BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email editorial.bmjopen@bmj.com

BMJ Open

Are risk factors for preterm and early term birth the same? A population-based study in France

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-018745
Article Type:	Research
Date Submitted by the Author:	26-Jul-2017
Complete List of Authors:	Delnord, M; INSERM, UMR1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité, 53 avenue de l'Observatoire Blondel, Béatrice; INSERM, UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité Prunet, Caroline; INSERM, UMR1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité, 53 avenue de l'Observatoire Zeitlin, Jennifer; INSERM, UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité; Paris-Descartes University,
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Obstetrics and gynaecology, Paediatrics, Public health
Keywords:	early term birth, preterm birth, Population prevention, Perinatal Health Survey, population risk factors

SCHOLARONE™
Manuscripts

Are risk factors for preterm and early term birth the same? A population-based study in France

Marie DELNORD[1]*MSc, MA; Béatrice BLONDEL[1], PhD; Caroline Prunet, MSc ; Jennifer ZEITLIN[1], DSc
*INSERM U1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, Research Center for Epidemiology and Biostatistics Sorbonne Paris Cité (CRESS)

Affiliations:

1. Inserm UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team (Epopé), Centre for Epidemiology and Statistics Sorbonne Paris Cité, DHU Risks in pregnancy, Paris Descartes University, Paris, France

***Corresponding author**:
Ms. Marie Delnord
INSERM U1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, Research Center for Epidemiology and Biostatistics Sorbonne Paris Cité (CRESS)
Maternité de Port Royal, 53 Avenue de l' Observatoire, 75014 Paris FRANCE
Tel : +33 1 42 34 55 86
Fax: +33 1 43 26 89 79
Marie.delnord@inserm.fr

Word count:
Abstract: 213/300 words

Main text: 2603/4000 words

Abstract

Objectives: To investigate whether risk factors for preterm (<37 weeks gestation) and early term birth (37 and 38 weeks gestation) are similar.

Design: Nationally representative cross-sectional study of births

Setting: France in 2010

Participants: Live singleton births (N=14 326)

Primary and secondary outcome measures: Preterm and early term birth rates overall and by mode of delivery (spontaneous and indicated). Risk factors were maternal sociodemographic characteristics, previous preterm birth, height, pre-pregnancy body mass index (BMI) and smoking, assessed using multinomial regression models with full term births 39 weeks and over as the reference group.

Results: There were 5.5% preterm and 22.5% early term births. Common risk factors were: a previous preterm delivery (adjusted odds ratio aOR=8.2 [95% CI: 6.2-10.7] and aOR=2.4 [95% CI: 2.0-3.0] respectively), short stature, an extreme BMI, a low educational level, and Sub Saharan African origin. In contrast, primiparity was a risk factor only for preterm birth, aOR=1.8 [95% CI: 1.5-2.2], while higher parity was associated with greater odds of early term birth.

Conclusions: Most population-level risk factors were common to both preterm and early term birth, with the exception of primiparity, and BMI which differed by mode of onset of delivery. Our results suggest that preterm and early term birth share similar etiologies and thus potentially common strategies for prevention.

<u>Strengths and limitations of this study:</u>

- We had detailed information on prenatal social and demographic characteristics collected using a standardized maternal interview in a representative sample of births in France.
- We had few missing data for which we corrected using multiple imputation.
- We used multinomial regression to estimate preterm and early term birth adjusted odds ratios and their 95% confidence intervals by maternal characteristics using births reaching full term (i.e. births 39 weeks and over) as the reference.
- Because very preterm births represented 0.6% of births in our sample, we do not report associations by preterm GA subgroups.
- Our sample size may have been too small to detect low to moderate associations in less prevalent sub groups of women, such as heavy smokers, for instance.

Funding:

This work was supported by Paris Descartes University, Paris, France.

The French National Perinatal Survey 2010 was funded by the French Ministry of Health.

The funding agencies were not involved in the study.

Competing interests: No competing interests

Introduction

Preterm birth, defined as birth before 37 weeks of gestation, is a leading cause of perinatal mortality and morbidity. Preterm infants represent 60% of all neonatal deaths and 75% of all infant deaths (1). They are at risk of short and long-term neurocognitive and motor impairments, and display higher rates of chronic disease and premature death compared to term infants (1, 2). The prevention of preterm birth is a global priority, however preterm births are not the only gestational age subgroup at risk of adverse health outcomes (1, 2). Compared to being born full term, defined as between 39 and 41 weeks, early term birth at 37 and 38 weeks is associated with higher risks of neonatal mortality, more intensive care unit admissions (3), and higher health-related costs well into childhood for obstructive airway diseases, visual and motor disabilities (4).

There are large differences in rates and trends of preterm and early term births among countries with similar levels of development (5-7). In Europe in 2010, preterm birth rates ranged between 4.1% and 8.2% while early term rates ranged between 15.6% and 30.8% (5); such heterogeneity across countries suggests that rate reductions may be possible. However, despite the significant public health burden (4, 8-10), little progress has been made in decreasing the number of these early births (6, 11, 12). The latest French recommendations for the prevention of spontaneous preterm birth focus on smoking cessation and on interventions for women with high risk pregnancies (i.e. cerclage, progesterone), but conclude that high quality evidence does not exist for other preventive strategies (13); this is partially due to the low predictive accuracy of diagnostic tools (11). As for early term birth, prevention efforts are recent, with a focus by professional societies in the United States on the reduction of indicated early term deliveries for non-medical reasons (14).

More research on the etiology of early delivery is required to orient prevention efforts and practice. We know that early term and late preterm births both have worse neonatal outcomes compared to full term births (15), but we do not know if maternal characteristics related to preterm birth risk (1, 11, 16, 17) are also related to early term birth. Thus in this study we aimed to identify population determinants of preterm and early term birth taking into consideration mode of onset of delivery, i.e. spontaneous or indicated, using nationally representative data on births from the French National Perinatal Survey in 2010.

Materials and Methods

The French National Perinatal Survey 2010 (*Enquête Nationale Périnatale*, ENP) is a study based on a representative sample of births in Metropolitan France. Data were collected on live and stillbirths starting at 22 weeks of gestation or weighing at least 500g over the course of one week in public and private maternity units (18). We studied singleton pregnancies ending in a live birth with a gestational age of 22 weeks or over (N=14,326 pregnant women in 2010). Multifetal pregnancies and stillbirths were excluded because of differences in delivery practices and etiology for these births.

Survey items on mothers' demographic characteristics (e.g. maternal age, parity), socioeconomic status (e.g. level of education), prenatal care and behaviors were collected during interviews in the postpartum ward. Other data on the delivery and newborn health were abstracted from the medical records. We defined indicated deliveries as those with a provider-initiated mode of onset, i.e. either induction of labor or prelabor cesarean section.

Our main outcomes were preterm and early term birth. These were defined respectively as births 22-36 completed weeks of gestation and 37-38 completed weeks overall and by mode of onset (spontaneous or indicated). Gestational age was based on the best obstetrical estimate. In France, nearly all women have a first trimester ultrasound for dating the pregnancy (18).

We selected risk factors based on a scoping review of the scientific literature, including recent research on preterm birth risk factors in France (17, 19). Some preterm birth exposures that were available in the French National Perinatal Survey were omitted from our study because of their low prevalence in the sample (i.e. use of fertility treatments and diabetes, <4% and <2% respectively).

We included the following variables in our analysis: maternal age (<20, 20-24, 25-29, 30-34, >=35 years old), parity (1,2-3,4+), previous preterm birth, nationality (French, Other European, North African, Sub-Saharan African, Other), maternal height presented in quartiles (Q1: 100-160cm, Q2: 161-165cm, Q3: 166-168cm, Q4:169-190cm), pre-pregnancy body mass index (defined as underweight, normal, overweight, and obese women for BMIs <18.5, 18.5-24.9, 25-29.9,≥30 respectively), level of education, and smoking during the third trimester. Level of completed education was defined based on the ISCED 2011 classification: low educational level ISCED 0-2 (i.e. up to lower secondary education completed), medium educational level ISCED 3-5 (i.e. upper secondary education or short cycle tertiary education completed), high educational level ISCED 6-7 (Bachelors' equivalent or higher) (20).

Analysis strategy

We first compared the distributions of preterm and early term births by maternal characteristics. We included all maternal exposures hypothesized to be associated with preterm delivery in the multivariate analyses (17). We used multinomial regression to estimate preterm and early term birth adjusted odds ratios and their 95% confidence intervals by maternal characteristics using births reaching full term (i.e. births 39 weeks and over) as the reference. In the mode of onset analyses, we computed odds of spontaneous and indicated preterm and early delivery using the same full term reference population (i.e. all births 39 weeks and over, regardless of mode of onset). Data were analysed using STATA 13.0 software (StataCorp LP, College Station, TX, USA).

There were 14 326 live singleton births in the survey of which 65 were missing GA data. We had less than 1% missing data on mode of onset of labor (i.e. spontaneous or provider-initiated delivery) and less than 5% missing sociodemographic data (i.e. nationality and level of education). There were 4% missing data on previous preterm birth and 6% missing on anthropometric characteristics (i.e. height or BMI). Although individual proportions of missing data were low, complete cases were only 86% of the total and therefore we imputed missing values (except the outcome) using multivariate imputation by chained equations. We performed 100 imputations using all available covariates (21). Descriptive and multivariate analyses were done on the imputed dataset.

Results

Table 1 provides descriptive statistics on our sample. We included 14 261 live singleton pregnancies with GA data available. The overall rate of preterm birth was 5.5% and early term birth was 22.6%. In the reference population of women with a full term birth, 2.4% were aged under 20 and 18.3% over 35 years of age; 44.1% were primiparous and 6.9% were parity 4 or more; 2.2% had a previous preterm birth, 7.8% were underweight, 9.4% were overweight and 16.4% smoked in the 3rd trimester of pregnancy. The risk profiles of mothers with a preterm and early term infant were different. These mothers were more likely to be older, have a previous preterm birth, be of shorter stature, with a lower level of education, and smoke. Mothers with a preterm birth were more likely to be primipara whereas mothers with an early term birth were more likely to be multipara, compared to mothers with a term birth.

