The impact of delayed maternity on foetal growth in Spain: An assessment by population attributable fraction

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Abstract

Background. Delayed childbearing is considered a risk factor for maternal-foetal health. As in other higher-income countries, in Spain age at maternity has steadily increased during the last two decades. **Aim**. To quantify the impact of the delay in the age at maternity on small for gestational age (SGA) categories of <3rd, 3rd-5th and 5th-10th percentiles. **Methods**. 2,672,350 singleton live births born to Spanish mothers in 2007-2015 were analysed. Adjusted relative risk was calculated by Poisson regressions to estimate the adjusted partial population attributable fractions (PAF$_p$) for primipara and multipara mothers aged 35-39 and ≥40 years for each category of SGA considering the interaction between age at maternity and parity. **Findings**. Primipara 35-39 years old mothers have the highest PAF$_p$ in the three categories of SGA, with the maximum value for SGA <3rd percentile (2.57%, 95% CI 2.25, 2.88). PAF$_p$ for both primipara and multipara ≥40 years old mothers were less than 1%. PAF$_p$ for the three categories of SGA increased significantly in 2007-2015 among primipara mature mothers, more clearly among those aged 35-39 years. The contribution of multipara mothers of both age groups did not increase significantly during the period. **Conclusion**. Delayed maternity is a significant adjusted risk factor for SGA, contributing to the increase of its prevalence. However, results also suggest a limited clinical impact of delayed maternity on foetal growth. Positive changes in maternal profile associated with the shift in maternal age might contribute to explain the discreet impact of mature mothers on negative birth outcome in Spain.

Key words

Introduction

Statement of Significance

Problem

Delayed childbearing is a trend across higher-income countries, being increasingly considered a major public health concern as an independent risk factor for maternal-foetal health, especially small-for-gestational age (SGA) newborns.

What is already known

Older age at childbearing is an obstetric, labour, and birth outcome risk factor, becoming more evident with increasing age over 40 years old. Some studies, however, find that its impact may be significantly reduced or eliminated after adjustment for potential confounders.

What this paper adds

Delayed maternity associated with primiparity is a significant adjusted risk factor for SGA, contributing to the increase of its prevalence. However, results suggest a limited clinical impact, perhaps as a consequence of the high socioeconomic status profile of older mothers.

The past decades have seen a remarkable trend in higher-income countries towards delaying childbirth to later reproductive years, a tendency driven by the free access to highly effective contraception, expanding opportunities for higher education and professional employment among women, and the subsequent option of assisted reproductive techniques (ART). Mature mothers (usually considered as women aged 35 years or older) may be psychologically and socially better prepared for childbearing, when compared to younger mothers, due to greater education, higher-income, and better prenatal care. Due to biological limits on fertility, mature mothers are more heavily involved in their "valuable pregnancies".[1] However, the trend to

delayed childbearing is being increasingly regarded as a major public health concern in higher-income countries, considering that it is an independent risk factor for maternal health and birth outcome. It has been suggested that delayed childbearing may be reversing the general improvement achieved during the previous decades in the health of mothers and neonates.[2] Moreover, the growing predominance of primipara mothers with an ever-increasing age at first maternity, and their growing rates of multiple pregnancies (twins, triplets) as a result of the rise in ART, have been proposed as the main explanations for the increasing rates of low birthweight (LBW) and preterm births described in almost all higher-income countries over the past two decades.[3]

Some biological mechanisms have been proposed to explain the potential negative effect of delayed maternity on maternal and foetal health and type of delivery. Uteroplacental perfusion decreases as women grow older independently of parity, affecting foetal growth and even determining a higher risk of perinatal mortality.[4] In a growing population of mature primipara mothers, primiparity contributes negatively to birth outcome mainly due to a lesser vascular uteroplacental capacity.[5] Additionally, the life course increasing prevalence of chronic medical diseases (diabetes and hypertension) and obesity among mature mothers contributes to poorer birth outcome and increased maternal health problems (pregnancy-induced hypertension, preeclampsia, and diabetes mellitus) compared with healthy younger women.[6] Finally, delayed childbirth has been associated with rising rates of intrapartum complications and, consequently, of Caesarean section (CS) and operative vaginal deliveries as a consequence of impaired myometrial function.[7]

The recent reviews by Carolan et al.[8,9] confirm that delayed maternity is significantly associated with an increased prevalence and risk of obstetric complications (placenta praevia and placental abruption), adverse labour (breech presentation, and operative vaginal or CS delivery), and negative birth outcome (stillbirths, preterm birth, and newborns with LBW or small for gestational age), although these associations are significantly reduced or disappeared after adjustment for potential confounders (parity, maternal health profile, and socioeconomic and

lifestyle factors), and are more evident with increasing age from ≥40 years old. Subsequent analyses in higher-income countries seem to confirm that delayed age at maternity is an independent obstetric, labour, and birth outcome risk factor,[10,11] although methodological disparities—specifically on the age groups compared and selection of confounders—make it difficult to draw strong conclusions.

