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# Incidence of stillbirth: effect of deprivation

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**KEYWORDS:** deprivation; pregnancy complication; race; screening; singleton pregnancy; socioeconomic status; stillbirth

## CONTRIBUTION

*What are the novel findings of this work?*
First, the incidence of stillbirth, particularly placental dysfunction-related stillbirth, is higher in women living in the most deprived areas in South East England. Second, in women living in the most deprived areas, there is a higher incidence of factors that contribute to stillbirth, including black race, increased body mass index, smoking, chronic hypertension and previous stillbirth. Third, in screening for stillbirth, inclusion of the index of multiple deprivation does not improve the prediction provided by race, other maternal characteristics and elements of medical history.

*What are the clinical implications of this work?*
Effective first-trimester prediction of stillbirth is provided by a combination of maternal characteristics and elements of medical history. Inclusion of the index of multiple deprivation does not improve prediction.

## ABSTRACT

***Objectives*** *To examine the relationship between the English index of multiple deprivation (IMD) and the incidence of stillbirth and assess whether IMD contributes to the prediction of stillbirth provided by the combination of maternal demographic characteristics and elements of medical history.*

***Methods*** *This was a prospective, observational study of 159 125 women with a singleton pregnancy who attended their first routine hospital visit at 11 + 0 to 13 + 6 weeks' gestation in two maternity hospitals in the UK. The inclusion criterion was delivery at ≥ 24 weeks' gestation of a fetus without major abnormality. Participants completed a questionnaire on demographic characteristics and obstetric and medical history. IMD was used as a measure of socioeconomic status, which takes into account income, employment, education, skills and training, health and disability, crime, barriers to housing and services, and living environment. Each neighborhood is ranked according to its level of deprivation relative to that of other areas into one of five equal groups, with Quintile 1 containing the 20% most deprived areas and Quintile 5 containing the 20% least deprived areas. Logistic regression analysis was used to determine whether IMD provided a significant independent contribution to stillbirth after adjustment for known maternal risk factors.*

***Results*** *The overall incidence of stillbirth was 0.35% (551/159 125), and this was significantly higher in the most deprived compared with the least deprived group (Quintile 1* vs *Quintile 5). The odds ratio (OR) in Quintile 1 was 1.57 (95% CI, 1.16–2.14) for any stillbirth, 1.64 (95% CI, 1.20–2.28) for antenatal stillbirth and 1.89 (95% CI, 1.23–2.98) for placental dysfunction-related stillbirth. In Quintile 1 (*vs *Quintile 5), there was a higher incidence of factors that contribute to stillbirth, including black race, increased body mass index, smoking, chronic hypertension and previous stillbirth. The OR of black (*vs *white) race was 2.58 (95% CI, 2.14–3.10) for any stillbirth, 2.62 (95% CI, 2.16–3.17) for antenatal stillbirth and 3.34 (95% CI, 2.59–4.28) for placental dysfunction-related stillbirth. Multivariate analysis showed that IMD did not have a significant contribution to the prediction of stillbirth provided by maternal race and other maternal risk factors. In contrast, in black (*vs *white) women, the risk of any and antenatal stillbirth was 2.4-fold higher and the risk of placental*

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*dysfunction-related stillbirth was 2.9-fold higher after adjustment for other maternal risk factors.*

***Conclusions*** *The incidence of stillbirth, particularly placental dysfunction-related stillbirth, is higher in women living in the most deprived areas in South East England. However, in screening for stillbirth, inclusion of IMD does not improve the prediction provided by race, other maternal characteristics and elements of medical history.*


## INTRODUCTION

The rate of stillbirth is a sensitive marker of the quality of care during pregnancy and birth. Globally, an estimated two million babies are stillborn every year, and the reported rates vary from 22.8 stillbirths per 1000 total births in West and Central Africa to 2.9 per 1000 total births in western Europe[1]. Stillbirths can be broadly classified into antenatal and intrapartum and are also subdivided into those thought to be the consequence of impaired placentation and those due to other causes or that are unexplained. The rationale for categorizing stillbirths according to the likely underlying cause is that antenatal intervention and preventive strategies can be undertaken more effectively[2–5].

We have reported previously that the risk for stillbirth has a U-shaped relationship with maternal age and increases with increasing body mass index, black race, smoking, medical history of chronic hypertension and diabetes mellitus, and a history of previous stillbirth[5,6]. Studies from countries with populations that are of predominantly white race have consistently reported that, in women of black race, the incidence of stillbirth is 2-fold higher than in white women; the risk for South or East Asians is usually not different from that in white women[6]. Women with lower socioeconomic status are also at increased risk for stillbirth[3,7], but it is uncertain whether there is an independent contribution to stillbirth risk from race and deprivation because black women living in high-income countries are more likely to live in areas of deprivation compared with white women[7].

The aims of this study were to examine the relationship between the English index of multiple deprivation (IMD) and the incidence of stillbirth in a cohort of racially diverse women with a singleton pregnancy living in South East England and to assess whether IMD improves the prediction of stillbirth provided by a combination of maternal race and other maternal risk factors.

## METHODS

### Study design and participants

The data for this study were derived from a cohort of 159 125 women with a singleton pregnancy who attended a routine hospital visit at 11 + 0 to 13 + 6 weeks' gestation at King's College Hospital, London, and Medway Maritime Hospital, Gillingham, UK, between March 2006 and November 2020. Gestational age was determined by the measurement of fetal crown–rump length at 11–13 weeks' gestation[8]. Women with a singleton pregnancy delivering a non-anomalous liveborn or stillborn fetus at ≥ 24 weeks' gestation were included. Pregnancies with aneuploidy or major fetal abnormality were excluded. Women gave written informed consent to take part in the study, which was conducted in accordance with the guidelines of the Declaration of Helsinki and was approved by the NHS research ethics committee on 11 March 2003 (REC reference: 02-03-033). The study population was used in our previous publication on the relationship between IMD and pre-eclampsia (PE)[9].