In multinomial multivariable models, most of these associations persisted; common population determinants for preterm and early term birth were: a previous preterm birth, shorter stature, underweight, sub-Saharan nationality, and a low level of education. There were some differences in the impact of these risk factors: a previous preterm birth was a stronger risk factor for preterm birth than early term birth (aOR 8.2 vs. 2.4 respectively); maternal underweight and Sub-Saharan nationality were also stronger risk factors for preterm compared to early term birth. Primipara were at risk for preterm birth only (aOR 1.8 [1.5-

2.2]), whereas grand multipara (parity 4+) were at higher risk of early term birth. After adjustment, advanced maternal age, and smoking during the third trimester were no longer associated with increased risks of delivery before 39 weeks.

In Table 2, we display the associations between spontaneous preterm, and early term births by maternal characteristics. Out of all births, 2.8% were spontaneous preterm births and 13.6% were spontaneous early term births. Common risk factors were: a previous preterm birth, short stature, maternal underweight, foreign nationality (i.e. Other European), and a low level of education. There were some differences in the impact of these risk factors. Underweight was a stronger risk factor for spontaneous preterm than early term birth: aOR 1.9[1.4-2.6] vs aOR 1.3[1.1-1.5] respectively, and overweight women displayed a reduced risk of spontaneous early term delivery. Primipara were at risk of preterm birth but not early term birth. Smoking during the third trimester was associated with a moderately increased risk of spontaneous preterm delivery, although the confidence interval included 1: aOR 1.5[1.0-2.2]. The aOR was lower and non-significant for early term birth: 1.2[0.9-1.5].

In Table 3, we display the associations between indicated preterm and early term birth by maternal characteristics. Out of all births, 2.6% were indicated preterm deliveries and 8.8% were indicated early term deliveries. Most risk factors were common to indicated preterm and early term birth including: advanced maternal age, a previous preterm birth, short stature, BMI over 30, sub-Saharan African origin (aOR 2.2[1.4-3.5] preterm, and aOR 1.6[1.2-2.2] for early term), and a low level of education, after adjusting on all other covariates. Primipara were only at risk for indicated preterm birth, aOR=2.1[1.6-2.7]; while parity 4+ was associated with greater odds of indicated early term birth aOR= 1.3 [1.1-1.6].

Discussion

Our study provides new insight into the population determinants of preterm and early term birth by mode of onset of delivery. We identified shared risk factors for delivery before 39 weeks which were: a previous preterm birth, short stature, a low level of education, underweight (overall and in spontaneous deliveries), obesity (in indicated deliveries only), and foreign origin (for other European and sub-Saharan nationals). The impact of most risk factors was greater for preterm birth compared to early term birth, and primiparity was a risk factor for preterm birth but not early term birth.

A strength of our study is the availability of detailed information on prenatal, social and demographic characteristics collected using a standardized maternal interview in a representative sample of births in France. We had few missing data for which we corrected using multiple imputation. Nonetheless, there were some limitations. Our sample size may have been too small to detect low to moderate associations in less prevalent subgroups of women, such as heavy smokers, for instance. We also did not correct for multiple comparisons in order to maintain adequate power to carry out the study (22). Because very preterm births (births <32 weeks: n=83) represented 0.6% of births in our sample, we did not report associations by preterm GA subgroups. It is possible that risk factors for this vulnerable subpopulation may differ from those for moderate and late preterm births at 32-36 weeks of gestation. Finally, we did not have data on the complications of pregnancy associated with earlier delivery (23).

The strongest single predictor of both preterm and early term delivery was a previous preterm birth, as confirmed in other population-based studies (24, 25) and a recent systematic review which showed a 30% risk of recurrent spontaneous preterm birth (sPTB) following sPTB in singleton pregnancies (26) . We also found that first-time mothers were more likely to deliver preterm, but not early term. Therefore, the shape of the risk distribution for early delivery in first-time mothers may slightly differ from the overall GA distribution which peaks around 38-40 weeks of gestation. These results indicate that within countries, fertility trends determining the proportion of primiparous women are likely to contribute to preterm and early term birth rates.

Socio-demographic characteristics were also associated with earlier delivery. Women with a lower level of education were more likely to deliver preterm and early term, confirming well known associations on education and preterm birth risk, and recent findings from Canada on the association with early term birth (27-29). Exposures related to mothers' general quality of life and well-being (i.e. living and employment conditions, air pollution, exposure to stress) could mediate the association with social status via physiological pathways (30-34). In France, Prunet et al. showed that social status was associated with preterm birth risk independently of use of medical care during pregnancy (17). As for the association with foreign origin, our results are consistent with the literature showing higher risks of preterm birth among women from Sub-Saharan Africa (35).

There were common anthropometric determinants of delivery before 39 weeks overall and by mode of onset of delivery. Our findings confirm previous research on the association between preterm birth and short stature (36, 37) and we provide new evidence on the association with early term birth. With respect to maternal pre-pregnancy weight, thinness is often associated with spontaneous preterm birth but the association between GA and overweight is less clear (38-40). A greater prevalence of comorbities in obese women could contribute to the excess in indicated delivery (41), which we observed. We also found a decreased risk of spontaneous preterm and early term delivery in women with BMIs over 30 which could be due to specific delivery practices, and greater levels of obstetrical interventions for obese women in general(42).

Finally, smoking and advanced maternal age are traditionally cited as preterm birth risk factors (43, 44); while there was an increased risk for spontaneous preterm birth in heavy smokers and an increased risk for indicated preterm and early term delivery in mothers over 35, we did not identify associations with either variable in the overall analyses. Previous data from France, also showed a limited impact of smoking on overall preterm birth risk whereas associations were stronger in studies from other countries (18, 19).

Our findings showing common risk patterns for preterm and early term births suggest a shared etiology for these births overall, with some exceptions for primiparous women and by mode of onset of delivery. These results are consistent with two reports documenting shared pregnancy complications for spontaneous preterm and early term deliveries (22), but a more heterogeneous etiology for medically indicated late preterm and early term delivery (i.e. chronic medical conditions like anemia and gastrointestinal disease were associated with late preterm but not early term delivery) (45). Future research associating maternal exposures with pregnancy complications such as: diabetes mellitus, infection and inflammation, placental ischemia, polyhydramnios and oligohydramnios, which are related to spontaneous and indicated preterm and early term births could provide insight into the mechanisms underpinning early delivery (23).

In conclusion, our population-based study showed that there are shared maternal prenatal and socio-demographic risk factors for delivery before full term (i.e. 39 weeks and over). Because strategies to reduce individual risk of preterm birth have had a limited impact on global rate reductions (11), investing in broader population-based interventions may be justified, including those targeting maternal pre-pregnancy BMI and social inequalities in health (41). Moreover, due to the large volume of births at 37-38 weeks, even small point percentage reductions are likely to impact on health and needs for educational and social services. Each additional week of gestation after 35 weeks reduces specific delays in communication, personal-social, fine-motor, and problem-solving skills up until 24 months of age, and the population attributable fraction for poor achievement in school is highest among early term births (46, 47). The existence of shared risk factors for both gestational age subgroups and the greater number of early term births compared to preterm births provides greater power to investigate the mechanisms leading to early delivery, and supports the use of a broader research paradigm for preterm birth prevention.

Contributions: MD, BB and JZ contributed to the study design, and interpretation of the data. MD, BB, and CP participated in the data collection and analysis. MD and JZ drafted the manuscript, BB provided critical revisions. All authors have read and approved the final version of the manuscript.

Data sharing statement: Instructions for applying for public access data from the French National Perinatal Survey are available upon request from the authors.

References

1. Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller AB, et al. Born too soon: the global epidemiology of 15 million preterm births. Reproductive health. 2013;10 Suppl 1:S2.
2. Zhang X, Kramer MS. Variations in mortality and morbidity by gestational age among infants born at term. The Journal of pediatrics. 2009;154(3):358-62, 62 e1.
3. Sengupta S, Carrion V, Shelton J, Wynn RJ, Ryan RM, Singhal K, et al. Adverse neonatal outcomes associated with early-term birth. JAMA pediatrics. 2013;167(11):1053-9.
4. Helle E, Andersson S, Hakkinen U, Jarvelin J, Eskelinen J, Kajantie E. Morbidity and Health Care Costs After Early Term Birth. Paediatric and perinatal epidemiology. 2016;30(6):533-40.
5. Euro-Peristat project with SCPE and EUROCAT, European Perinatal Health Report. The health and care of pregnant women and babies in Europe in 2010. 2013 May 2013. Report No.
6. Richards JL, Kramer MS, Deb-Rinker P, Rouleau J, Mortensen L, Gissler M, et al. Temporal Trends in Late Preterm and Early Term Birth Rates in 6 High-Income Countries in North America and Europe and Association With Clinician-Initiated Obstetric Interventions. Jama. 2016;316(4):410-9.
7. Zeitlin J, Szamotulska K, Drewniak N, Mohangoo AD, Chalmers J, Sakkeus L, et al. Preterm birth time trends in Europe: a study of 19 countries. BJOG : an international journal of obstetrics and gynaecology. 2013;120(11):1356-65.
8. Jacob J, Lehne M, Mischker A, Klinger N, Zickermann C, Walker J. Cost effects of preterm birth: a comparison of health care costs associated with early preterm, late preterm, and full-term birth in the first 3 years after birth. The European journal of health economics : HEPAC : health economics in prevention and care. 2016.
9. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. Lancet. 2008;371(9608):261-9.
10. Crump C, Sundquist K, Winkleby MA, Sundquist J. Early-term birth (37-38 weeks) and mortality in young adulthood. Epidemiology. 2013;24(2):270-6.
11. Chang HH, Larson J, Blencowe H, Spong CY, Howson CP, Cairns-Smith S, et al. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. Lancet. 2013;381(9862):223-34.