Spain is currently one of the European countries with the highest mean age at first maternity.[12] Between 1996 and 2015, age at first maternity among Spanish national mothers increased from 29.23 to 32.21 years old, and mean age at maternity (all parities considered) increased from 30.03 to 33.30 years old (compiled by the authors from the Spanish Birth Statistical Bulletin), a trend strengthened during the current economic crisis beginning in 2007.[13] Simultaneously, throughout the decade prior to the economic crisis, Spain registered the greatest increase in LBW among the European countries in spite of the reduction in the prevalence of preterm births.[3] The aim of this study is to quantify the possible impact of delaying maternity on foetal growth (small for gestational age —SGA—) in Spain during the period 2007-2015 by the assessment of adjusted partial population attributable fraction (PAF_p) for primipara and multipara mothers with advanced (35-39 years old) and high (≥40 years old) age at maternity considering previous evidences on the interaction between age at maternity and parity on birth outcome.[11]

Methods

Data analysed came from the Spanish birth certificate (Spanish Birth Statistical Bulletin, *Boletín Estadístico de Partos*), the compulsory civil registration of all births. Since 1996 the Spanish birth certificate includes the nationality of parents, and in the revised version of 2007 includes new variables of interest, including marital status, level of education of both parents, and type of delivery. Validation studies have concluded that data provided by the Spanish birth certificate are highly reliable when compared with hospital birth statistics.[14] The three main groups of immigrant mothers in Spain (Latin-American, North African, and Eastern European women)

have very different lifestyles, cultural practices, nutritional behaviour and genetic heritage, showing different trends in reproductive profile and birth outcome compared with Spanish mothers.[15] As in other high income countries,[3] delayed maternity is associated in Spain with an increased access to ART and the consequent increase in multiple pregnancies, so that 70% of twin pregnancies are estimated to be due to fertility treatment.[16] Due to these reasons, analysis was restricted to Spanish women that delivered singleton live births (final sample n=2,672,350, 64.9% of all births registered in the analysed period: Figure 1).

SGA <3rd, 3rd-5th and 5th-10th percentiles were considered the dependent variables. Values of the three SGA categories have been established according to national birthweight charts by parity and type of delivery for the 2010-2014 period.[17] Age at maternity was considered the independent variable and categorised in six age groups: <20 years old, 20-24 years old, 25-29 years old, 30-34 years old, 35-39 years old, and ≥40 years old. Potential confounding variables included in the analysis were maternal education (primary education, secondary education, or university education), maternal occupation (professionals, administrative employees, service sector workers, primary sector workers, qualified workers, unskilled workers, students or housewives), marital status (married, with stable partner or with non-stable partner), residence of the mother (rural or urban residence), parity (primipara or multipara mothers), sex of the newborn, type of delivery (vaginal or CS delivery), and year of birth. Following descriptive analysis, adjusted PAF_p by parity and maternal age group on the three categories of SGA were calculated.

Firstly, interactions between pairs of potential confounders on birth outcome were checked by bivariate Poisson regressions. Interaction between age at maternity and parity on the three categories of SGA was confirmed. No other interactions between potential confounders on birth outcome were detected.

Secondly, to avoid unnecessary adjustment when performing multivariable analysis, bivariate Poisson regressions on each category of SGA have been carried out between age at maternity and the aforementioned maternal-foetal variables in order to identify the confounders of the effect of age at maternity on birth outcomes. Because the conventional change-in-estimate (CIE)

criterion of 10% between unadjusted and adjusted relative risk (RR) has been questioned,[18] models established by this criterion were compared with those based on the z-score test, considering significant a change between unadjusted and adjusted regression coefficients [Ln(RR)] with a *p*-value <0.05. Goodness-of-fit of adjusted models was checked by the likelihood ratio test and accuracy was checked by analysing Area Under ROC Curve (AUC). Both for primipara and for multipara mothers CIE criterion based on *p*-value <0.05 yield models with the highest Log-Likelihood and accuracy. Maternal occupation, maternal education, marital status, gestational age, type of birth, parity and the interaction term between age at maternity and parity were identified as confounders of age at maternity on the three categories of SGA and included in the model.

Finally, adjusted PAF_p were calculated. Unadjusted and adjusted relative risks (RR) of maternal age, parity and the interaction between both variables on the different categories of SGA were calculated (Supporting Information Table S1) considering the maternal groups with the lowest prevalence of the three categories of SGA (30-34 years old mothers, multipara, and 30-34 years old multipara mothers, respectively) as the reference categories. Adjusted partial PAF (PAF_p) and their confidence intervals (CI) were then calculated according to Rothman et al. (2008)[18] in order to evaluate the contribution of age at maternity, parity and their interaction to the prevalence of the three categories of SGA in the Spanish population during the period 2007-2015. Adjusted PAF_p by year between 2007 and 2015 were also calculated to evaluate the temporal trends in the contribution of mothers aged 35-39 and ≥40 years on the prevalence of SGA categories. Considering 2007 as the year of reference, a temporal change in adjusted PAF_p was considered significant when CI did not overlap.

Results

Temporal trends in maternal-foetal variables for the years 2007, 2010 and 2015 are shown in Table 1. Spanish mothers that delivered singleton births have become predominantly older women (44.1% over 35 years old in 2015) and highly qualified professionals (54.9% of women

professional or administrative employees in 2015), with a substantial reduction of the contribution of housewives (from 21.6% in 2007 to 15.3% in 2015). Associated with these trends in age at maternity and occupation, the percentage of mothers with university education increased from 34.2% to 41.4% between 2007 and 2015. Spanish mothers were predominantly urban dwellers and married or with a stable partner, although the percentage of women with non-stable partnerships increased significantly from 7.6% to 17.9% in the analysed period. Although still predominant, the rate of primiparity has been reduced from 59.1% to 53.6%, while CS deliveries remained over 25%. The prevalence of preterm births decreased significantly from 6.1% to 5.4%. In contrast, the overall prevalence of SGA ($<10^{th}$) increased significantly during the worst year of the economic crisis, 2010 (10.3%).

The association between age at maternity and maternal profile and birth outcome is shown in Table 2. Both quality of employment and education level increased significantly with age at maternity, in such a way that more than half of the mothers over 35 years old were professionals or administrative employees, and college educated, while women under 24 years old were predominantly housewives and with low educational levels. Likewise, marital stability increased with age at maternity. As expected, primiparity reduced with age at maternity (at a minimum of 37.9%, in mothers over 40 years old), while the rate of CS delivery increased from 14.1% in mothers <20 years old to 33.8% among those over 39 years old. The prevalence of preterm births and SGA $<10^{th}$ percentile newborns were higher among younger mothers (9.1%, and 11.7%, respectively), decreasing with maternal age and increasing again slightly in 35-39 years old women (5.7, and 9.9%, respectively), and more sharply among ≥40 years old women (7.1%, and 10.6%, respectively).