### Race and other maternal characteristics

The first-trimester visit included recording of maternal demographic characteristics and medical history, measurement of maternal weight and height, and ultrasound examination for fetal anatomy and biometry. Participants completed a questionnaire, which was then reviewed by a doctor together with the woman. When there was a language barrier, professional translation services were offered to participants. Patient characteristics included maternal age, race, method of conception (natural or using assisted reproductive technology, defined as *in-vitro* fertilization or use of ovulation drugs), cigarette smoking during pregnancy, medical history of chronic hypertension, diabetes mellitus and lupus erythematosus (SLE) or antiphospholipid syndrome (APS), family history of PE (woman's mother affected) and obstetric history, which included parity (parous or nulliparous if no previous pregnancy at ≥ 24 weeks' gestation) and, for parous women, history of PE and interpregnancy interval. Chronic hypertension was defined as hypertension (i.e. systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg) diagnosed before pregnancy or before 20 weeks' gestation. In relation to race, patients were asked to self-describe as white, black, South Asian, East Asian or mixed race.

### Index of multiple deprivation (IMD)

IMD was used as a measure of socioeconomic status. IMD is the official measure of relative deprivation for small areas (or neighborhoods) in England. IMD is designed to identify aspects of deprivation across seven domains: (i) income, which measures the proportion of the population with low income; (ii) employment, which measures the proportion of the working-age population in an area involuntarily excluded from the labor market; (iii) education, skills and training, which measures the lack of attainment and skills in the local population; (iv), health and disability, which measures the risk of premature death and impairment of quality of life through poor physical or mental health; (v) crime, which measures the risk of personal and material victimization at local level; (vi) barriers to housing and services, which measures the physical and financial

 

accessibility of housing and local services; and (vii) living environment, which measures the quality of the local environment. These domains are combined, using appropriate weights, to calculate the IMD of each neighborhood in England. Each neighborhood is ranked according to its level of deprivation relative to that of other areas and categorized into one of five equal groups, with Quintile 1 containing the 20% most deprived areas and Quintile 5 containing the 20% least deprived areas. The postcode of each patient was used to determine their IMD (https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019).

### Outcome measure

Data on pregnancy outcome were obtained from the hospital maternity records or women's general practitioner. Stillbirths were divided into those that occurred antenatally, those that were associated with placental dysfunction (PE or birth weight $< 10^{th}$ percentile) and those due to other causes or that were unexplained.

The Fetal Medicine Foundation fetal and neonatal population weight charts were used to define the $10^{th}$ birth-weight percentile[10], and the diagnosis of PE was based on the criteria of the American College of Obstetricians and Gynecologists[11]. According to this definition, diagnosis of PE requires the presence of chronic or gestational hypertension (i.e. systolic blood pressure $\geq$ 140 mmHg or diastolic blood pressure $\geq$ 90 mmHg on at least two occasions 4 h apart developing after 20 weeks' gestation in a previously normotensive woman) and at least one of the following: proteinuria ($\geq$ 300 mg/24 h, protein-to-creatinine ratio $\geq$ 30 mg/mmol or urinary dipstick testing $\geq$ 2+), renal insufficiency with serum creatinine $>$ 97 µmol/L in the absence of underlying renal disease, hepatic dysfunction with blood concentration of transaminases more than twice the upper limit of normal ($\geq$ 65 IU/L for our laboratory), thrombocytopenia (platelet count $<$ 100 000/µL), neurological complications (e.g. cerebral or visual symptoms) and pulmonary edema[11].

### Statistical analysis

Data were expressed as mean ± SD for continuous variables and *n* (%) for categorical variables. Student's *t*-test and chi-square test or Fisher's exact test were used for comparing outcome groups for continuous and categorical data, respectively.

Univariate logistic regression analysis was performed to examine the association between IMD and stillbirth using Quintile 5 (least deprived group) as the reference. Multiple logistic regression analysis was performed for stillbirth using race, age, body mass index, mode of conception, smoking, history of chronic hypertension, diabetes mellitus, APS or SLE and obstetric history. The latter was subdivided into the following groups: nulliparous without previous miscarriage, nulliparous with previous miscarriage at $<$ 16 weeks' gestation, nulliparous with previous miscarriage at 16 + 0 to 23 + 6 weeks, parous without previous miscarriage or stillbirth, parous with previous miscarriage at $<$ 16 weeks' gestation, parous with previous miscarriage at 16 + 0 to 23 + 6 weeks' gestation and parous with previous stillbirth. The statistical software R version 4.1.2 was used for data analysis[12].

## RESULTS

### Study participants

In the study population of 159 125 singleton pregnancies, there were 551 (0.35%) stillbirths, including 504 (91.5%) that were antenatal and 283 (51.4%) that were placental dysfunction-related.

Maternal and pregnancy characteristics of the study population according to IMD quintile are summarized, and patient characteristics in Quintiles 1–4 are compared with those in Quintile 5 (the least deprived group) in Table 1. The incidence of stillbirth (any, antenatal and placental dysfunction-related) was significantly higher in Quintiles 1 and 2 (*vs* Quintile 5). In Quintile 1 (*vs* Quintile 5), there was a higher incidence of factors that contribute to stillbirth, including black race, increased body mass index, smoking, chronic hypertension and previous stillbirth. In Quintiles 1–4 (*vs* Quintile 5), there were lower mean maternal age, higher mean body mass index, lower proportions of white, South Asian and East Asian women, higher proportions of black and mixed race women, higher rate of natural conception and higher proportion of cigarette smokers. In Quintiles 1–3 (*vs* Quintile 5), there were higher proportions of women with chronic hypertension, parous women with previous stillbirth and nulliparous women with previous late miscarriage. In Quintiles 1 and 2 (*vs* Quintile 5), there were higher proportions of women with Type-II diabetes mellitus and parous women with previous late miscarriage.