12. Lawn JE, Kinney MV, Belizan JM, Mason EM, McDougall L, Larson J, et al. Born too soon: accelerating actions for prevention and care of 15 million newborns born too soon. Reproductive health. 2013;10 Suppl 1:S6.
13. Sentilhes L, Senat MV, Ancel PY, Azria E, Benoist G, Blanc J, et al. Prevention of spontaneous preterm birth: Guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). European journal of obstetrics, gynecology, and reproductive biology. 2017;210:217-24.
14. ACOG Committee Opinion No 579: Definition of term pregnancy. Obstetrics and gynecology. 2013;122(5):1139-40.
15. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Neonatal morbidity associated with late preterm and early term birth: the roles of gestational age and biological determinants of preterm birth. International journal of epidemiology. 2014;43(3):802-14.
16. Delnord M, Blondel B, Zeitlin J. What contributes to disparities in the preterm birth rate in European countries? Current opinion in obstetrics & gynecology. 2015;27(2):133-42.
17. Prunet C, Delnord M, Saurel-Cubizolles MJ, Goffinet F, Blondel B. Risk factors of preterm birth in France in 2010 and changes since 1995: Results from the French National Perinatal Surveys. Journal de gynecologie, obstetrique et biologie de la reproduction. 2016.
18. Blondel B, Lelong N, Kermarrec M, Goffinet F, National Coordination Group of the National Perinatal S. Trends in perinatal health in France from 1995 to 2010. Results from the French National Perinatal Surveys. Journal de gynecologie, obstetrique et biologie de la reproduction. 2012;41(4):e1-e15.
19. Prunet C, Delnord M, Saurel-Cubizolles MJ, Goffinet F, Blondel B. Risk factors of preterm birth in France in 2010 and changes since 1995: Results from the French National Perinatal Surveys. Journal of gynecology obstetrics and human reproduction. 2017;46(1):19-28.
20. Statistics OEUIf. ISCED 2011 Operational Manual: OECD Publishing.
21. Graham JW, Olchowski AE, Gilreath TD. How many imputations are really needed? Some practical clarifications of multiple imputation theory. Prevention science : the official journal of the Society for Prevention Research. 2007;8(3):206-13.
22. Feise RJ. Do multiple outcome measures require p-value adjustment? BMC medical research methodology. 2002;2:8.
23. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Biological determinants of spontaneous late preterm and early term birth: a retrospective cohort study. BJOG : an international journal of obstetrics and gynaecology. 2015;122(4):491-9.
24. Yang J, Baer RJ, Berghella V, Chambers C, Chung P, Coker T, et al. Recurrence of Preterm Birth and Early Term Birth. Obstetrics and gynecology. 2016;128(2):364-72.
25. Ferrero DM, Larson J, Jacobsson B, Di Renzo GC, Norman JE, Martin JN, Jr., et al. Cross-Country Individual Participant Analysis of 4.1 Million Singleton Births in 5 Countries with Very High Human Development Index Confirms Known Associations but Provides No Biologic Explanation for 2/3 of All Preterm Births. PloS one. 2016;11(9):e0162506.
26. Phillips C, Velji Z, Hanly C, Metcalfe A. Risk of recurrent spontaneous preterm birth: a systematic review and meta-analysis. BMJ open. 2017;7(6):e015402.
27. Auger N, Leduc L, Naimi AI, Fraser WD. Delivery at Term: Impact of University Education by Week of Gestation. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC. 2016;38(2):118-24.
28. Oftedal AM, Busterud K, Irgens LM, Haug K, Rasmussen S. Socio-economic risk factors for preterm birth in Norway 1999-2009. Scandinavian journal of public health. 2016;44(6):587-92.
29. Poulsen G, Strandberg-Larsen K, Mortensen L, Barros H, Cordier S, Correia S, et al. Exploring educational disparities in risk of preterm delivery: a comparative study of 12 European birth cohorts. Paediatric and perinatal epidemiology. 2015;29(3):172-83.
30. Stieb DM, Chen L, Eshoul M, Judek S. Ambient air pollution, birth weight and preterm birth: a systematic review and meta-analysis. Environmental research. 2012;117:100-11.

31. Staneva A, Bogossian F, Pritchard M, Wittkowski A. The effects of maternal depression, anxiety, and perceived stress during pregnancy on preterm birth: A systematic review. Women and birth : journal of the Australian College of Midwives. 2015;28(3):179-93.
32. Ncube CN, Enquobahrie DA, Albert SM, Herrick AL, Burke JG. Association of neighborhood context with offspring risk of preterm birth and low birthweight: A systematic review and meta-analysis of population-based studies. Social science & medicine. 2016;153:156-64.
33. Zeitlin J, Combier E, Levaillant M, Lasbeur L, Pilkington H, Charreire H, et al. Neighbourhood socio-economic characteristics and the risk of preterm birth for migrant and non-migrant women: a study in a French district. Paediatric and perinatal epidemiology. 2011;25(4):347-56.
34. Sorbye IK, Daltveit AK, Sundby J, Vangen S. Preterm subtypes by immigrants' length of residence in Norway: a population-based study. BMC pregnancy and childbirth. 2014;14:239.
35. Gagnon AJ, Zimbeck M, Zeitlin J, Collaboration R, Alexander S, Blondel B, et al. Migration to western industrialised countries and perinatal health: a systematic review. Social science & medicine. 2009;69(6):934-46.
36. Derraik JG, Lundgren M, Cutfield WS, Ahlsson F. Maternal Height and Preterm Birth: A Study on 192,432 Swedish Women. PLoS One. 2016;11(4):e0154304.
37. Han Z, Lutsiv O, Mulla S, McDonald SD. Maternal height and the risk of preterm birth and low birth weight: a systematic review and meta-analyses. J Obstet Gynaecol Can. 2012;34(8):721-46.
38. Cnattingius S, Villamor E, Johansson S, Edstedt Bonamy AK, Persson M, Wikstrom AK, et al. Maternal obesity and risk of preterm delivery. Jama. 2013;309(22):2362-70.
39. Torloni MR, Betran AP, Daher S, Widmer M, Dolan SM, Menon R, et al. Maternal BMI and preterm birth: a systematic review of the literature with meta-analysis. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2009;22(11):957-70.
40. Lynch AM, Hart JE, Agwu OC, Fisher BM, West NA, Gibbs RS. Association of extremes of prepregnancy BMI with the clinical presentations of preterm birth. American journal of obstetrics and gynecology. 2014;210(5):428 e1-9.
41. Gould JB, Mayo J, Shaw GM, Stevenson DK, March of Dimes Prematurity Research Center at Stanford University School of M. Swedish and American studies show that initiatives to decrease maternal obesity could play a key role in reducing preterm birth. Acta paediatrica. 2014;103(6):586-91.
42. Hermann M, Le Ray C, Blondel B, Goffinet F, Zeitlin J. The risk of prelabor and intrapartum cesarean delivery among overweight and obese women: possible preventive actions. American journal of obstetrics and gynecology. 2015;212(2):241 e1-9.
43. Savitz DA, Murnane P. Behavioral influences on preterm birth: a review. Epidemiology. 2010;21(3):291-9.
44. Luke B, Brown MB. Elevated risks of pregnancy complications and adverse outcomes with increasing maternal age. Human reproduction. 2007;22(5):1264-72.
45. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Maternal, fetal, and placental conditions associated with medically indicated late preterm and early term delivery: a retrospective study. BJOG : an international journal of obstetrics and gynaecology. 2016;123(5):763-70.
46. Dueker G, Chen J, Cowling C, Haskin B. Early developmental outcomes predicted by gestational age from 35 to 41weeks. Early human development. 2016;103:85-90.
47. Searle AK, Smithers LG, Chittleborough CR, Gregory TA, Lynch JW. Gestational age and school achievement: a population study. Archives of disease in childhood Fetal and neonatal edition. 2017.

Table 1: Associations between maternal characteristics and risks of preterm and early term birth

		<37 wks GA % N=782	37-38 wks GA % N=3010	≥39 wks GA % N=10269	p[a]	<37 weeks GA aORs[b]	<37 weeks GA 95% CI	37-38 weeks GA aORs[b]	37-38 weeks GA 95% CI
Maternal age									
<20 years	346	3.9	2.3	2.4	0.005	1.0	0.7-1.6	0.9	0.7-1.2
20-24 years	2078	16.3	14.5	14.5		0.9	0.8-1.2	1.0	0.9-1.2
25-29 years	4737	32.8	31.7	33.7		1	-	1	-
30-34 years	4380	27.9	30.1	31.1		1.0	0.8-1.2	1.0	0.9-1.1
>=35 years	2720	19.1	21.4	18.3		1.1	0.9-1.4	1.2	1.0-1.3
Parity					<0.001				
1	6165	49.8	38.9	44.1		1.8	1.5-2.2	0.9	0.8-1.0
2-3	6980	39.8	50.8	49.1		1		1	-
4+	1116	10.4	10.3	6.9		1.2	0.9-1.6	1.2	1.1-1.4
Previous preterm birth					<0.001				
No	13740	86.6	94.1	97.8		8.2	6.2-10.7	2.4	2.0-3.0
Yes	521	13.4	5.9	2.2		1	-	1	-
Maternal height					<0.001				
Q1: 100-160 cm	4365	37.7	34.6	28.8		1.4	1.1-1.7	1.4	1.2-1.6
Q2: 161-165 cm	4143	25.9	29.9	29.0		1.0	0.8-1.2	1.2	1.1-1.4
Q3: 166-168 cm	2440	15.2	15.2	17.9		0.9	0.7-1.2	1.0	0.9-1.2
Q4: 169-190 cm	3313	21.3	20.4	24.3		1	-	1	-
Pre-pregnancy BMI					0.307				
<18.5	1177	12.9	8.5	7.8		1.7	1.3-2.2	1.1	1.0-1.3
18.5-25.9	9190	59.9	63.6	65.0		1	-	1	-
25-29.9	2472	15.5	16.6	17.7		0.9	0.7-1.1	0.9	0.8-1.0
>=30	1422	11.7	11.2	9.4		1.2	1.0-1.6	1.1	1.0-1.3
Nationality					0.043				
French	12360	84.0	86.3	87.0		1	-	1	-
Other European	470	4.2	3.3	3.2		1.2	0.8-1.8	1.0	0.8-1.2
North African	685	4.9	4.4	4.9		1.1	0.7-1.5	0.8	0.7-1.0
Sub-Saharan Africa	392	4.5	3.3	2.4		1.8	1.2-2.6	1.3	1.0-1.6
Other	354	2.5	2.7	2.4		1.0	0.6-1.6	1.1	0.8-1.4
Level of education									
Low ISCED 0-2	4054	37.5	31.9	26.7	<0.001	1.7	1.3-2.1	1.2	1.1-1.4
Medium ISCED 3-5	5883	38.8	40.6	41.7		1.2	1.0-1.5	1.1	1.0-1.2
High ISCED 6+	4324	23.7	27.6	31.7		1	-	1	-
Smoking n° cigarettes/day during the 3rd trimester					<0.001				
0	11814	79.1	81.4	83.6		1	-	1	-
1-9 cigarettes	1757	13.9	12.8	12.1		1.0	0.8-1.3	1.0	0.9-1.2
>=10 cigarettes	690	7.0	5.8	4.4		1.3	0.9-1.8	1.1	0.9-1.4

a. F-test b. Adjusted Relative Risk Ratio

Table 2: Associations between maternal characteristics and risks of spontaneous preterm and early term birth