Table 3 shows the adjusted PAF_p for the three categories of SGA by age at maternity, parity and their interaction. The highest adjusted PAF_p for age at maternity was found among SGA $<3^{rd}$ percentile (1.90%, 95% CI 1.15, 2.60), and for parity among SGA 3rd-5th percentile (4.29%, 95% CI 3.16, 5.40). Considering the interaction between age at maternity and parity, total adjusted PAF_p for SGA $<3^{rd}$ percentile increased to 7.22% (95% CI 6.41, 8.03). Compared with the category of reference (multipara 30-34 years old mothers), primipara 35-39 years old mothers

showed the highest contributions in the three categories of SGA, with the maximum value to SGA <3rd percentile (2.57%, 95% CI 2.25, 2.88). The maternal group with the second highest PAF$_p$ was 30-34 years old primipara women, with the highest contribution to SGA <3rd percentile (1.99%, 95% CI 1.50, 2.47). In contrast, the PAF$_p$ for both primipara and multipara ≥40 years old mothers were <1% regarding the three categories of SGA.

Figures 2.a-d. show the temporal trend in the adjusted PAF$_p$ for SGA categories considering the interaction between age at maternity and parity in both groups of mature mothers. During the analysed period, adjusted PAF$_p$ for the three categories of SGA increased significantly among primipara 35-39 years old mothers (Figure 2.a, and Supporting Information Table S2), with a maximum contribution in 2015 to SGA <3rd percentile of 4.23% (95% CI 3.08, 5.37). Furthermore, the contribution of primipara ≥40 years old mothers to the prevalence of the three categories of SGA increased also significantly, although adjusted PAF$_p$ were substantial lower and the temporal trend is less clear (Figure 2.c, and Supporting Information Table S2). In contrast, PAF$_p$ for multipara mothers, both 35-39 years old (Figure 2.b, and Supporting Information Table S2) and ≥40 years old women (Figure 2.d, and Supporting Information Table S2) did not show a significant increase for any category of SGA.

Discussion

Spain is one of the higher-income countries with a more recent and sharper trend in postponing childbearing.[12] This study examined the impact of delayed childbearing on birth outcome in the country during the period of economic crisis (2007-2015), calculating adjusted PAF$_p$ for SGA considering the interaction between age at maternity and parity. Results confirm that the contribution to national fertility of mothers of advanced (35-39 years old) and high (≥40 years old) age at maternity increased during the analysed period, up to 44.1% in 2015, an increase which was far beyond previous estimations for European countries (~25% by 2015).[19] Between 2007 and 2015, the category of 35-39 years old mothers increased by one third, and that of ≥40 years old mothers almost doubled. Delayed maternity was clearly associated with a higher

socioeconomic status and marital stability, increased obstetric intervention (higher rate of CS deliveries), and a slightly higher prevalence of SGA among mature mothers—although lower than shown by mothers under 25 years old.

Results confirm that delayed maternity is a significant adjusted risk factor for foetal growth that is contributing to the increase of the prevalence of SGA newborns in Spain. Although younger mothers showed the highest prevalence of the three categories of SGA considered, the adjusted PAF_p for both primipara and multipara mothers ≥35 years old were higher, a consequence of their increasing demographic predominance among Spanish mothers and their higher adjusted RR. Results also confirm the need to consider the interaction between parity and age at maternity when assessing the impact of a delayed childbearing on birth outcome. Thus, primipara 35-39 years old mothers had the highest adjusted PAF_p for the three categories of SGA, showing the most clear and sustained upward trend in the prevalence of SGA categories, especially for SGA <3rd percentile. The contributions to the prevalence of SGA categories by primipara ≥40 years old mothers were more discrete, and there were no significant temporal increase from multipara mothers of both categories of mature mothers.

More than half of the Spanish mothers were primipara. Although primiparity reduced with age at maternity, as a consequence of the sustained trend to delay childbearing in the country, an ever-growing proportion of primipara mothers are also mature mothers. Between 2007 and 2015, the percentage of primipara mothers aged 35 years or older rose from 21.1% (n=38,521) to 34.2% (n=51,130)—an increase of 62.1%—, while decreased among mothers of younger age. However, despite the steady, ever-growing contribution of primipara mature women to childbearing in Spain, results also suggest a limited clinical impact of delayed childbearing on birth outcome, as other studies have highlighted.[20,21] Coinciding with previous studies,[11,22] the contribution to the prevalence of SGA by primipara mature mothers was discreet, well below those PAF_p obtained for the effect of harmful behaviours,[23] poor maternal weight gain,[24] or the exposure to air pollution[25] during pregnancy.

Positive changes in maternal profile associated with the shift in maternal age might contribute to explain this discreet impact of mature mothers on negative birth outcome in Spain. Delayed maternity is clearly associated with an increasing contribution of educated and wealthy women, a profile associated with greater stability and resources, lesser pregnancy anxiety, and better maternal care,[26] and, finally, with better perinatal indicators.[27] A favourable socioeconomic maternal profile reduces significantly, or cancels, the adverse effects of advanced maternal age on pregnancy and birth outcomes.[9,10] This socioeconomic bias in maternal profile—strongly associated with the tendency to postpone childbearing—is deepening in Spain as a consequence of the economic crisis [13] and might explain the temporal trends of PAF_p described. Moreover, overall prevalence of SGA (and those of SGA <3rd) percentile rise during the worst years of the economic crisis with a further reduction, perhaps an indication that this increase was due to the impact of the economic crisis on foetal growth through increased maternal stress,[13] more than to the effect of delayed maternity, an hypothesis that requires a more extended time series analysis to be confirmed.

