Supplementary Information

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Additional file 1. Characteristics of the study population included in the analysis and incidence rates. An alcohol unit was defined as 10 mL of pure alcohol. Substance misuse refers to illicit drug use or misuse of prescribed medications as recorded in maternity records. Complex social factors were defined according to NICE CG110 and recorded in the NHS Digital dataset. Inherited disorders reflect NHS Digital coding and include genetic or chromosomal conditions present in the mother or fetus. Maternal ethnicity was derived from raw NHS Digital ethnicity codes and categorised into nine groups to balance statistical power and clinical relevance. Pakistani women were retained as a separate category due to sufficient sample size and known differences in maternal and perinatal outcomes compared with other South Asian groups; Indian and Bangladeshi women were combined due to smaller numbers and similar risk profiles. Remaining ethnicities were grouped to ensure stable estimates while preserving clinically meaningful distinctions.

Additional file 2. Characteristics of the imputed study population and incidence rates. Data were multiply imputed to account for missing values, with results representing pooled estimates across all imputed datasets. Comparisons between observed and missing groups were performed using chi-squared tests. Variables with no missing data or identical category distributions returned $p = 1$. Variable definitions and ethnicity categorisation were consistent with additional file: Table 1.

Additional file 3. Univariable analysis of risk factors for stillbirth, comparing results from complete-case analysis and the imputed dataset.

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Authors' contributions

AH and BT are joint co-first authors. EL and AJ are joint co-last authors. AH, EL and BT conceived the study. AH performed the data analysis. AH, EL and BT drafted the first version of the manuscript. RM, CB, VC, JS, MV, LB, DA, CW, TD and AJ contributed to interpretation of the results and critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Data availability

The data that supports the findings of this study are available from the Maternity Information Systems (MIS) data following approval from (DARS-NIC-430380-F7L4Z-v1.2). Restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

Declarations

Ethics approval and consent to participate

This study was conducted using routinely collected, de-identified maternity data. Approval to access and use the data was granted by NHS Digital through the Data Access Request Service (DARS) (reference DARS-NIC-430380-F7L4Z-v1.2). As the study involved secondary analysis of anonymised data, individual consent was not required.

RCOG Disclaimer: "Within this document [paper] we use the terms woman and women's health. However, it is important to acknowledge that it is not only women for whom it is necessary to access women's health and reproductive services in order to maintain their gynaecological health and reproductive well-being. Gynaecological and obstetric services and delivery of care must therefore be appropriate, inclusive and sensitive to the needs of those individuals whose gender identity does not align with the sex they were assigned at birth".

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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