	<37 weeks GA % N=405	37-38 weeks GA % N=1949	p[a]	<37 weeks GA aORs[b]	95% CI	37-38 weeks GA aORs[b]	95% CI
Maternal age							
<20 years	3.7	2.5	0.002	1.0	0.6-1.8	1.0	0.7-1.4
20-24 years	19.1	16.2		1.1	0.8-1.5	1.1	0.9-1.3
25-29 years.	34.9	34.4		1	-	1	-
30-34 years	24.2	30.1		0.8	0.6-1.0	0.9	0.8-1.0
>=35 years	18.1	16.8		1.0	0.7-1.3	0.8	0.7-1.0
Parity							
1	48.4	40.5	0.004	1.6	1.3-2.1	0.9	0.8-1.0
2-3	40.8	51.1		1	-	1	
4	10.8	8.3		1.3	0.9-1.9	1.2	1.0-1.4
Previous preterm birth							
No	84.6	94.5	<0.001	1	-	1	-
Yes	15.4	5.5		9.3	6.6-13.0	2.4	1.9-3.1
Maternal height							
Q1: 100-160 cm	38.2	33.0	<0.001	1.4	1.1-1.9	1.3	1.1-1.5
Q2: 161-165 cm	26.4	30.1		1.0	0.8-1.4	1.2	1.0-1.4
Q3: 166-168 cm	14.5	15.7		0.9	0.6-1.3	1.0	0.9-1.2
Q4: 169-190 cm	21.0	21.1		1	-	1	-
Pre-pregnancy BMI							
<18.5	15.3	10.4	<0.001	1.9	1.4-2.6	1.3	1.1-1.5
18.5-24.9	61.9	67.1		1	-	1	-
25-29.9	13.6	14.7		0.8	0.6-1.0	0.8	0.7-0.9
>=30	9.3	7.8		0.9	0.6-1.3	0.7	0.6-0.9
Nationality							
French	83.7	87.1	0.6213	1	-	1	-
Other Europe	5.4	3.7		1.5	1.0-2.5	1.1	0.8-1.4
North African	5.7	3.9		1.2	0.8-2.0	0.8	0.6-1.0
sub-Saharan Africa	3.1	2.5		1.2	0.7-2.3	1.0	0.7-1.4
Other	2.1	2.8		0.8	0.4-1.7	1.1	0.8-1.5
Level of education							
Low ISCED 0-2	37.1	30.4	<0.001	1.4	1.0-1.9	1.1	0.9-1.3
Medium ISCED 3-5	38.4	39.7		1.1	0.8-1.4	1.0	0.9-1.1
High ISCED 6+	24.5	30.0		1	-	1	-
Smoking n° cigarettes/day during the 3[rd] trimester							
0	78.0	82.2	<0.001	1	-	1	-
1-9	13.5	11.9		1.0	0.7-1.3	0.9	0.8-1.1
>=10	8.5	5.9		1.5	1.0-2.2	1.2	0.9-1.5

a. F-test b. Adjusted Relative Risk Ratio

Table 3: Associations between maternal characteristics and risks of indicated preterm and early term

birth

	<37 weeks GA % N=374	37-38 weeks GA % N=1259	p[a]	<37 weeks GA aORs[b]	<37 weeks GA 95% CI	37-38 weeks GA aORs[b]	37-38 weeks GA 95% CI
Maternal age							
<20 yo	4.1	1.9	0.0000	1.1	0.6-2.0	0.9	0.6-1.4
20-24 yo	13.5	11.9		0.8	0.6-1.1	0.9	0.8-1.2
25-29 yo.	30.5	27.6		1	-	1	-
30-34 yo	31.6	30.1		1.3	1.0-1.7	1.2	1.0-1.4
>=35 yo	20.3	28.4		1.4	1.0-1.9	1.8	1.5-2.1
Parity							
1	51.5	36.6	0.0000	2.1	1.6-2.7	1.0	0.9-1.2
2-3	38.8	50.3		1	-	1	-
4	9.7	13.2		1.1	0.7-1.6	1.3	1.1-1.6
Previous preterm birth							
Yes	89.0	93.5	0.0000	6.6	4.5-9.7	2.5	1.9-3.3
No	11.0	6.5		1	-	1	-
Maternal height							
Q1: 100-160 cm	37.2	36.9	0.0000	1.3	1.0-1.8	1.5	1.3-1.8
Q2: 161-165 cm	25.2	29.3		1.0	0.7-1.3	1.2	1.0-1.5
Q3: 166-168 cm	15.9	14.4		1.0	0.7-1.4	1.0	0.8-1.3
Q4: 169-190 cm	21.6	19.3		1	-	1	-
Pre-pregnancy BMI							
<18.5	10.4	5.6	0.0000	1.4	1.0-2.1	0.8	0.6-1.1
18.5-24.9	57.7	58.3		1	-	1	-
25-29.9	17.6	19.6		1.0	0.8-1.4	1.1	0.9-1.3
>=30	14.4	16.5		1.6	1.1-2.2	1.7	1.4-2.0
Nationality							
French	84.2	84.9	0.0044	1	-	1	-
Other Europe	2.9	2.8		0.8	0.4-1.6	0.8	0.6-1.2
North African	4.1	5.1		0.8	0.5-1.5	0.9	0.7-1.2
sub-Saharan Africa	5.9	4.6		2.2	1.4-3.5	1.6	1.2-2.2
Other	2.9	2.6		1.2	0.6-2.2	1.1	0.8-1.6
Level of education							
Low ISCED 0-2	38.0	34.2	0.0000	2.0	1.5-2.8	1.5	1.3-1.8
Medium ISCED 3-5	39.4	42.0		1.4	1.0-1.8	1.3	1.1-1.5
High ISCED 6+	22.7	23.8		1	-	-	1
Smoking n° cigarettes/day during the 3rd trimester							
0	80.5	80.3	0.0068	1	-	1	-
1-9	14.1	14.1		1.1	0.8-1.5	1.2	1.0-1.4
>=10	5.4	5.6		1.0	0.6-1.6	1.1	0.9-1.5

a. F-test b. Adjusted Relative Risk Ratio

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6-7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-9
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Are risk factors for preterm and early term live singleton birth the same? A population-based study in France

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-018745.R1
Article Type:	Research
Date Submitted by the Author:	04-Oct-2017
Complete List of Authors:	Delnord, Marie; INSERM, UMR1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité, 53 avenue de l'Observatoire Blondel, Béatrice; INSERM, UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité Prunet, Caroline; INSERM, UMR1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité, 53 avenue de l'Observatoire Zeitlin, Jennifer; INSERM, UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité; Paris-Descartes University,
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Obstetrics and gynaecology, Paediatrics, Public health
Keywords:	early term birth, preterm birth, Population prevention, Perinatal Health Survey, population risk factors

SCHOLARONE™ Manuscripts

Are risk factors for preterm and early term live singleton birth the same? A population-based study in France

Marie DELNORD[1]*MSc, MA; Béatrice BLONDEL[1], PhD; Caroline PRUNET, MSc; Jennifer ZEITLIN[1], DSc
*INSERM U1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, Research Center for Epidemiology and Biostatistics Sorbonne Paris Cité (CRESS)

Affiliations:

1. Inserm UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team (Epopé), Centre for Epidemiology and Statistics Sorbonne Paris Cité, DHU Risks in pregnancy, Paris Descartes University, Paris, France

***Corresponding author**:
Ms. Marie Delnord
INSERM U1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, Research Center for Epidemiology and Biostatistics Sorbonne Paris Cité (CRESS)
Maternité de Port Royal, 53 Avenue de l' Observatoire, 75014 Paris FRANCE
Tel : +33 1 42 34 55 86 Fax: +33 1 43 26 89 79
Marie.delnord@inserm.fr

Word count:
Abstract: 222/300 words

Main text: 3233/4000 words

Abstract

Objectives: To investigate whether risk factors for preterm (<37 weeks gestation) and early term birth (37 and 38 weeks gestation) are similar.

Design: Nationally representative cross-sectional study of births

Setting: France in 2010

Participants: Live singleton births (N=14 326)

Primary and secondary outcome measures: Preterm and early term birth rates overall and by mode of delivery (spontaneous and indicated). Risk factors were maternal sociodemographic characteristics, previous preterm birth, height, pre-pregnancy body mass index (BMI) and smoking, assessed using multinomial regression models with full term births 39 weeks and over as the reference group.

Results: There were 5.5% preterm and 22.5% early term births. Common risk factors were: a previous preterm delivery (adjusted relative risk ratio aRRR=8.2 [95% CI: 6.2-10.7] and aRRR=2.4 [95% CI: 2.0-3.0] respectively), short stature, underweight (overall and in spontaneous deliveries), obesity (in indicated deliveries only), a low educational level, and Sub Saharan African origin. In contrast, primiparity was a risk factor only for preterm birth, aRRR=1.8 [95% CI: 1.5-2.2], while higher parity was associated with greater risk of early term birth.

Conclusions: Most population-level risk factors were common to both preterm and early term birth with the exception of primiparity, and BMI which differed by mode of onset of delivery. Our results suggest that preterm and early term birth share similar etiologies and thus potentially common strategies for prevention.

Strengths and limitations of this study:

- We had detailed information on prenatal social and demographic characteristics collected using a standardized maternal interview in a representative sample of births in France.
- We had few missing data for which we corrected using multiple imputation.
- We used multinomial regression to estimate preterm and early term birth adjusted relative risk ratios and their 95% confidence intervals by maternal characteristics using births reaching full term (i.e. births 39 weeks and over) as the reference.
- Because very preterm births represented 0.6% of births in our sample, we do not report associations by preterm GA subgroups.
- Our sample size may have been too small to detect low to moderate associations in less prevalent sub groups of women, such as heavy smokers, for instance.

Funding:

This work was supported by Paris Descartes University, Paris, France.

The French National Perinatal Survey 2010 was funded by the French Ministry of Health.

The funding agencies were not involved in the study.