Results might challenge the consideration that the growing number of older primipara mothers represents as a specific obstetric risk group and, consequently, subjected to unnecessary or excessive obstetric interventionism.[28] Our published analyses of data from one of the main maternity hospitals in Spain support the consideration that increasing obstetric interventions mainly on mature primipara mothers might be contributing to the reduction in birthweight though changes in the distribution of gestational age among term newborns,[15] with a significant increase in births born at 37 and 38 weeks, and a decrease in those born at ≥39 weeks, as have been described for other higher-income countries.[29] This consideration might also explain the striking fact that birthweight is decreasing among newborns to Spanish mothers while the prevalence of preterm birth is decreasing.[3]

Limitations of our study include that the analysis carried out was necessarily restricted to those maternal-foetal variables available in the Spanish birth certificate, and data concerning some possible relevant confounding factors in the evaluation of birth outcome—namely

anthropometry and health conditions of the mother, healthy behaviours, and weight gain during pregnancy—were not available. We have published a complementary analysis of the Spanish population using a data set based on hospital records that addresses some of these limitations.[15] Strength of our study is that it is based on a large nationwide data set including all births in Spain from 2007 to 2015. Large-scale population-based data allows evaluating national temporal trends in maternal profile and in obstetric practice that could be having offsetting effects on birth outcome, both prior and during the current economic crisis.

Conclusion

Current demographic and reproductive trends affecting maternal profile and age at childbearing seem to be depth in Spain as in other higher-income countries, reinforced during the current economic crisis. Public health policies should focus on re-assessing the characterization of mature primipara mothers as a risk group with the goals of identifying their specific needs and concerns,[30] and reversing the trend of increasing obstetric intervention over them, especially their extremely high rates of CS deliveries. As Panagopoulous et al. (2006) suggested,[1] advanced maternal age should be considered as a *risk indicator* rather than a *risk factor*.