The proportion of black women in the most deprived Quintiles 1 and 2 (73.9%, 17 942/24 291) was significantly higher compared with that of white (42.0%, 50 393/120 065), South Asian (43.7%, 3255/7446) and East Asian (45.2%, 1404/3107) women (all $P < 0.0001$).

### Prediction of stillbirth

Tables 2–4 present the results of univariate and multiple logistic regression analyses demonstrating the association of maternal characteristics, including IMD and race, with stillbirth. The overall incidence of stillbirth was 0.35% (551/159 125), and this was significantly higher in the most, compared with the least, deprived group (Quintile 1 *vs* Quintile 5). The odds ratio (OR) in Quintile 1 (*vs* Quintile 5) was 1.57 (95% CI, 1.16–2.14) for any stillbirth (Table 2), 1.64 (95% CI, 1.20–2.28) for antenatal stillbirth (Table 3) and 1.89 (95% CI, 1.23–2.98) for placental dysfunction-related stillbirth (Table 4). The OR of black (*vs* white) race was 2.58

 

(95% CI, 2.14–3.10) for any stillbirth, 2.62 (95% CI, 2.16–3.17) for antenatal stillbirth and 3.34 (95% CI, 2.59–4.28) for placental dysfunction-related stillbirth. The OR of smoking (*vs* no smoking) was 1.77 (95% CI, 1.39–2.23) for any stillbirth, 1.76 (95% CI, 1.37–2.25) for antenatal stillbirth and 1.56 (95% CI, 1.09–2.18) for placental dysfunction-related stillbirth. The OR of chronic hypertension (*vs* no chronic hypertension) was 4.00 (95% CI, 2.66–5.74) for any stillbirth, 4.39 (95% CI, 2.93–6.32) for antenatal stillbirth and 7.56 (95% CI, 4.92–11.11) for placental dysfunction-related stillbirth. The OR of history of previous stillbirth (*vs* no previous stillbirth) was 4.08 (95% CI, 2.55–6.17) for any stillbirth, 3.54 (95% CI, 2.04–5.70) for antenatal stillbirth and 3.75 (95% CI, 1.84–6.79) for placental dysfunction-related stillbirth.

Multivariate analysis showed that IMD did not have a significant contribution to the prediction of stillbirth provided by maternal race and other maternal risk factors. Increased risk for any stillbirth was provided

**Table 1** Maternal and pregnancy characteristics of study population according to quintile of index of multiple deprivation