Competing interests: No competing interests

Introduction

Preterm birth, defined as birth before 37 weeks of gestation, is a leading cause of perinatal mortality and morbidity. Preterm infants represent 60% of all neonatal deaths and 75% of all infant deaths (1). They are at risk of short and long-term neurocognitive and motor impairments, and display higher rates of chronic disease and premature death compared to term infants (1, 2). The prevention of preterm birth is a global priority, however preterm births are not the only gestational age subgroup at risk of adverse health outcomes (1, 2). Compared to being born full term, defined as between 39 and 41 weeks, early term birth at 37 and 38 weeks is associated with higher risks of neonatal mortality, more intensive care unit admissions (3), and higher health-related costs well into childhood for obstructive airway diseases, visual and motor disabilities (4).

There are large differences in rates and trends of preterm and early term births among countries with similar levels of development (5-7). In Europe in 2010, preterm birth rates ranged between 4.1% and 8.2% while early term rates ranged between 15.6% and 30.8% (5); such heterogeneity across countries suggests that rate reductions may be possible. However, despite the significant public health burden (4, 8-10), little progress has been made in decreasing the number of these early births (6, 11, 12). The latest French recommendations for the prevention of spontaneous preterm birth focus on smoking cessation and on interventions for women with high risk pregnancies (i.e. cerclage, progesterone), but conclude that high quality evidence does not exist for other preventive strategies (13); this is partially due to the low predictive accuracy of diagnostic tools (11). As for early term birth, prevention efforts are recent, with a focus by professional societies in the United States on the reduction of indicated early term deliveries for non-medical reasons (14).

More research on the etiology of early delivery is required to orient prevention efforts and practice. There is recent evidence that in high-income countries, moderate and late preterm birth rates are associated with rates of early term birth(15). Positive associations between preterm and early term birth country rates suggest that common population-level determinants could underpin shifts in the gestational age distribution towards early delivery. There are known maternal characteristics that contribute significantly to preterm birth rates and trends within countries, including maternal age, underweight and obesity and socioeconomic status (16) . In addition, we know that early term and late preterm births both have worse neonatal outcomes compared to full term births (17). However, what is not known is which maternal characteristics related to preterm birth risk (1, 11, 16, 18) could also relate to early term birth(19). Thus in this study we aimed to identify maternal population determinants of preterm and early term birth taking into consideration mode of onset of delivery, i.e. spontaneous or indicated, using nationally representative data on births from the French National Perinatal Survey in 2010.

Materials and Methods

The French National Perinatal Survey 2010 (*Enquête Nationale Périnatale*, ENP) is a study based on a representative sample of births in Metropolitan France. The National Perinatal Surveys have been conducted periodically since 1995 and constitute part of the routine health information system for the surveillance of mothers and newborns in France (20). They include all live and stillbirths starting at 22 weeks of gestation or weighing at least 500g over the course of one week in all public and private maternity units. In 2010, there were 535 maternity units operating in metropolitan France of which one refused to participate (20) . For this study, we included singleton pregnancies ending in a live birth with a gestational age of 22 weeks or over (N=14,326 pregnant women). Multifetal pregnancies and stillbirths were excluded because of differences in delivery practices and etiology for these births.

Survey items on mothers' demographic characteristics (e.g. maternal age, parity), socioeconomic status (e.g. level of education), prenatal care and behaviors were collected during interviews with midwives or nurses in the postpartum ward. Other data on the delivery and newborn health were abstracted from the medical records by medical staff, and include information on the mode of onset of delivery, pre-existing maternal medical conditions (hypertension, diabetes), as well as routine indicators of neonatal health at birth(20). We defined indicated deliveries as those with a provider-initiated mode of onset, i.e. either induction of labor or prelabor cesarean section. Although there may have been differences in the distribution of maternal characteristics by region, our total sample size precluded us carrying out more detailed analyses (24 regions in total, N min=58 and N max= 1312 live singleton births).

Our main outcomes were preterm and early term birth. These were defined respectively as births 22-36 completed weeks of gestation and 37-38 completed weeks overall and by mode of onset (spontaneous or indicated). Gestational age was based on the best obstetrical estimate. In France, nearly all women have a first trimester ultrasound for dating the pregnancy (20). The upper limit of gestational age included in the sample was 44 weeks, but very few deliveries were postterm (N=49, 0.4% at 42 weeks and over). We also do not report associations by preterm GA subgroups, in particular for very preterm births (N=122, 0.9%)

We selected risk factors based on a scoping review of the scientific literature, including recent research on preterm birth risk factors in France (18, 21). Some preterm birth exposures that were available in the French National Perinatal Survey were omitted from our study because of their low prevalence in the sample (i.e. use of fertility treatments : <4%, diabetes: <2%, and chronic hypertension: 2%).

We included the following variables in our analysis: maternal age (<20, 20-24, 25-29, 30-34, >=35 years old), parity (1,2-3,4+), previous preterm birth, nationality (French, Other European, North African, Sub-Saharan African, Other), maternal height presented in quartiles

(Q1: 100-160cm, Q2: 161-165cm, Q3: 166-168cm, Q4:169-190cm), pre-pregnancy body mass index (defined as underweight, normal, overweight, and obese women for BMIs <18.5, 18.5-24.9, 25-29.9,≥30 respectively), level of education, and smoking during the third trimester. Level of completed education was defined based on the ISCED 2011 classification: low educational level ISCED 0-2 (i.e. up to lower secondary education completed), medium educational level ISCED 3-5 (i.e. upper secondary education or short cycle tertiary education completed), high educational level ISCED 6-7 (Bachelors' equivalent or higher) . BMI is a measure of body mass that is independent of height in adults; therefore both variables were included in the study (22).

The National Council on Statistical Information (Comité du Label) and the French Commission on Information Technology and Liberties (CNIL) approved the French National Perinatal Surveys (Enquête Nationale Périnatale 2010)

Analysis strategy

We first compared the distributions of preterm and early term births by maternal characteristics. We included all maternal exposures hypothesized to be associated with preterm delivery in the multivariate analyses (18). We used multinomial regression to estimate preterm and early term birth adjusted relative risk ratios (RRR) and their 95% confidence intervals by maternal characteristics using births reaching full term (i.e. births 39 weeks and over) as the reference. Adjusted relative risk ratios are similar to adjusted odds ratios in binary logistic regression.

In the mode of onset analyses, we computed relative risk ratios of spontaneous and indicated preterm and early delivery using the same full term reference population (i.e. all births 39 weeks and over, regardless of mode of onset). We used this reference population as we considered spontaneous and indicated births as two sub-types of our outcome (early delivery). Indicated deliveries at full term are principally for prolonged pregnancy, previous cesarean section and can be based on maternal request, indications which are much less common before 39 weeks(23, 24). Data were analysed using STATA 13.0 software (StataCorp LP, College Station, TX, USA).

There were 14 326 live singleton births in the survey of which 65 were missing GA data. We had less than 1% missing data on mode of onset of labor (i.e. spontaneous or provider-initiated delivery) and less than 5% missing sociodemographic data (i.e. nationality and level of education). There were 4% missing data on previous preterm birth and 6% missing on anthropometric characteristics (i.e. height or BMI). Although individual proportions of missing data were low, complete cases were only 86% of the total and therefore we imputed missing values (except the outcome) using multivariate imputation by chained equations. We performed 100 imputations using all available covariates (25). Descriptive and multivariate analyses were done on the imputed dataset. Because data were imputed, we used F-tests to look at differences in the distributions of maternal characteristics by GA subgroup(26).

Results

Table 1 provides descriptive statistics on our sample. We included 14 261 live singleton pregnancies with GA data available. The overall rate of preterm birth was 5.5% and early term birth was 22.6%. In the reference population of women with a full term birth, 2.4% were aged under 20 and 18.3% over 35 years of age; 44.1% were primiparous and 6.9% were parity 4 or more; 2.2% had a previous preterm birth, 7.8% were underweight, 9.4% were overweight and 16.4% smoked in the 3rd trimester of pregnancy. The risk profiles of mothers with a preterm and early term infant were different. These mothers were more likely to be older, have a previous preterm birth, be of shorter stature, with a lower level of education, and smoke. Mothers with a preterm birth were more likely to be primipara whereas mothers with an early term birth were more likely to be multipara, compared to mothers with a term birth.

In multinomial multivariable models, most of these associations persisted; common population determinants for preterm and early term birth were: a previous preterm birth, shorter stature, underweight, sub-Saharan nationality, and a low level of education. There were some differences in the impact of these risk factors: a previous preterm birth was a stronger risk factor for preterm birth than early term birth (aRRR 8.2 vs. 2.4 respectively); maternal underweight and Sub-Saharan nationality were also stronger risk factors for preterm compared to early term birth. Primipara were at risk for preterm birth only (aRRR 1.8 [1.5-2.2]), whereas grand multipara (parity 4+) were at higher risk of early term birth. After adjustment, advanced maternal age, and smoking during the third trimester were no longer associated with increased risks of delivery before 39 weeks.

In Table 2, we display the associations between spontaneous preterm, and early term births by maternal characteristics. Out of all births, 2.8% were spontaneous preterm births and 13.6% were spontaneous early term births. Common risk factors were: a previous preterm birth, short stature, maternal underweight, foreign nationality (i.e. Other European), and a low level of education. There were some differences in the impact of these risk factors. Underweight was a stronger risk factor for spontaneous preterm than early term birth: aRRR 1.9[1.4-2.6] vs aRRR 1.3[1.1-1.5] respectively, and overweight women displayed a reduced risk of spontaneous early term delivery. Primipara were at risk of preterm birth but not early term birth. Smoking during the third trimester was associated with a moderately increased risk of spontaneous preterm delivery, although the confidence interval included 1: aRRR 1.5[1.0-2.2]. The aRRR was lower and non-significant for early term birth: 1.2[0.9-1.5].

In Table 3, we display the associations between indicated preterm and early term birth by maternal characteristics. Out of all births, 2.6% were indicated preterm deliveries and 8.8% were indicated early term deliveries. Most risk factors were common to indicated preterm and early term birth including: advanced maternal age, a previous preterm birth, short stature, obesity (aRRR 1.6(1.1-2.2] preterm, and aRRR 1.7[1.4-2.0] early term), sub-Saharan African origin (aRRR 2.2[1.4-3.5] preterm, and aRRR 1.6[1.2-2.2] for early term), and a low level of education, after adjusting on all other covariates. Primipara were only at risk for indicated preterm birth, aRRR=2.1[1.6-2.7]; while parity 4+ was associated with greater risk of indicated early term birth aRRR= 1.3 [1.1-1.6].