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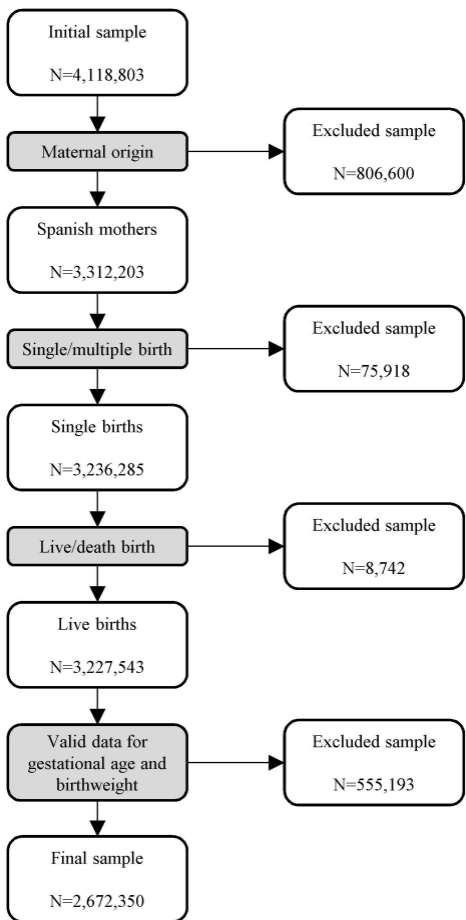
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┌─────────────────────┐
│   Initial sample    │
│   N=4,118,803       │
└─────────────────────┘
          │
┌─────────────────────┐        ┌─────────────────────┐
│   Maternal origin   │───────▶│   Excluded sample   │
└─────────────────────┘        │   N=806,600         │
          │                    └─────────────────────┘
┌─────────────────────┐
│   Spanish mothers   │
│   N=3,312,203       │
└─────────────────────┘
          │
┌─────────────────────┐        ┌─────────────────────┐
│ Single/multiple birth│──────▶│   Excluded sample   │
└─────────────────────┘        │   N=75,918          │
          │                    └─────────────────────┘
┌─────────────────────┐
│   Single births     │
│   N=3,236,285       │
└─────────────────────┘
          │
┌─────────────────────┐        ┌─────────────────────┐
│  Live/death birth   │───────▶│   Excluded sample   │
└─────────────────────┘        │   N=8,742           │
          │                    └─────────────────────┘
┌─────────────────────┐
│    Live births      │
│    N=3,227,543      │
└─────────────────────┘
          │
┌─────────────────────┐        ┌─────────────────────┐
│   Valid data for    │───────▶│   Excluded sample   │
│  gestational age and│        │   N=555,193         │
│    birthweight      │        └─────────────────────┘
└─────────────────────┘
          │
┌─────────────────────┐
│    Final sample     │
│    N=2,672,350      │
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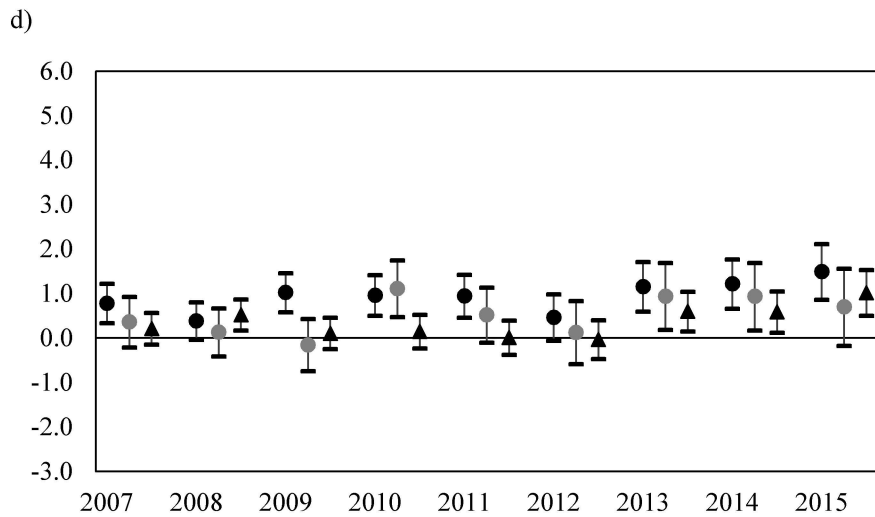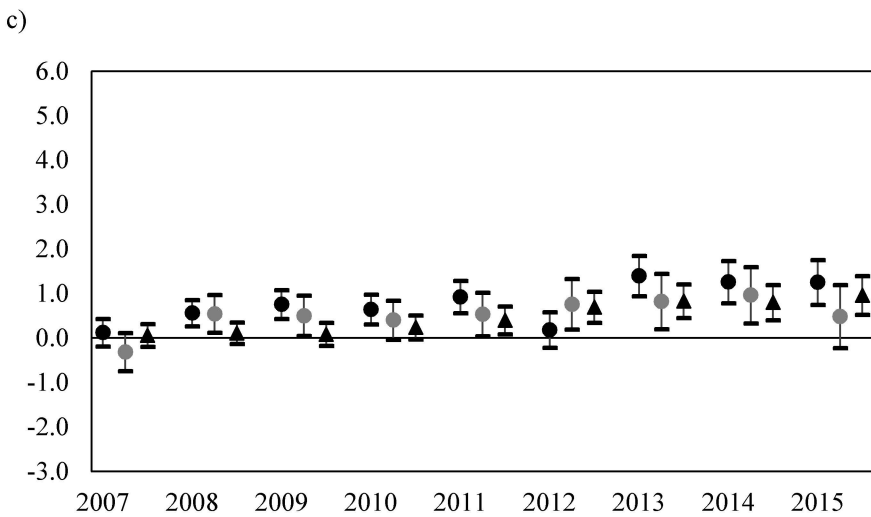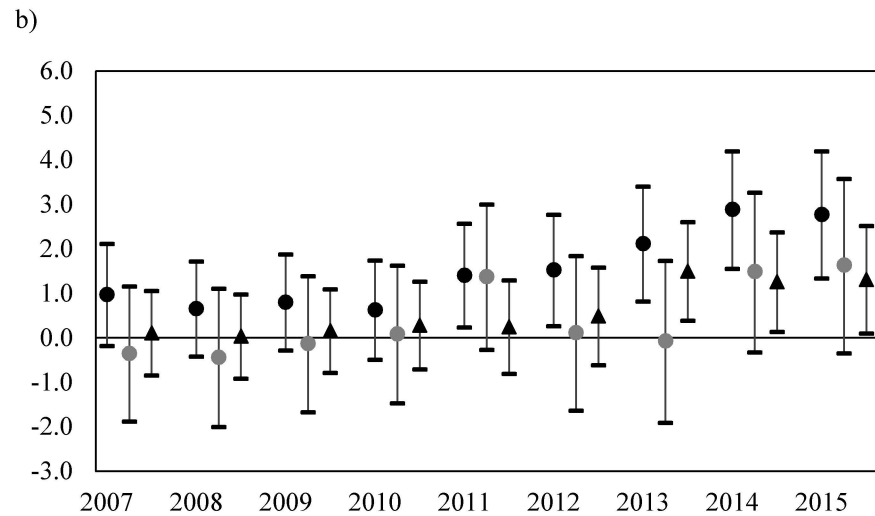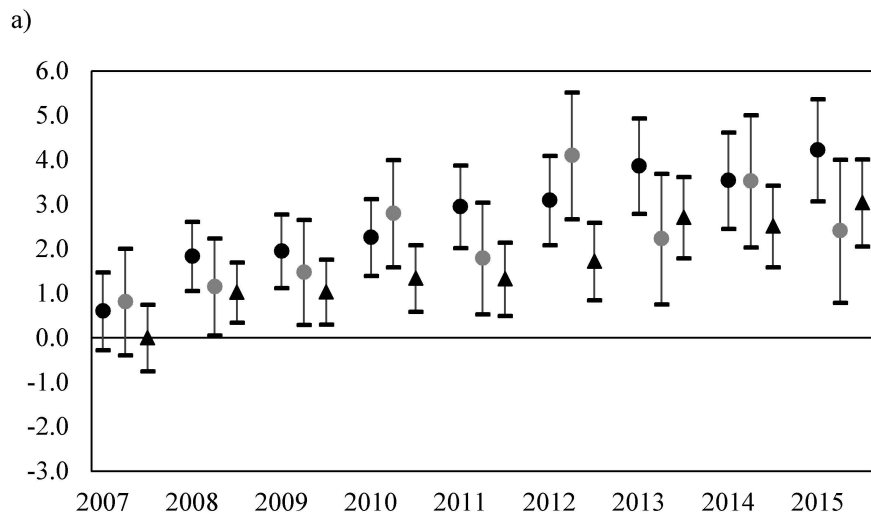
Table S1. Distribution and adjusted relative risk of SGA <3rd, SGA 3rd-5th, and SGA 5th-10th by age and parity (live single births, Spanish mothers, 2007-2015, data from Spanish Birth Statistical Bulletin).