| | *Index of multiple deprivation* | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | *Quintile 1* | | *Quintile 2* | | *Quintile 3* | | *Quintile 4* | | *Quintile 5* |
| *Characteristic* | *(n = 30 123)* | P | *(n = 45 142)* | P | *(n = 36 091)* | P | *(n = 27 315)* | P | *(n = 20 454)* |
| Stillbirth | | | | | | | | | |
| All | 136 (0.5) | 0.003 | 183 (0.4) | 0.022 | 103 (0.3) | 0.935 | 70 (0.3) | 0.533 | 59 (0.3) |
| Antenatal | 128 (0.4) | 0.003 | 162 (0.4) | 0.045 | 98 (0.3) | 0.849 | 63 (0.2) | 0.595 | 53 (0.3) |
| Placental dysfunction-related | 75 (0.2) | 0.006 | 92 (0.2) | 0.057 | 57 (0.2) | 0.512 | 32 (0.1) | 0.745 | 27 (0.1) |
| Age | 28.8 ± 6.07 | < 0.001 | 30.2 ± 5.95 | < 0.001 | 31.6 ± 5.55 | < 0.001 | 31.9 ± 5.26 | < 0.001 | 32.4 ± 4.95 |
| < 20 years | 2239 (7.4) | < 0.001 | 2159 (4.8) | < 0.001 | 1007 (2.8) | < 0.001 | 531 (1.9) | 0.030 | 219 (1.1) |
| 20–40 years | 26 881 (89.2) | < 0.001 | 41 074 (91.0) | < 0.001 | 33 337 (92.4) | 0.014 | 25 434 (93.1) | 0.068 | 19 148 (93.6) |
| ≥ 40 years | 1003 (3.3) | < 0.001 | 1909 (4.2) | < 0.001 | 1747 (4.8) | < 0.001 | 1350 (4.9) | < 0.001 | 1087 (5.3) |
| Body mass index (kg/m$^2$) | 27.0 ± 6.14 | < 0.001 | 26.3 ± 5.73 | < 0.001 | 25.4 ± 5.18 | 0.002 | 25.4 ± 4.96 | < 0.001 | 25.1 ± 4.68 |
| Underweight (< 18.5 kg/m$^2$) | 794 (2.6) | < 0.001 | 1054 (2.3) | < 0.001 | 792 (2.2) | 0.002 | 502 (1.8) | 0.809 | 369 (1.8) |
| Normal (18.5–24.9 kg/m$^2$) | 12 788 (42.5) | < 0.001 | 21 399 (47.4) | < 0.001 | 19 825 (54.9) | < 0.001 | 15 014 (55.0) | < 0.001 | 11 588 (56.7) |
| Overweight (25–29.9 kg/m$^2$) | 8548 (28.4) | 0.688 | 12 737 (28.2) | 0.993 | 9692 (26.9) | 0.001 | 7553 (27.7) | 0.180 | 5770 (28.2) |
| Obese (≥ 30 kg/m$^2$) | 7993 (26.5) | < 0.001 | 9952 (22.0) | < 0.001 | 5782 (16.0) | < 0.001 | 4246 (15.5) | < 0.001 | 2727 (13.3) |
| Race | | | | | | | | | |
| White | 19 942 (66.2) | < 0.001 | 30 451 (67.5) | < 0.001 | 28 585 (79.2) | < 0.001 | 23 297 (85.3) | < 0.001 | 17 790 (87.0) |
| Black | 7507 (24.9) | < 0.001 | 10 435 (23.1) | < 0.001 | 4280 (11.9) | < 0.001 | 1432 (5.2) | < 0.001 | 637 (3.1) |
| South Asian | 1266 (4.2) | < 0.001 | 1989 (4.4) | < 0.001 | 1543 (4.3) | < 0.001 | 1461 (5.3) | 0.032 | 1187 (5.8) |
| East Asian | 562 (1.9) | 0.004 | 842 (1.9) | 0.002 | 705 (2.0) | 0.022 | 540 (2.0) | 0.049 | 458 (2.2) |
| Mixed | 846 (2.8) | < 0.001 | 1425 (3.2) | < 0.001 | 978 (2.7) | < 0.001 | 585 (2.1) | 0.036 | 382 (1.9) |
| Conception | | | | | | | | | |
| Spontaneous | 29 509 (98.0) | < 0.001 | 43 801 (97.0) | < 0.001 | 34 551 (95.7) | < 0.001 | 26 069 (95.4) | 0.001 | 19 389 (94.8) |
| *In-vitro* fertilization | 381 (1.3) | < 0.001 | 941 (2.1) | < 0.001 | 1193 (3.3) | 0.004 | 931 (3.4) | 0.034 | 772 (3.8) |
| Ovulation drugs | 233 (0.8) | < 0.001 | 400 (0.9) | < 0.001 | 347 (1.0) | < 0.001 | 315 (1.2) | 0.007 | 293 (1.4) |
| Smoker | 4899 (16.3) | < 0.001 | 4602 (10.2) | < 0.001 | 2332 (6.5) | < 0.001 | 1403 (5.1) | < 0.001 | 737 (3.6) |
| Medical history | | | | | | | | | |
| Chronic hypertension | 546 (1.8) | < 0.001 | 712 (1.6) | < 0.001 | 416 (1.2) | 0.009 | 262 (1.0) | 0.667 | 188 (0.9) |
| Type-I DM | 126 (0.4) | 0.492 | 199 (0.4) | 0.752 | 136 (0.4) | 0.149 | 130 (0.5) | 0.839 | 94 (0.5) |
| Type-II DM | 340 (1.1) | < 0.001 | 413 (0.9) | < 0.001 | 228 (0.6) | 0.956 | 159 (0.6) | 0.550 | 128 (0.6) |
| SLE/APS | 63 (0.2) | 0.628 | 107 (0.2) | 0.931 | 78 (0.2) | 0.780 | 55 (0.2) | 0.548 | 47 (0.2) |
| Parity | | | | | | | | | |
| Nulliparous | 12 731 (42.3) | < 0.001 | 21 277 (47.1) | 0.116 | 18 067 (50.1) | < 0.001 | 13 423 (49.1) | < 0.001 | 9505 (46.5) |
| Nulliparous, previous miscarriage < 16 weeks | 2129 (7.1) | < 0.001 | 3672 (8.1) | 0.433 | 3123 (8.7) | 0.173 | 2328 (8.5) | 0.425 | 1701 (8.3) |
| Nulliparous, previous miscarriage 16–23 weeks | 125 (0.4) | < 0.001 | 180 (0.4) | < 0.001 | 115 (0.3) | 0.048 | 72 (0.3) | 0.456 | 46 (0.2) |
| Parous, previous stillbirth | 357 (1.2) | < 0.001 | 404 (0.9) | < 0.001 | 305 (0.8) | < 0.001 | 150 (0.5) | 0.852 | 115 (0.6) |
| Parous, previous miscarriage < 16 weeks | 4356 (14.5) | 0.071 | 6154 (13.6) | < 0.001 | 4821 (13.4) | < 0.001 | 3759 (13.8) | < 0.001 | 3077 (15.0) |
| Parous, previous miscarriage 16–23 weeks | 313 (1.0) | < 0.001 | 371 (0.8) | < 0.001 | 207 (0.6) | 0.053 | 123 (0.5) | 1 | 92 (0.4) |

Data are given as *n* (%) or mean ± SD. Data in Quintiles 1–4 were compared with those in Quintile 5. APS, antiphospholipid syndrome; DM, diabetes mellitus; SLE, systemic lupus erythematosus.

 

by black race, low and high maternal age, increasing body mass index, conception after the use of ovulation drugs, cigarette smoking, Type-I diabetes mellitus, chronic hypertension and previous pregnancy affected by stillbirth; the risk was reduced in parous women without previous miscarriage or stillbirth (Table 2). Similar findings were observed for antenatal stillbirth (Table 3) and placental dysfunction-related stillbirth (Table 4).

Subgroup analysis in the black racial group showed that IMD did not have a significant contribution to the prediction of stillbirth provided by other maternal risk factors. The adjusted OR for any stillbirth was 2.29 (95% CI, 0.71–14.03) for Quintile 1, 2.60 (95% CI, 0.82–15.80) for Quintile 2, 1.52 (95% CI, 0.44–9.54) for Quintile 3 and 1.30 (95% CI, 0.30–8.90) for Quintile 4, indicating no statistically significant difference compared with Quintile 5.

Figure 1 illustrates the OR for any stillbirth in IMD Quintiles 1–4 compared with Quintile 5, each racial group compared with white women, each body mass index group compared with normal weight (18.5–24.9 kg/m$^2$) and those with (*vs* without) medical conditions, smoking and previous stillbirth. On unadjusted analysis, Quintiles 1 and 2 were associated with a significantly increased incidence of stillbirth, but this was not the case after adjustment for race as well as race plus other maternal risk factors.