When we compare findings from our mode of onset analyses, Table 2 and 3 show that risk factors for delivery before 39 weeks are the same in spontaneous preterm and early term deliveries, and indicated preterm and early term deliveries - with the exception of BMI. Underweight was a risk factor for spontaneous delivery before 39 weeks (aRRR 1.9[1.4-2.6] for preterm and aRRR 1.3[1.1-1.5] for early term), whereas overweight was a risk factor for indicated delivery before 39 weeks (aRRR 1.6(1.1-2.2] preterm, and aRRR 1.7[1.4-2.0] early term).

Discussion

Our study provides new insight into the population determinants of preterm and early term birth by mode of onset of delivery. We identified shared risk factors for delivery before 39 weeks which were: a previous preterm birth, short stature, a low level of education, underweight (overall and in spontaneous deliveries), obesity (in indicated deliveries only), and foreign origin (for other European and sub-Saharan nationals). The impact of most risk factors was greater for preterm birth compared to early term birth, and primiparity was a risk factor for preterm birth but not early term birth.

A strength of our study is the availability of detailed population-based information on prenatal, social and demographic characteristics collected using a standardized maternal interview in a representative sample of births in France. We had few missing data for which we corrected using multiple imputation. In this study, our focus was on the broader population determinants of early delivery that contribute to global rates of preterm and early term birth in France. We were able to conduct analyses for spontaneous and indicated deliveries separately in order to highlight potential differences in risk factors between these subtypes of preterm birth for which some medical maternal and fetal factors differ (27). We did not include pregnancy complications in our analyses as these are pathways between our population risk factors and preterm and early term deliveries. (28, 29),

Our study also has some limitations. Our sample size may have been too small to detect low to moderate associations in less prevalent subgroups of women, such as heavy smokers, for instance. Similarly, we were not able to include risk factors with low prevalence (i.e. preexisting medical conditions: diabetes, hypertension) or carry out analyses by region although there may have been differences in the distribution of maternal characteristics. We did not carry out separate analyses for very preterm births, and it is possible that risk factors for this vulnerable subpopulation may differ from those for moderate and late preterm births at 32-36 weeks of gestation. Finally, we did not correct for multiple comparisons in order to maintain adequate power to carry out the study (30).

The strongest single predictor of both preterm and early term delivery was a previous preterm birth overall and by mode of onset of delivery, as confirmed in other population-based studies (31, 32) and a recent systematic review which showed a 30% risk of recurrent spontaneous preterm birth (sPTB) following sPTB in singleton pregnancies (33) . In contrast, first-time mothers were more likely to deliver preterm, but not early term indicating that the shape of the risk distribution for early delivery in primipara may slightly differ from the overall GA distribution which peaks around 38-40 weeks of gestation.Fertility trends determining the proportion of primiparous women may therefore contribute to differences in preterm and early term birth rates across countries.

Socio-demographic characteristics, measured by a lower level of education and mother's country of birth, were also associated with earlier delivery overall and by mode of onset of delivery. Maternal educational level is a well documented risk factor for preterm birth risk and recent findings from Canada have shown an association with early term birth (34-36). Exposures related to mothers' general quality of life and well-being (i.e. living and employment conditions, air pollution, exposure to stress) could mediate the association with social status via physiological pathways (37-41). In France, Prunet et al. showed that social status was associated with preterm birth risk independently of use of medical care during pregnancy (18). As for the association with foreign origin, our results are consistent with the literature showing higher risks of preterm birth among women from Sub-Saharan Africa (42).

There were common anthropometric determinants of delivery before 39 weeks overall, however there were differences by mode of onset of delivery. Our findings confirm previous research on the association between preterm birth and short stature (43, 44) and we provide new evidence on the association with early term birth. With respect to maternal pre-pregnancy weight, thinness is often associated with spontaneous preterm birth but the association between GA and overweight is less clear (45-47). A greater prevalence of comorbities in obese women could contribute to the excess in indicated delivery (48), which we observed. In contrast, the decreased risk of spontaneous preterm and early term delivery in women with BMIs over 30 could be due to specific delivery practices, and greater levels of obstetrical interventions for obese women in general(49).

Finally, smoking and advanced maternal age are traditionally cited as preterm birth risk factors (50, 51); while there was an increased risk for spontaneous preterm birth in heavy smokers and an increased risk for indicated preterm and early term delivery in mothers over 35, we did not identify associations with either variable in the overall analyses. Previous data from France, also showed a limited impact of smoking on overall preterm birth risk whereas associations were stronger in studies from other countries (20, 21).

Our findings showing common risk patterns for preterm and early term births suggest a shared etiology for these births overall, with some exceptions for primiparous women and by mode of onset of delivery for BMI. These results raise questions about the appropriate definition of preterm birth, and the GA thresholds which should be used (52). Our findings by mode of onset of delivery are also consistent with two reports documenting shared pregnancy complications for spontaneous preterm and early term deliveries (28, 29). Delivery following spontaneous labour even close to full term may be a result of pathological processes (28), with a slightly more heterogeneous etiology for medically indicated late preterm and early term phenotypes (i.e. anemia and gastrointestinal disease were associated with late preterm but not early term delivery) (29). Future research associating maternal exposures with pregnancy complications such as: diabetes mellitus, infection and inflammation, placental ischemia, polyhydramnios and oligohydramnios, which are related to spontaneous and indicated preterm and early term births could provide insight into the mechanisms underpinning early delivery (28).

In conclusion, our population-based study showed that there are several shared maternal prenatal and socio-demographic risk factors for delivery before full term (i.e. 39 weeks and over). Because strategies to reduce individual risk of preterm birth have had a limited impact on global rate reductions (11), investing in broader population-based interventions may be justified, including those targeting maternal pre-pregnancy BMI and social inequalities in health (48). Moreover, due to the large volume of births at 37-38 weeks, even small point percentage reductions are likely to impact on health and needs for educational and social services. Each additional week of gestation after 35 weeks reduces specific delays in communication, personal-social, fine-motor, and problem-solving skills up until 24 months of age, and the population attributable fraction for poor achievement in school is highest among early term births (53, 54). The existence of shared risk factors for both gestational age subgroups and the greater number of early term births compared to preterm births provides greater power to investigate the mechanisms leading to early delivery, and supports the use of a broader research paradigm for preterm birth prevention.

Contributions: MD, BB and JZ contributed to the study design, and interpretation of the data. MD, BB, and CP participated in the data collection and analysis. MD and JZ drafted the manuscript, BB provided critical revisions. All authors have read and approved the final version of the manuscript.

Data sharing statement: Instructions for applying for public access data from the French National Perinatal Survey are available upon request from the authors.

References

1. Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller AB, et al. Born too soon: the global epidemiology of 15 million preterm births. Reproductive health. 2013;10 Suppl 1:S2.
2. Zhang X, Kramer MS. Variations in mortality and morbidity by gestational age among infants born at term. The Journal of pediatrics. 2009;154(3):358-62, 62 e1.
3. Sengupta S, Carrion V, Shelton J, Wynn RJ, Ryan RM, Singhal K, et al. Adverse neonatal outcomes associated with early-term birth. JAMA pediatrics. 2013;167(11):1053-9.
4. Helle E, Andersson S, Hakkinen U, Jarvelin J, Eskelinen J, Kajantie E. Morbidity and Health Care Costs After Early Term Birth. Paediatric and perinatal epidemiology. 2016;30(6):533-40.
5. Euro-Peristat project with SCPE and EUROCAT, European Perinatal Health Report. The health and care of pregnant women and babies in Europe in 2010. 2013 May 2013. Report No.
6. Richards JL, Kramer MS, Deb-Rinker P, Rouleau J, Mortensen L, Gissler M, et al. Temporal Trends in Late Preterm and Early Term Birth Rates in 6 High-Income Countries in North America and Europe and Association With Clinician-Initiated Obstetric Interventions. JAMA. 2016;316(4):410-9.
7. Zeitlin J, Szamotulska K, Drewniak N, Mohangoo AD, Chalmers J, Sakkeus L, et al. Preterm birth time trends in Europe: a study of 19 countries. BJOG. 2013;120(11):1356-65.
8. Jacob J, Lehne M, Mischker A, Klinger N, Zickermann C, Walker J. Cost effects of preterm birth: a comparison of health care costs associated with early preterm, late preterm, and full-term birth in the first 3 years after birth. The European journal of health economics : HEPAC : health economics in prevention and care. 2016.
9. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. Lancet. 2008;371(9608):261-9.
10. Crump C, Sundquist K, Winkleby MA, Sundquist J. Early-term birth (37-38 weeks) and mortality in young adulthood. Epidemiology. 2013;24(2):270-6.
11. Chang HH, Larson J, Blencowe H, Spong CY, Howson CP, Cairns-Smith S, et al. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. Lancet. 2013;381(9862):223-34.