	SGA <3rd		SGA 3rd-5th		SGA 5th-10th	
	n (%)	RR[a] (95% CI)	n (%)	RR[a] (95% CI)	n (%)	RR[a] (95% CI)
Age at maternity						
30-34 years old (reference)	33,284 (36.5)	1.00	18,402 (37.5)	1.00	47,545 (37.8)	1.00
<20 years old	2,618 (2.9)	0.83 (0.79, 0.87)	1,316 (2.7)	0.84 (0.78, 0.90)	3,321 (2.6)	0.94 (0.90, 0.98)
20-24 years old	5,335 (5.8)	0.90 (0.87, 0.93)	2,781 (5.7)	0.89 (0.85, 0.94)	6,628 (5.3)	0.92 (0.89, 0.94)
25-29 years old	15,322 (16.8)	0.94 (0.92, 0.97)	8,248 (16.8)	0.94 (0.91, 0.97)	20,826 (16.6)	0.95 (0.94, 0.97)
35-39 years old	27,520 (30.1)	1.10 (1.08, 1.12)	14,701 (29.9)	1.06 (1.04, 1.09)	38,081 (30.3)	1.05 (1.04, 1.07)
≥40 years old	7,200 (7.9)	1.21 (1.18, 1.24)	3,682 (7.5)	1.12 (1.08, 1.17)	9,264 (7.4)	1.09 (1.06, 1.12)
Parity						
Multipara (reference)	40,568 (44.4)	1.00	21,451 (43.7)	1.00	55,487 (44.2)	1.00
Primipara	50,711 (55.6)	1.08 (1.06, 1.09)	27,679 (56.3)	1.08 (1.06, 1.11)	70,178 (55.8)	1.05 (1.03, 1.06)
Age at maternity and parity						
30-34 years old multipara (reference)	13,378 (14.7)	1.00	7,330 (14.9)	1.00	19,126 (15.2)	1.00
<20 years old primipara	2,258 (2.5)	0.89 (0.84, 0.94)	1,124 (2.3)	0.88 (0.82, 0.96)	2,882 (2.3)	0.98 (0.94, 1.03)
20-24 years old primipara	3,655 (4.0)	0.94 (0.90, 0.98)	1,973 (4.0)	0.94 (0.88,0.99)	4,660 (3.7)	0.93 (0.89, 0.96)
25-29 years old primipara	10,166 (11.1)	0.99 (0.96, 1.02)	5,587 (11.4)	0.98 (0.95, 1.02)	14,225 (11.3)	0.97 (0.89, 0.99)
30-34 years old primipara	19,906 (21.8)	1.10 (1.07, 1.13)	11,072 (22.5)	1.07 (0.95, 1.02)	28,419 (22.6)	1.05 (1.03, 1.07)
35-39 years old primipara	11,938 (13.1)	1.24 (1.21, 1.28)	6,469 (13.2)	1.20 (1.16, 1.24)	16,304 (13.0)	1.14 (1.11, 1.16)
≥40 years old primipara	2,788 (3.1)	1.32 (1.26, 1.38)	1,454 (3.0)	1.21 (1.13, 1.28)	3,688 (2.9)	1.17 (1.13, 1.22)
<20 years old multipara	360 (0.4)	1.03 (0.92, 1.17)	192 (0.4)	1.02 (0.86, 1.22)	439 (0.3)	1.03 (0.92, 1.15)
20-24 years old multipara	1,680 (1.8)	1.05 (0.99, 1.11)	808 (1.6)	0.97 (0.89, 1.05)	1,968 (1.6)	1.02 (0.97, 1.08)
25-29 years old multipara	5,156 (5.6)	1.05 (1.01, 1.08)	2,661 (5.4)	1.02 (0.97, 1.07)	6,601 (5.3)	1.03 (0.99, 1.06)
35-39 years old multipara	15,582 (17.1)	1.09 (1.06, 1.11)	8,232 (16.8)	1.02 (0.99, 1.06)	21,777 (17.3)	1.03 (1.01, 1.05)
≥40 years old multipara	4,412 (4.8)	1.22 (1.18, 1.27)	2,228 (4.5)	1.12 (1.07, 1.18)	5,576 (4.4)	1.08 (1.04, 1.11)

SGA, small for gestational age; RR, relative risk; CI, confidence interval.

[a] Adjusted by maternal occupation, maternal education, marital status, gestational age, type of birth, parity and the interaction term between age at maternity and parity.

Table S2. Adjusted population attributable fraction for SGA <3rd, SGA 3rd-5th, and SGA 5th-10th by age at maternity and parity (live single births, Spanish mothers, 2007-2015, data from Spanish Birth Statistical Bulletin).