## DISCUSSION

### Main findings

There are three main findings of this study of 159 125 pregnancies in the racially and socioeconomically diverse South East of England. First, univariate analysis demonstrated that the risk of stillbirth (any, antenatal and placental dysfunction-related) was higher in women living in the most (*vs* least) deprived areas. Such a relationship between IMD and the risk of stillbirth is likely to be mediated by several maternal characteristics and elements from maternal history that were found to be associated with increased risk of stillbirth (Tables 2–4) and were more common in women living in the most (*vs* least) deprived areas (Table 1). Thus, in the most (*vs* least) deprived areas, the mean maternal age was lower (28.8 *vs* 32.4 years), median body mass index was higher (27.0 *vs* 25.1 kg/m$^2$)

**Table 2** Univariate and multivariate analyses of relationship between maternal characteristics and stillbirth of any type

| | *Univariate* | | *Multivariate* | |
|---|---|---|---|---|
| *Characteristic* | *OR (95% CI)* | P | *OR (95% CI)* | P |
| Intercept | — | — | 0.01 (0.00–0.04) | < 0.001 |
| Maternal age (in years) | 0.79 (0.72–0.88) | < 0.001 | 0.87 (0.78–0.97) | 0.007 |
| Maternal age (in years)$^2$ | 1.00 (1.00–1.01) | < 0.001 | 1.00 (1.00–1.00) | 0.004 |
| Body mass index (in kg/m$^2$) | 1.05 (1.04–1.07) | < 0.001 | 1.04 (1.02–1.05) | < 0.001 |
| Race (reference: white) | | | | |
| Black | 2.58 (2.14–3.10) | < 0.001 | 2.37 (1.93–2.90) | < 0.001 |
| South Asian | 1.07 (0.67–1.60) | 0.774 | 1.20 (0.76–1.81) | 0.408 |
| East Asian | 1.28 (0.66–2.22) | 0.425 | 1.55 (0.79–2.70) | 0.157 |
| Mixed | 1.03 (0.54–1.74) | 0.930 | 1.03 (0.55–1.75) | 0.921 |
| Method of conception (reference: spontaneous) | | | | |
| *In-vitro* fertilization | 1.18 (0.70–1.85) | 0.503 | 1.15 (0.66–1.86) | 0.597 |
| Ovulation drugs | 1.85 (0.92–3.27) | 0.055 | 1.91 (1.02–3.58) | 0.045 |
| Smoker (reference: no) | | | | |
| Yes | 1.77 (1.39–2.23) | < 0.001 | 2.01 (1.55–2.58) | < 0.001 |
| Diabetes mellitus (reference: no) | | | | |
| Type I | 3.49 (1.58–6.56) | < 0.001 | 3.39 (1.53–6.42) | 0.001 |
| Type II | 2.82 (1.50–4.78) | < 0.001 | 1.43 (0.75–2.48) | 0.239 |
| Chronic hypertension (reference: no) | | | | |
| Yes | 4.00 (2.66–5.74) | < 0.001 | 2.20 (1.44–3.25) | < 0.001 |
| SLE/APS (reference: no) | | | | |
| Yes | 2.50 (0.62–6.54) | 0.116 | 1.94 (0.48–5.16) | 0.258 |
| Obstetric history (reference: nulliparous) | | | | |
| Nulliparous, previous miscarriage < 16 weeks | 0.95 (0.69–1.28) | 0.742 | 0.85 (0.61–1.16) | 0.315 |
| Nulliparous, previous miscarriage 16–23 weeks | 2.36 (0.84–5.16) | 0.058 | 1.41 (0.50–3.13) | 0.453 |
| Parous, no previous miscarriage/stillbirth | 0.80 (0.67–0.97) | 0.023 | 0.68 (0.55–0.83) | < 0.001 |
| Parous, previous miscarriage < 16 weeks | 0.87 (0.67–1.12) | 0.292 | 0.71 (0.53–0.93) | 0.014 |
| Parous, previous miscarriage 16–23 weeks | 0.85 (0.26–2.00) | 0.750 | 0.53 (0.16–1.26) | 0.208 |
| Parous, previous stillbirth | 4.08 (2.55–6.17) | < 0.001 | 2.09 (1.21–3.38) | 0.004 |
| Index of multiple deprivation (reference: Quintile 5) | | | | |
| Quintile 1 | 1.57 (1.16–2.14) | 0.004 | 1.03 (0.75–1.43) | 0.855 |
| Quintile 2 | 1.41 (1.06–1.90) | 0.023 | 0.99 (0.73–1.35) | 0.949 |
| Quintile 3 | 0.99 (0.72–1.37) | 0.948 | 0.84 (0.61–1.16) | 0.278 |
| Quintile 4 | 0.89 (0.63–1.26) | 0.503 | 0.84 (0.59–1.19) | 0.314 |

APS, antiphospholipid syndrome; OR, odds ratio; SLE, systemic lupus erythematosus.

 

and there was a higher incidence of black race (24.9% *vs* 3.1%), smoking (16.3% *vs* 3.6%), chronic hypertension (1.8% *vs* 0.9%) and history of previous stillbirth (1.2% *vs* 0.6%).

Second, on multivariate analysis, there was no significant contribution from IMD to the prediction of stillbirth provided by race, other maternal characteristics and elements of medical history (Tables 2–4, Figure 1). Significant prediction of stillbirth was provided by black race, low and high maternal age, increasing body mass index, conception after the use of ovulation drugs, smoking, chronic hypertension, Type-I diabetes mellitus and previous stillbirth.

Third, in black (*vs* white) women, after adjustment for other maternal risk factors, the risk of any and antenatal stillbirth was 2.4-fold higher and the risk of placental dysfunction-related stillbirth was 2.9-fold higher (Tables 2–4, Figure 1). The increased risk of stillbirth in black women after accounting for confounding variables, such as lower maternal age, higher body mass index, chronic hypertension and previous stillbirth, which are more common in black compared with white women[6], may be the consequence of social deprivation not captured by IMD or may be due to genetic susceptibility. The latter may be associated with vascular disease resulting in placental dysfunction and increased risk of PE and small-for-gestational-age (SGA) neonate, which are more common in black compared with white women[9,13]. The ORs of black (*vs* white) women were particularly increased for placental dysfunction-related stillbirth (Table 4).

## Comparison with results of previous studies

We found that the risk of stillbirth is higher in women living in the most (*vs* least) deprived neighborhoods. This is consistent with findings of a meta-analysis of seven studies, including 2 579 032 pregnancies, which reported that the OR for stillbirth in the most (*vs* least) deprived neighborhood quintile was 1.33 (95% CI, 1.21–1.45)[7]. Similarly, a systematic review and meta-analysis of five studies including a combined total of 12 642 203 births reported that there were significantly increased odds of stillbirth in women from lower (*vs* highest) levels of occupation/social classes (OR, 1.40 (95% CI, 1.23–1.59))[14].