12. Lawn JE, Kinney MV, Belizan JM, Mason EM, McDougall L, Larson J, et al. Born too soon: accelerating actions for prevention and care of 15 million newborns born too soon. Reproductive health. 2013;10 Suppl 1:S6.
13. Sentilhes L, Senat MV, Ancel PY, Azria E, Benoist G, Blanc J, et al. Prevention of spontaneous preterm birth: Guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). European journal of obstetrics, gynecology, and reproductive biology. 2017;210:217-24.
14. ACOG Committee Opinion No 579: Definition of term pregnancy. Obstetrics and gynecology. 2013;122(5):1139-40.
15. Delnord M, Mortensen L, Hindori-Mohangoo AD, Blondel B, Gissler M, Kramer MR, et al. International variations in the gestational age distribution of births: an ecological study in 34 high-income countries. The European Journal of Public Health. 2017:ckx131.
16. Delnord M, Blondel B, Zeitlin J. What contributes to disparities in the preterm birth rate in European countries? Current opinion in obstetrics & gynecology. 2015;27(2):133-42.
17. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Neonatal morbidity associated with late preterm and early term birth: the roles of gestational age and biological determinants of preterm birth. International journal of epidemiology. 2014;43(3):802-14.
18. Prunet C, Delnord M, Saurel-Cubizolles MJ, Goffinet F, Blondel B. Risk factors of preterm birth in France in 2010 and changes since 1995: Results from the French National Perinatal Surveys. Journal de gynecologie, obstetrique et biologie de la reproduction. 2016.
19. Raju TN. Moderately preterm, late preterm and early term infants: research needs. Clinics in perinatology. 2013;40(4):791-7.
20. Blondel B, Lelong N, Kermarrec M, Goffinet F, National Coordination Group of the National Perinatal S. Trends in perinatal health in France from 1995 to 2010. Results from the French National Perinatal Surveys. Journal de gynecologie, obstetrique et biologie de la reproduction. 2012;41(4):e1-e15.
21. Prunet C, Delnord M, Saurel-Cubizolles MJ, Goffinet F, Blondel B. Risk factors of preterm birth in France in 2010 and changes since 1995: Results from the French National Perinatal Surveys. Journal of gynecology obstetrics and human reproduction. 2017;46(1):19-28.
22. Heymsfield SB, Heo M, Thomas D, Pietrobelli A. Scaling of body composition to height: relevance to height-normalized indexes. The American journal of clinical nutrition. 2011;93(4):736-40.
23. Roman H, Blondel B, Breart G, Goffinet F. Do risk factors for elective cesarean section differ from those of cesarean section during labor in low risk pregnancies? Journal of perinatal medicine. 2008;36(4):297-305.
24. Coulm B, Blondel B, Alexander S, Boulvain M, Le Ray C. Elective induction of labour and maternal request: a national population-based study. BJOG : an international journal of obstetrics and gynaecology. 2016;123(13):2191-7.
25. Graham JW, Olchowski AE, Gilreath TD. How many imputations are really needed? Some practical clarifications of multiple imputation theory. Prevention science : the official journal of the Society for Prevention Research. 2007;8(3):206-13.
26. van Ginkel JR, Kroonenberg PM. Analysis of Variance of Multiply Imputed Data. Multivariate behavioral research. 2014;49(1):78-91.
27. Savitz DA, Dole N, Herring AH, Kaczor D, Murphy J, Siega-Riz AM, et al. Should spontaneous and medically indicated preterm births be separated for studying aetiology? Paediatric and perinatal epidemiology. 2005;19(2):97-105.
28. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Biological determinants of spontaneous late preterm and early term birth: a retrospective cohort study. BJOG : an international journal of obstetrics and gynaecology. 2015;122(4):491-9.
29. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Maternal, fetal, and placental conditions associated with medically indicated late preterm and early term delivery: a retrospective study. BJOG : an international journal of obstetrics and gynaecology. 2016;123(5):763-70.

30. Feise RJ. Do multiple outcome measures require p-value adjustment? BMC medical research methodology. 2002;2:8.
31. Yang J, Baer RJ, Berghella V, Chambers C, Chung P, Coker T, et al. Recurrence of Preterm Birth and Early Term Birth. Obstetrics and gynecology. 2016;128(2):364-72.
32. Ferrero DM, Larson J, Jacobsson B, Di Renzo GC, Norman JE, Martin JN, Jr., et al. Cross-Country Individual Participant Analysis of 4.1 Million Singleton Births in 5 Countries with Very High Human Development Index Confirms Known Associations but Provides No Biologic Explanation for 2/3 of All Preterm Births. PloS one. 2016;11(9):e0162506.
33. Phillips C, Velji Z, Hanly C, Metcalfe A. Risk of recurrent spontaneous preterm birth: a systematic review and meta-analysis. BMJ open. 2017;7(6):e015402.
34. Auger N, Leduc L, Naimi AI, Fraser WD. Delivery at Term: Impact of University Education by Week of Gestation. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC. 2016;38(2):118-24.
35. Oftedal AM, Busterud K, Irgens LM, Haug K, Rasmussen S. Socio-economic risk factors for preterm birth in Norway 1999-2009. Scandinavian journal of public health. 2016;44(6):587-92.
36. Poulsen G, Strandberg-Larsen K, Mortensen L, Barros H, Cordier S, Correia S, et al. Exploring educational disparities in risk of preterm delivery: a comparative study of 12 European birth cohorts. Paediatric and perinatal epidemiology. 2015;29(3):172-83.
37. Stieb DM, Chen L, Eshoul M, Judek S. Ambient air pollution, birth weight and preterm birth: a systematic review and meta-analysis. Environmental research. 2012;117:100-11.
38. Staneva A, Bogossian F, Pritchard M, Wittkowski A. The effects of maternal depression, anxiety, and perceived stress during pregnancy on preterm birth: A systematic review. Women and birth : journal of the Australian College of Midwives. 2015;28(3):179-93.
39. Ncube CN, Enquobahrie DA, Albert SM, Herrick AL, Burke JG. Association of neighborhood context with offspring risk of preterm birth and low birthweight: A systematic review and meta-analysis of population-based studies. Social science & medicine. 2016;153:156-64.
40. Zeitlin J, Combier E, Levaillant M, Lasbeur L, Pilkington H, Charreire H, et al. Neighbourhood socio-economic characteristics and the risk of preterm birth for migrant and non-migrant women: a study in a French district. Paediatric and perinatal epidemiology. 2011;25(4):347-56.
41. Sorbye IK, Daltveit AK, Sundby J, Vangen S. Preterm subtypes by immigrants' length of residence in Norway: a population-based study. BMC pregnancy and childbirth. 2014;14:239.
42. Gagnon AJ, Zimbeck M, Zeitlin J, Collaboration R, Alexander S, Blondel B, et al. Migration to western industrialised countries and perinatal health: a systematic review. Social science & medicine. 2009;69(6):934-46.
43. Derraik JG, Lundgren M, Cutfield WS, Ahlsson F. Maternal Height and Preterm Birth: A Study on 192,432 Swedish Women. PloS one. 2016;11(4):e0154304.
44. Han Z, Lutsiv O, Mulla S, McDonald SD. Maternal height and the risk of preterm birth and low birth weight: a systematic review and meta-analyses. J Obstet Gynaecol Can. 2012;34(8):721-46.
45. Cnattingius S, Villamor E, Johansson S, Edstedt Bonamy AK, Persson M, Wikstrom AK, et al. Maternal obesity and risk of preterm delivery. Jama. 2013;309(22):2362-70.
46. Torloni MR, Betran AP, Daher S, Widmer M, Dolan SM, Menon R, et al. Maternal BMI and preterm birth: a systematic review of the literature with meta-analysis. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2009;22(11):957-70.
47. Lynch AM, Hart JE, Agwu OC, Fisher BM, West NA, Gibbs RS. Association of extremes of prepregnancy BMI with the clinical presentations of preterm birth. American journal of obstetrics and gynecology. 2014;210(5):428 e1-9.
48. Gould JB, Mayo J, Shaw GM, Stevenson DK, March of Dimes Prematurity Research Center at Stanford University School of M. Swedish and American studies show that initiatives to decrease maternal obesity could play a key role in reducing preterm birth. Acta paediatrica. 2014;103(6):586-91.

49. Hermann M, Le Ray C, Blondel B, Goffinet F, Zeitlin J. The risk of prelabor and intrapartum cesarean delivery among overweight and obese women: possible preventive actions. American journal of obstetrics and gynecology. 2015;212(2):241 e1-9.

50. Savitz DA, Murnane P. Behavioral influences on preterm birth: a review. Epidemiology. 2010;21(3):291-9.

51. Luke B, Brown MB. Elevated risks of pregnancy complications and adverse outcomes with increasing maternal age. Human reproduction. 2007;22(5):1264-72.

52. Kirby RS, Wingate MS. Late preterm birth and neonatal outcome: is 37 weeks' gestation a threshold level or a road marker on the highway of perinatal risk? Birth. 2010;37(2):169-71.

53. Dueker G, Chen J, Cowling C, Haskin B. Early developmental outcomes predicted by gestational age from 35 to 41weeks. Early human development. 2016;103:85-90.

54. Searle AK, Smithers LG, Chittleborough CR, Gregory TA, Lynch JW. Gestational age and school achievement: a population study. Archives of disease in childhood Fetal and neonatal edition. 2017.

Table 1: Associations between maternal characteristics and risks of preterm (<37 weeks) and early term birth (37-38 weeks) using births reaching full term (i.e. 39 weeks and over) as the reference in a representative sample of births in France in 2010

		<37 wks GA %	37-38 wks GA %	≥39 wks GA %		<37 weeks GA		37-38 weeks GA	
		N=782	N=3010	N=10269	p[a]	aRRRs[b]	95% CI	aRRRs[b]	95% CI
Maternal age									
<20 years	346	3.9	2.3	2.4	0.005	1.0	0.7-1.6	0.9	0.7-1.2
20-24 years	2078	16.3	14.5	14.5		0.9	0.8-1.2	1.0	0.9-1.2
25-29 years	4737	32.8	31.7	33.7		1	-	1	-
30-34 years	4380	27.9	30.1	31.1		1.0	0.8-1.2	1.0	0.9-1.1
>=35 years	2720	19.1	21.4	18.3		1.1	0.9-1.4	1.2	1.0-1.3
Parity					<0.001				
1	6165	49.8	38.9	44.1		1.8	1.5-2.2	0.9	0.8-1.0
2-3	6980	39.8	50.8	49.1		1		1	-
4+	1116	10.4	10.3	6.9		1.2	0.9-1.6	1.2	1.1-1.4
Previous preterm birth					<0.001				
No	13740	86.6	94.1	97.8		1	-	1	-
Yes	521	13.4	5.9	2.2		8.2	6.2-10.7	2.4	2.0-3.0
Maternal height					<0.001				
Q1: 100-160 cm	4365	37.7	34.6	28.8		1.4	1.1-1.7	1.4	1.2-1.6
Q2: 161-165 cm	4143	25.9	29.9	29.0		1.0	0.8-1.2	1.2	1.1-1.4
Q3: 166-168 cm	2440	15.2	15.2	17.9		0.9	0.7-1.2	1.0	0.9-1.2
Q4: 169-190 cm	3313	21.3	20.4	24.3		1	-	1	-
Pre-pregnancy BMI					0.307				
<18.5	1177	12.9	8.5	7.8		1.7	1.3-2.2	1.1	1.0-1.3
18.5-25.9	9190	59.9	63.6	65.0		1	-	1	-
25-29.9	2472	15.5	16.6	17.7		0.9	0.7-1.1	0.9	0.8-1.0
>=30	1422	11.7	11.2	9.4		1.2	1.0-1.6	1.1	1.0-1.3
Nationality					0.043				
French	12360	84.0	86.3	87.0		1	-	1	-
Other European	470	4.2	3.3	3.2		1.2	0.8-1.8	1.0	0.8-1.2
North African	685	4.9	4.4	4.9		1.1	0.7-1.5	0.8	0.7-1.0
Sub-Saharan Africa	392	4.5	3.3	2.4		1.8	1.2-2.6	1.3	1.0-1.6
Other	354	2.5	2.7	2.4		1.0	0.6-1.6	1.1	0.8-1.4
Level of education									
Low ISCED 0-2	4054	37.5	31.9	26.7	<0.001	1.7	1.3-2.1	1.2	1.1-1.4
Medium ISCED 3-5	5883	38.8	40.6	41.7		1.2	1.0-1.5	1.1	1.0-1.2
High ISCED 6+	4324	23.7	27.6	31.7		1	-	1	-
Smoking n° cigarettes/day during the 3rd trimester					<0.001				
0	11814	79.1	81.4	83.6		1	-	1	-
1-9 cigarettes	1757	13.9	12.8	12.1		1.0	0.8-1.3	1.0	0.9-1.2
>=10 cigarettes	690	7.0	5.8	4.4		1.3	0.9-1.8	1.1	0.9-1.4

a. F-test b. Adjusted Relative Risk Ratio

Note: ISCED 2011, International Standard Classification of Education 2011.