Age at maternity 35-39 years old	Primipara			Multipara		
	SGA <3rd PAF^a (95% CI)	SGA 3rd-5th PAF^a (95% CI)	SGA 5th-10th PAF^a (95% CI)	SGA <3rd PAF^a (95% CI)	SGA 3rd-5th PAF^a (95% CI)	SGA 5th-10th PAF^a (95% CI)
2007	0.61 (-0.27, 1.48)	0.89 (-0.39, 2.01)	0.00 (-0.75, 0.75)	0.97 (-0.18, 2.11)	-0.35 (-1.88, 1.16)	0.11 (-0.84, 1.06)
2008	1.84 (1.06, 2.61)	1.15 (0.06, 2.24)	1.02 (0.35, 1.70)	0.66 (-0.42, 1.72)	-0.43 (-2.00, 1.11)	0.04 (-0.91, 0.98)
2009	1.96 (1.13, 2.78)	1.48 (0.29, 2.66)	1.04 (0.30, 1.76)	0.80 (-0.28, 1.88)	-0.13 (-1.67, 1.39)	0.16 (-0.78, 1.10)
2010	2.27 (1.40, 3.13)	2.80 (1.59, 4.00)	1.34 (0.59, 2.09)	0.63 (-0.49, 1.74)	0.09 (-1.47, 1.63)	0.29 (-0.70, 1.27)
2011	2.96 (2.02, 3.88)	1.79 (0.53, 3.04)	1.33 (0.50, 2.15)	1.41 (0.24, 2.57)	1.38 (-0.27, 3.00)	0.25 (-0.80, 1.30)
2012	3.10 (2.09, 4.09)	4.10 (2.67, 5.52)	1.73 (0.85, 2.59)	1.53 (0.27, 2.77)	0.12 (-1.64, 1.84)	0.49 (-0.61, 1.58)
2013	3.87 (2.80, 4.94)	2.23 (0.75, 3.69)	2.71 (1.79, 3.62)	2.12 (0.82, 3.41)	-0.07 (-1.91, 1.74)	1.50 (0.39, 2.61)
2014	3.54 (2.45, 4.62)	3.53 (2.04, 5.01)	2.51 (1.59, 3.43)	2.89 (1.56, 4.20)	1.49 (-0.32, 3.27)	1.26 (0.14, 2.38)
2015	4.23 (3.08, 5.37)	2.41 (0.79, 4.01)	3.04 (2.06, 4.02)	2.78 (1.34, 4.20)	1.64 (-0.35, 3.58)	1.32 (0.10, 2.52)
Age at maternity ≥40 years old	Primipara			Multipara		
	SGA <3rd PAF^a (95% CI)	SGA 3rd-5th PAF^a (95% CI)	SGA 5th-10th PAF^a (95% CI)	SGA <3rd PAF^a (95% CI)	SGA 3rd-5th PAF^a (95% CI)	SGA 5th-10th PAF^a (95% CI)
2007	0.13 (-0.18, 0.43)	-031 (-0.74, 0.11)	0.06 (-0.19, 0.32)	0.79 (0.34, 1.23)	0.36 (-0.21, 0.93)	0.22 (-0.14, 0.57)
2008	0.57 (0.27, 0.86)	0.55 (0.12, 0.97)	0.12 (-0.13, 0.36)	0.39 (-0.03, 0.81)	0.13 (-0.41, 0.67)	0.53 (0.18, 0.87)
2009	0.76 (0.44, 1.09)	0.51 (0.05, 0.96)	0.09 (-0.17, 0.35)	1.03 (0.58, 1.46)	-0.15 (-0.74, 0.43)	0.11 (-0.25, 0.46)
2010	0.65 (0.31, 0.98)	0.41 (-0.03, 0.84)	0.24 (-0.03, 0.51)	0.97 (0.51, 1.42)	1.12 (0.48, 1.75)	0.15 (-0.23, 0.53)
2011	0.93 (0.56, 1.29)	0.54 (0.05, 1.03)	0.40 (0.09, 0.72)	0.95 (0.46, 1.43)	0.53 (-0.10, 1.14)	0.02 (-0.37, 0.40)
2012	0.19 (-0.21, 0.58)	0.76 (0.19, 1.33)	0.70 (0.35, 1.04)	0.47 (-0.06, 0.99)	0.13 (-0.58, 0.84)	-0.03 (-0.47, 0.41)
2013	1.40 (0.95, 1.85)	0.83 (0.20, 1.45)	0.84 (0.46, 1.21)	1.16 (0.60, 1.71)	0.94 (0.19, 1.69)	0.60 (0.15, 1.05)
2014	1.27 (0.79, 1.74)	0.97 (0.33, 1.60)	0.80 (0.40, 1.20)	1.22 (0.66, 1.77)	0.94 (0.18, 1.69)	0.59 (0.12, 1.06)
2015	1.26 (0.75, 1.76)	0.49 (-0.22, 1.20)	0.97 (0.53, 1.40)	1.50 (0.87, 2.12)	0.70 (-0.17, 1.56)	1.02 (0.50, 1.54)

SGA, small for gestational age; PAF, population attributable fraction; CI, confidence interval.

[a] Adjusted by maternal occupation, maternal education, marital status, gestational age, type of birth, parity and the interaction term between age at maternity and parity.

Table 1. Temporal trends in maternal-foetal variables (live single births, Spanish mothers, selected years 2007, 2010, 2015, data from Spanish Birth Statistical Bulletin).

	2007 n (%)	2010 n (%)	2015 n (%)	Chi-sq. test p-value
Distribution	308,877 (34.5)	305,927 (34.2)	279,234 (31.2)	
Age at maternity				
<20 years old	5,479 (1.8)	4,627 (1.5)	3,654 (1.3)	
20-24 years old	19,427 (6.3)	17,871 (5.8)	14,239 (5.1)	
25-29 years old	59,697 (19.3)	49,742 (16.3)	40,106 (14.4)	
30-34 years old	128,635 (41.6)	122,799 (40.1)	98,167 (35.2)	<0.001
35-39 years old	79,972 (25.9)	91,442 (29.9)	95,788 (34.3)	
≥40 years old	15,667 (5.1)	19,446 (6.4)	27,280 (9.8)	
Maternal occupation				
Professionals	68,476 (25.6)	89,020 (29.8)	85,786 (34.0)	
Administrative employees	64,245 (24.1)	72,346 (24.2)	52,835 (20.9)	
Service sector workers	48,291 (18.1)	54,077 (18.1)	49,890 (19.8)	
Primary sector workers	3,092 (1.2)	3,075 (1.0)	2,602 (1.0)	
Qualified workers	8,968 (3.4)	9,021 (3.0)	6,292 (2.5)	<0.001
Unskilled workers	13,589 (5.1)	16,440 (5.5)	12,303 (4.9)	
Students	2,808 (1.1)	3,702 (1.2)	4,163 (1.6)	
Housewives	57,589 (21.6)	51,283 (17.2)	38,627 (15.3)	
Maternal education				
University education	100,035 (34.2)	117,296 (39.1)	104,500 (41.4)	
Secondary education	165,088 (56.4)	155,830 (51.9)	124,080 (49.2)	<0.001
Primary education	27,398 (9.4)	27,039 (9.0)	23,625 (9.4)	
Marital status				
Married	221,512 (75.7)	199,433 (69.9)	150,350 (61.6)	
Unmarried with a stable partner	48,881 (16.7)	51,027 (17.9)	49,915 (20.5)	<0.001
Unmarried with non-stable partner	22,389 (7.6)	35,052 (12.3)	43,637 (17.9)	
Residence				
Rural	250,849 (18.8)	249,497 (18.4)	50,043 (17.9)	<0.001
Sex of newborn				
Male	159,577 (51.7)	157,736 (51.6)	143,732 (51.5)	n.s.
Parity				
Primipara	182,521 (59.1)	167,587 (54.8)	149,634 (53.6)	<0.001
Type of birth				
CS delivery	74,182 (25.4)	78,909 (25.8)	70,132 (25.1)	<0.001
Gestational age				
Preterm birth	18,726 (6.1)	17,670 (5.8)	15,209 (5.4)	<0.001
Weight for gestational age				
SGA (<10th)	28,751 (9,8)	31,162 (10.3)	27,863 (10,0)	<0.001
SGA (<3rd)	9,647 (3.3)	10,899 (3.6)	9,162 (3.3)	<0.001
SGA (3rd-5th)	5,452 (1.9)	5,712 (1.9)	5,231 (1.9)	n.s.
SGA (5th-10th)	13,652 (4.7)	14,551 (4.8)	13,470 (4.8)	<0.050