**Table 3** Univariate and multivariate analyses of relationship between maternal characteristics and antenatal stillbirth

| | *Univariate* | | *Multivariate* | |
|---|---|---|---|---|
| *Characteristic* | *OR (95% CI)* | P | *OR (95% CI)* | P |
| Intercept | — | — | 0.01 (0.00–0.04) | < 0.001 |
| Maternal age (in years) | 0.80 (0.72–0.89) | < 0.001 | 0.87 (0.78–0.98) | 0.018 |
| Maternal age (in years)$^2$ | 1.00 (1.00–1.01) | < 0.001 | 1.00 (1.00–1.00) | 0.011 |
| Body mass index (in kg/m$^2$) | 1.05 (1.04–1.07) | < 0.001 | 1.04 (1.02–1.05) | < 0.001 |
| Race (reference: white) | | | | |
| Black | 2.62 (2.16–3.17) | < 0.001 | 2.41 (1.95–2.97) | < 0.001 |
| South Asian | 1.13 (0.70–1.71) | 0.602 | 1.28 (0.79–1.95) | 0.279 |
| East Asian | 1.41 (0.73–2.45) | 0.261 | 1.73 (0.88–3.01) | 0.078 |
| Mixed | 1.14 (0.60–1.93) | 0.667 | 1.14 (0.60–1.94) | 0.656 |
| Method of conception (reference: spontaneous) | | | | |
| *In-vitro* fertilization | 1.06 (0.59–1.73) | 0.834 | 1.04 (0.57–1.75) | 0.903 |
| Ovulation drugs | 1.81 (0.87–3.30) | 0.078 | 1.87 (0.89–3.41) | 0.065 |
| Smoker (reference: no) | | | | |
| Yes | 1.76 (1.37–2.25) | < 0.001 | 2.02 (1.53–2.61) | < 0.001 |
| Diabetes mellitus (reference: no) | | | | |
| Type I | 3.81 (1.73–7.17) | < 0.001 | 3.72 (1.68–7.04) | < 0.001 |
| Type II | 2.57 (1.28–4.55) | 0.003 | 1.27 (0.62–2.30) | 0.473 |
| Chronic hypertension (reference: no) | | | | |
| Yes | 4.39 (2.93–6.32) | < 0.001 | 2.47 (1.61–3.66) | < 0.001 |
| SLE/APS (reference: no) | | | | |
| Yes | 2.73 (0.68–7.16) | 0.084 | 2.13 (0.52–5.66) | 0.200 |
| Obstetric history (reference: nulliparous) | | | | |
| Nulliparous, previous miscarriage < 16 weeks | 0.92 (0.65–1.27) | 0.637 | 0.84 (0.59–1.16) | 0.302 |
| Nulliparous, previous miscarriage 16–23 weeks | 2.72 (1.12–6.64) | 0.027 | 1.51 (0.53–3.36) | 0.367 |
| Parous, no previous miscarriage/stillbirth | 0.80 (0.65–0.98) | 0.031 | 0.67 (0.54–0.83) | < 0.001 |
| Parous, previous miscarriage < 16 weeks | 0.85 (0.64–1.12) | 0.268 | 0.67 (0.50–0.89) | 0.007 |
| Parous, previous miscarriage 16–23 weeks | 0.79 (0.20–2.08) | 0.687 | 0.42 (0.10–1.12) | 0.138 |
| Parous, previous stillbirth | 3.54 (2.04–5.70) | < 0.001 | 2.09 (1.19–3.42) | 0.006 |
| Index of multiple deprivation (reference: Quintile 5) | | | | |
| Quintile 1 | 1.64 (1.20–2.28) | 0.002 | 1.07 (0.77–1.51) | 0.702 |
| Quintile 2 | 1.39 (1.02–1.91) | 0.039 | 0.97 (0.70–1.34) | 0.831 |
| Quintile 3 | 1.05 (0.75–1.47) | 0.784 | 0.88 (0.63–1.24) | 0.458 |
| Quintile 4 | 0.89 (0.62–1.29) | 0.532 | 0.84 (0.58–1.21) | 0.336 |

APS, antiphospholipid syndrome; OR, odds ratio; SLE, systemic lupus erythematosus.

Our findings indicating increased risk of stillbirth in black (*vs* white) women and in the most (*vs* least) deprived IMD quintile are consistent with those of a study examining registry data of all 4 391 569 singleton births at ≥ 24 + 0 weeks' gestation in the UK between 2014 and 2019[15]. The study reported that the stillbirth rate per 1000 was higher in black women (7.58 (95% CI, 7.19–7.99)) compared with white women (3.40 (95% CI, 3.33–3.47)) and in the most deprived socioeconomic quintile (4.80 (95% CI, 4.64–4.96)) compared with the least deprived quintile (2.70 (95% CI, 2.58 to 2.81)). An additional finding of the study was that, after adjustment for race and maternal age, neonates born to mothers living in the most (*vs* least) deprived quintile had an increased absolute rate difference of 1.5 (95% CI, 1.32–1.67) stillbirths per 1000 total births. An association of stillbirth with both black race and social deprivation was also reported in a population-based observational study in Spain, which included 970 740 live births and 2464 stillbirths from 2007 to 2008[16]. The study reported that the risk ratio (RR) for stillbirth adjusted for maternal age, education, country of origin, parity and gestational age was 2.13 (95% CI, 1.74–2.60) among mothers having secondary or lower education (*vs* tertiary education) and 1.75 (95% CI, 1.54–2.00) among African (*vs* Spanish) mothers. The RR of stillbirth was 3.74 (95% CI, 3.00–4.70) in African women with only secondary or lower education and 1.75 (95% CI, 1.54–2.00) in those with tertiary education; the respective values for Spanish women were 2.13 (95% CI, 1.74–2.60) and 1.0.

In our study, although both black race and social deprivation were associated with increased risk of stillbirth on univariate analysis, which was similar to the findings of the two abovementioned studies[15,16], our multivariate analysis found no significant contribution to stillbirth prediction from IMD after adjustment for other maternal characteristics and elements from medical history, in contrast to the two studies.

A population-based registry study examined single births in Sweden between 1992 and 2005, including 219 832 births to foreign-born women and 1 094 146 births to Swedish-born women[17]. Logistic regression analysis demonstrated that, in women from Africa, compared with Swedish women, the OR of stillbirth adjusted for year of birth, parity, income in quintiles (as an indicator of socioeconomic living conditions)

**Table 4** Univariate and multivariate analyses of relationship between maternal characteristics and placental dysfunction-related stillbirth

| | *Univariate* | | *Multivariate* | |
|---|---|---|---|---|
| *Characteristic* | *OR (95% CI)* | P | *OR (95% CI)* | P |
| Intercept | — | — | 0.01 (0.00–0.06) | < 0.001 |
| Maternal age (in years) | 0.77 (0.67–0.89) | < 0.001 | 0.85 (0.74–0.98) | 0.024 |
| Maternal age (in years)$^2$ | 1.00 (1.00–1.01) | < 0.001 | 1.00 (1.00–1.01) | 0.021 |
| Body mass index (in kg/m$^2$) | 1.05 (1.03–1.07) | < 0.001 | 1.03 (1.01–1.05) | 0.001 |
| Race (reference: white) | | | | |
| Black | 3.34 (2.59–4.28) | < 0.001 | 2.92 (2.21–3.85) | < 0.001 |
| South Asian | 1.58 (0.89–2.60) | 0.090 | 1.80 (1.01–2.97) | 0.032 |
| East Asian | 1.77 (0.75–3.50) | 0.140 | 2.13 (0.90–4.25) | 0.052 |
| Mixed | 0.93 (0.33–2.04) | 0.874 | 0.91 (0.32–2.00) | 0.839 |
| Method of conception (reference: spontaneous) | | | | |
| *In-vitro* fertilization | 0.66 (0.24–1.44) | 0.363 | 0.62 (0.22–1.41) | 0.315 |
| Ovulation drugs | 1.41 (0.44–3.31) | 0.495 | 1.46 (0.45–3.44) | 0.457 |
| Smoker (reference: no) | | | | |
| Yes | 1.56 (1.09–2.18) | 0.011 | 1.85 (1.26–2.64) | 0.001 |
| Diabetes mellitus (reference: no) | | | | |
| Type I | 0.83 (0.05–3.69) | 0.854 | 0.80 (0.05–3.58) | 0.826 |
| Type II | 2.70 (1.07–5.55) | 0.016 | 1.13 (0.44–2.41) | 0.774 |
| Chronic hypertension (reference: no) | | | | |
| Yes | 7.56 (4.92–11.11) | < 0.001 | 4.51 (2.83–6.91) | < 0.001 |
| SLE/APS (reference: no) | | | | |
| Yes | 1.61 (0.09–7.16) | 0.635 | 1.08 (0.06–4.95) | 0.938 |
| Obstetric history (reference: nulliparous) | | | | |
| Nulliparous, previous miscarriage < 16 weeks | 1.00 (0.64–1.49) | 0.984 | 0.92 (0.59–1.39) | 0.718 |
| Nulliparous, previous miscarriage 16–23 weeks | 1.85 (0.30–5.82) | 0.390 | 0.90 (0.15–2.89) | 0.883 |
| Parous, no previous miscarriage/stillbirth | 0.69 (0.52–0.91) | 0.009 | 0.57 (0.42–0.76) | < 0.001 |
| Parous, previous miscarriage < 16 weeks | 0.81 (0.55–1.15) | 0.253 | 0.62 (0.41–0.91) | 0.016 |
| Parous, previous miscarriage 16–23 weeks | 0.90 (0.15–2.82) | 0.879 | 0.45 (0.07–1.43) | 0.263 |
| Parous, previous stillbirth | 3.75 (1.84–6.79) | < 0.001 | 1.99 (1.02–3.88) | 0.044 |
| Index of multiple deprivation (reference: Quintile 5) | | | | |
| Quintile 1 | 1.89 (1.23–2.98) | 0.005 | 1.12 (0.72–1.81) | 0.622 |
| Quintile 2 | 1.55 (1.02–2.42) | 0.047 | 0.99 (0.64–1.57) | 0.951 |
| Quintile 3 | 1.20 (0.76–1.92) | 0.442 | 0.96 (0.61–1.54) | 0.855 |
| Quintile 4 | 0.89 (0.53–1.49) | 0.648 | 0.82 (0.49–1.38) | 0.456 |

APS, antiphospholipid syndrome; OR, odds ratio; SLE, systemic lupus erythematosus.

and urban/rural place of residence was 2.27 (95% CI, 1.84–2.80). The authors concluded that the increased risk of stillbirth in women from Africa cannot be explained by available socioeconomic factors but acknowledged that income is a crude socioeconomic indicator.

### Consequences for clinical practice

Development of preventive strategies for stillbirth necessitates recognition that, first, the etiology is heterogeneous and often unknown and, second, the majority of stillbirths are related to placental dysfunction, reflected by the increased incidence of SGA fetus and/or PE in affected cases, and important components of screening for SGA fetuses and PE are the same as those identified as predictors of stillbirth in the current study.