Chi-sq. test, chi-square test; CS delivery, caesarean section delivery; LBW, low birthweight; SGA, small for gestational age; n.s., not significant.

Table 2. Maternal and foetal characteristics by age at maternity (live single births, Spanish mothers, 2007-2015, data from Spanish Birth Statistical Bulletin).

	<20 years old n (%)	20-24 years old n (%)	25-29 years old n (%)	30-34 years old n (%)	35-39 years old n (%)	≥40 years old n (%)	Chi-sq. test p-value
Distribution	39,958 (1.5)	151,274 (5.7)	432,254 (16.2)	1,040,304 (38.9)	818,125 (30.6)	190,435 (7.1)	
Maternal occupation							
Professionals	1,245 (3.4)	8,203 (5.8)	72,745 (17.9)	327,391 (32.9)	296,623 (37.7)	69,146 (37.8)	
Administrative employees	1,199 (3.3)	10,457 (7.4)	74,995 (18.4)	250,198 (25.2)	210,172 (26.7)	46,118 (25.2)	
Service sector workers	2,624 (7.1)	31,741 (22.6)	109,296 (26.8)	184,338 (18.5)	116,093 (14.8)	24,864 (13.6)	
Primary sector workers	326 (0.9)	2,451 (1.7)	6,165 (1.5)	9,733 (1.0)	6,426 (0.8)	1,555 (0.9)	<0.001
Qualified workers	331 (0.9)	3,120 (2.2)	14,885 (3.7)	33,122 (3.3)	22,760 (2.9)	4,847 (2.7)	
Unskilled workers	2,279 (6.2)	12,524 (8.9)	29,198 (7.2)	47,073 (4.7)	32,895 (4.2)	8,544 (4.7)	
Students	9,424 (25.6)	10,787 (7.7)	6,889 (1.7)	6,084 (0.6)	109 (0.0)	14 (0.0)	
Housewives	19,410 (52.7)	61,156 (43.5)	93,004 (22.8)	135,881 (13.7)	101,181 (12.9)	27,669 (15.9)	
Maternal education							
University education	205 (0.6)	3,575 (2.5)	77,617 (18.7)	430,002 (42.9)	403,782 (51.5)	89,205 (49.6)	
Secondary education	10,975 (30.4)	76,256 (53.8)	277,359 (66.9)	526,776 (52.5)	352,141 (44.9)	81,406 (45.2)	<0.001
Primary education	24,884 (69.0)	61,980 (43.7)	59,906 (14.4)	45,698 (4.6)	28,561 (3.6)	9,414 (5.2)	
Marital status							
Married	1,867 (5.7)	26,131 (20.6)	225,933 (58.3)	731,606 (75.3)	579,078 (75.7)	120,153 (68.6)	
Unmarried with a stable partner	15,496 (47.3)	54,553 (43.1)	94,236 (24.3)	143,988 (14.8)	113,230 (14.8)	33,296 (19.0)	<0.001
Unmarried with non-stable partner	15,379 (47.0)	45,979 (36.3)	67,563 (17.4)	95,817 (9.9)	72,875 (9.5)	21,683 (12.4)	
Residence							
Rural	5,607 (14.0)	25,853 (17.1)	90,129 (20.9)	199,844 (19.2)	136,656 (16.7)	29,380 (15.4)	<0.001
Sex of newborn							
Male	20,762 (52.0)	78,356 (51.8)	223,216 (51.6)	537,515 (51.7)	421,472 (51.5)	97,236 (51.1)	<0.001
Parity							
Primipara	36,311 (90.9)	112,232 (74.2)	304,822 (70.5)	618,698 (59.5)	333,201 (40.7)	72,197 (37.9)	<0.001
Type of birth							
CS delivery	5,607 (14.1)	25,735 (17.1)	89,203 (20.8)	235,045 (22.7)	209,852 (25.8)	64,089 (33.8)	<0.001
Gestational age							
Preterm birth	3,653 (9.1)	10,138 (6.7)	24,023 (5.6)	54,200 (5.2)	46,755 (5.7)	13,586 (7.1)	<0.001
Weight for gestational age							
SGA (<10th)	4,617 (11.7)	17,382 (11.6)	44,396 (10.4)	99,231 (9.6)	80,302 (9.9)	20,146 (10.6)	<0.001
SGA (<3rd)	1,689 (4.3)	6,264 (4.2)	15,322 (3.6)	33,284 (3.2)	27,520 (3.4)	7,200 (3.8)	<0.001
SGA (3rd-5th)	820 (2.1)	3,277 (2.2)	8,248 (1.9)	18,402 (1.8)	14,701 (1.8)	3,682 (1.9)	<0.001
SGA (5th-10th)	2,108 (5.3)	7,841 (5.2)	20,826 (4.9)	47,545 (4.6)	38,081 (4.7)	9,264 (4.9)	<0.001

Chi-sq. test, chi-square test; CS delivery, caesarean section delivery; LBW, low birthweight; SGA, small for gestational age.