A high proportion of placental dysfunction-related stillbirths can potentially be prevented by a three-stage strategy. The first stage is screening for PE at 11–13 weeks' gestation and treatment of the high-risk group with aspirin; this is effective in the prevention of preterm PE as well as early SGA in the absence of PE[18–23]. The second stage is screening during the routine mid-trimester scan by a combination of maternal risk factors, estimated fetal weight and uterine artery pulsatility index, which identifies a high-risk group that contains a high proportion of placental dysfunction-related stillbirths that occur at 24–37 weeks' gestation; close monitoring of these pregnancies for early diagnosis of SGA fetuses may prevent at least some of such stillbirths by defining the best monitoring approach and timing of delivery[5,24,25]. The third stage is routine ultrasound examination at 36 weeks' gestation because screening at midgestation provides poor prediction of stillbirth at term; the detection rate for term SGA by assessment at 36 weeks' gestation is twice as high as with screening at midgestation[26,27].

### Strengths and limitations

The strengths of this study are, first, prospective examination of a large multiracial population of pregnant women with a singleton pregnancy attending for routine pregnancy care at 11–13 weeks' gestation, second, accurate recording of maternal and pregnancy characteristics and medical history to identify known risk factors for stillbirth and, third, use of multiple regression analysis to identify independent predictors of stillbirth and define the relative predictive value of each factor.

There are two main limitations of this study. First, race was classified into five broad categories, and it is likely

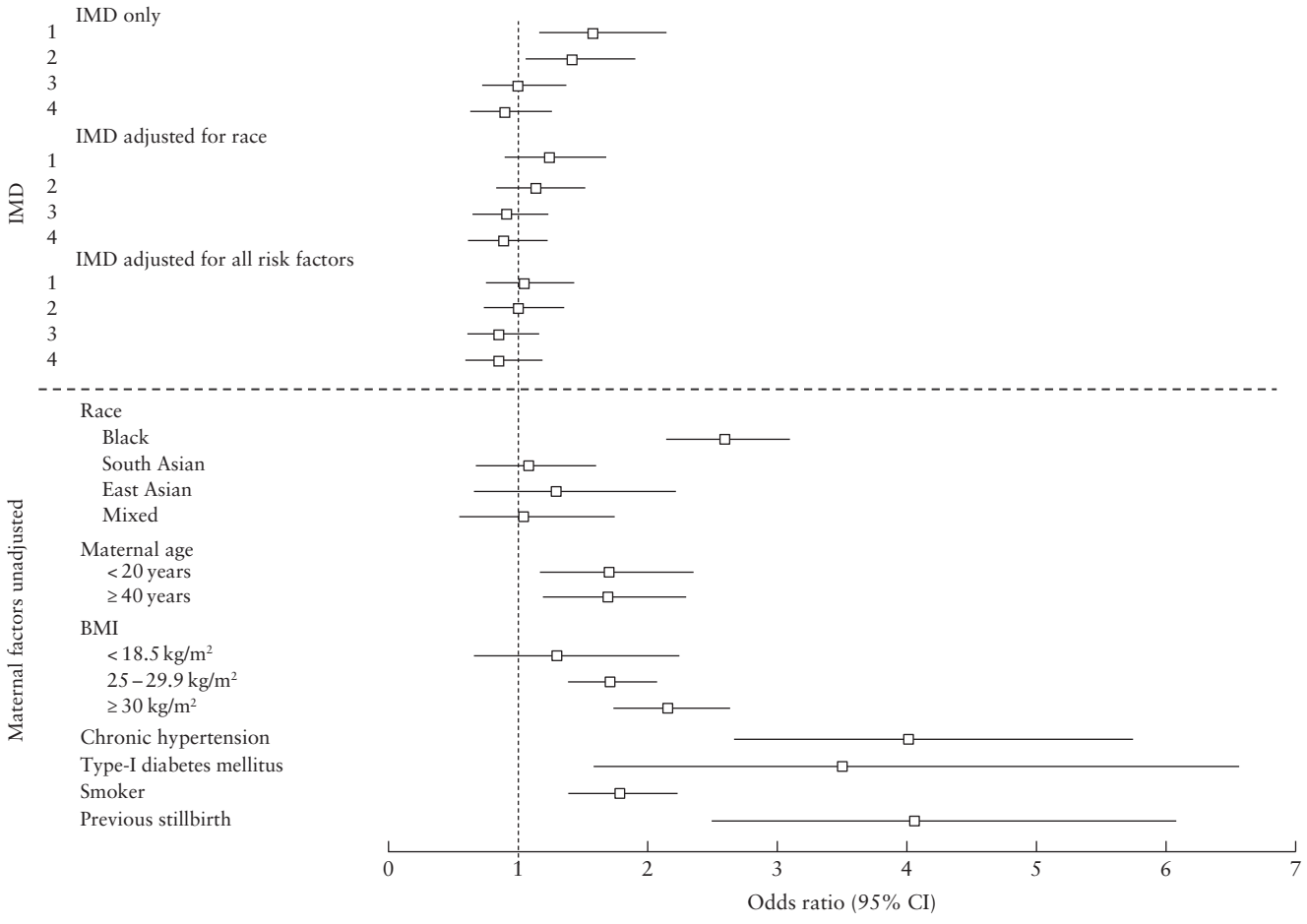


**Figure 1** Odds ratio, with 95% CI, for stillbirth of any type in index of multiple deprivation (IMD) Quintiles 1–4 (*vs* Quintile 5), each racial group (*vs* white race), each body mass index (BMI) group (*vs* group with normal BMI) and those with (*vs* without) medical history of chronic hypertension or Type-I diabetes mellitus, smoking and previous stillbirth.

 

that there would be variations in outcome in subgroups within each category; for example, in women classified as black, there may be differences between those who came to England from different regions in Africa, as opposed to the Caribbean, as well as differences between those who are first-, second- or third-generation immigrants in England. Second, IMD is not a suitable tool for targeting individuals, but a measure of relative deprivation based on the postcode of residence; not every person in a highly deprived area is necessarily deprived and some deprived people live in the least deprived areas.

## Conclusions

The incidence of stillbirth, particularly placental dysfunction-related stillbirth, is higher in women living in the most deprived areas in South East England. However, in screening for stillbirth, inclusion of IMD does not improve the prediction provided by race, other maternal characteristics and elements of medical history.

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