Table 2: Associations between maternal characteristics and risks of spontaneous preterm (<37 weeks) and early term birth (37-38 weeks) using births reaching full term (i.e. 39 weeks and over, N=10269) as the reference in a representative sample of births in France in 2010

	<37 weeks GA %	37-38 weeks GA %		<37 weeks GA		37-38 weeks GA	
	N=405	N=1949	p[a]	aRRRs[b]	95% CI	aRRRs[b]	95% CI
Maternal age							
<20 years	3.7	2.5	0.002	1.0	0.6-1.8	1.0	0.7-1.4
20-24 years	19.1	16.2		1.1	0.8-1.5	1.1	0.9-1.3
25-29 years.	34.9	34.4		1	-	1	-
30-34 years	24.2	30.1		0.8	0.6-1.0	0.9	0.8-1.0
>=35 years	18.1	16.8		1.0	0.7-1.3	0.8	0.7-1.0
Parity							
1	48.4	40.5	0.004	1.6	1.3-2.1	0.9	0.8-1.0
2-3	40.8	51.1		1	-	1	
4	10.8	8.3		1.3	0.9-1.9	1.2	1.0-1.4
Previous preterm birth							
No	84.6	94.5	<0.001	1	-	1	-
Yes	15.4	5.5		9.3	6.6-13.0	2.4	1.9-3.1
Maternal height							
Q1: 100-160 cm	38.2	33.0	<0.001	1.4	1.1-1.9	1.3	1.1-1.5
Q2: 161-165 cm	26.4	30.1		1.0	0.8-1.4	1.2	1.0-1.4
Q3: 166-168 cm	14.5	15.7		0.9	0.6-1.3	1.0	0.9-1.2
Q4: 169-190 cm	21.0	21.1		1	-	1	-
Pre-pregnancy BMI							
<18.5	15.3	10.4	<0.001	1.9	1.4-2.6	1.3	1.1-1.5
18.5-24.9	61.9	67.1		1	-	1	-
25-29.9	13.6	14.7		0.8	0.6-1.0	0.8	0.7-0.9
>=30	9.3	7.8		0.9	0.6-1.3	0.7	0.6-0.9
Nationality							
French	83.7	87.1	0.6213	1	-	1	-
Other Europe	5.4	3.7		1.5	1.0-2.5	1.1	0.8-1.4
North African	5.7	3.9		1.2	0.8-2.0	0.8	0.6-1.0
Sub-Saharan Africa	3.1	2.5		1.2	0.7-2.3	1.0	0.7-1.4
Other	2.1	2.8		0.8	0.4-1.7	1.1	0.8-1.5
Level of education							
Low ISCED 0-2	37.1	30.4	<0.001	1.4	1.0-1.9	1.1	0.9-1.3
Medium ISCED 3-5	38.4	39.7		1.1	0.8-1.4	1.0	0.9-1.1
High ISCED 6+	24.5	30.0		1	-	1	-
Smoking n° cigarettes/day during the 3rd trimester							
0	78.0	82.2	<0.001	1	-	1	-
1-9	13.5	11.9		1.0	0.7-1.3	0.9	0.8-1.1
>=10	8.5	5.9		1.5	1.0-2.2	1.2	0.9-1.5

a. F-test b. Adjusted Relative Risk Ratio

Note: ISCED 2011, International Standard Classification of Education 2011.

Table 3: Associations between maternal characteristics and risks of indicated preterm (<37 weeks) and early term birth (37-38 weeks) using births reaching full term (i.e. 39 weeks and over, N=10269) as the reference in a representative sample of births in France in 2010

	<37 weeks GA %	37-38 weeks GA %		<37 weeks GA		37-38 weeks GA	
	N=374	N=1259	p[a]	aRRRs[b]	95% CI	aRRRs[b]	95% CI
Maternal age							
<20 years	4.1	1.9	0.0000	1.1	0.6-2.0	0.9	0.6-1.4
20-24 years	13.5	11.9		0.8	0.6-1.1	0.9	0.8-1.2
25-29 years	30.5	27.6		1	-	1	-
30-34 years	31.6	30.1		1.3	1.0-1.7	1.2	1.0-1.4
>=35 years	20.3	28.4		1.4	1.0-1.9	1.8	1.5-2.1
Parity							
1	51.5	36.6	0.0000	2.1	1.6-2.7	1.0	0.9-1.2
2-3	38.8	50.3		1	-	1	-
4	9.7	13.2		1.1	0.7-1.6	1.3	1.1-1.6
Previous preterm birth							
Yes	89.0	93.5	0.0000	6.6	4.5-9.7	2.5	1.9-3.3
No	11.0	6.5		1	-	1	-
Maternal height							
Q1: 100-160 cm	37.2	36.9	0.0000	1.3	1.0-1.8	1.5	1.3-1.8
Q2: 161-165 cm	25.2	29.3		1.0	0.7-1.3	1.2	1.0-1.5
Q3: 166-168 cm	15.9	14.4		1.0	0.7-1.4	1.0	0.8-1.3
Q4: 169-190 cm	21.6	19.3		1	-	1	-
Pre-pregnancy BMI							
<18.5	10.4	5.6	0.0000	1.4	1.0-2.1	0.8	0.6-1.1
18.5-24.9	57.7	58.3		1	-	1	-
25-29.9	17.6	19.6		1.0	0.8-1.4	1.1	0.9-1.3
>=30	14.4	16.5		1.6	1.1-2.2	1.7	1.4-2.0
Nationality							
French	84.2	84.9	0.0044	1	-	1	-
Other Europe	2.9	2.8		0.8	0.4-1.6	0.8	0.6-1.2
North African	4.1	5.1		0.8	0.5-1.5	0.9	0.7-1.2
Sub-Saharan Africa	5.9	4.6		2.2	1.4-3.5	1.6	1.2-2.2
Other	2.9	2.6		1.2	0.6-2.2	1.1	0.8-1.6
Level of education							
Low ISCED 0-2	38.0	34.2	0.0000	2.0	1.5-2.8	1.5	1.3-1.8
Medium ISCED 3-5	39.4	42.0		1.4	1.0-1.8	1.3	1.1-1.5
High ISCED 6+	22.7	23.8		1	-	-	1
Smoking n° cigarettes/day during the 3rd trimester							
0	80.5	80.3	0.0068	1	-	1	-
1-9	14.1	14.1		1.1	0.8-1.5	1.2	1.0-1.4
>=10	5.4	5.6		1.0	0.6-1.6	1.1	0.9-1.5

a. F-test b. Adjusted Relative Risk Ratio

Note: ISCED 2011, International Standard Classification of Education 2011.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	6

Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6-7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	Described in the response to reviewer 2 (see comment 2) and reviewer 3 (see comment 4)
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	8-10

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-10
		(*b*) Report category boundaries when continuous variables were categorized	6-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Described in the response to reviewer 2 (see comment 2) and reviewer 3 (see comment 4)
Discussion			
Key results	18	Summarise key results with reference to study objectives	9-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Are risk factors for preterm and early term live singleton birth the same? A population-based study in France

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-018745.R2
Article Type:	Research
Date Submitted by the Author:	21-Nov-2017
Complete List of Authors:	Delnord, Marie; INSERM, UMR1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité, 53 avenue de l'Observatoire Blondel, Béatrice; INSERM, UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité Prunet, Caroline; INSERM, UMR1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité, 53 avenue de l'Observatoire Zeitlin, Jennifer; INSERM, UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, (Epopé). Center for Epidemiology and Statistics Sorbonne Paris Cité; Paris-Descartes University,
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Obstetrics and gynaecology, Paediatrics, Public health
Keywords:	early term birth, preterm birth, Population prevention, Perinatal Health Survey, population risk factors

SCHOLARONE™ Manuscripts

Are risk factors for preterm and early term live singleton birth the same? A population-based study in France

Marie DELNORD[1]*MSc, MA; Béatrice BLONDEL[1], PhD; Caroline PRUNET, MSc; Jennifer ZEITLIN[1], DSc
*INSERM U1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, Research Center for Epidemiology and Biostatistics Sorbonne Paris Cité (CRESS)

Affiliations:

1. Inserm UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team (Epopé), Centre for Epidemiology and Statistics Sorbonne Paris Cité, DHU Risks in pregnancy, Paris Descartes University, Paris, France

***Corresponding author**:
Ms. Marie Delnord
INSERM U1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, Research Center for Epidemiology and Biostatistics Sorbonne Paris Cité (CRESS)
Maternité de Port Royal, 53 Avenue de l' Observatoire, 75014 Paris FRANCE
Tel : +33 1 42 34 55 86 Fax: +33 1 43 26 89 79
Marie.delnord@inserm.fr

Word count:
Abstract: 222/300 words

Main text: 3230/4000 words

Abstract

Objectives: To investigate whether risk factors for preterm (<37 weeks gestation) and early term birth (37 and 38 weeks gestation) are similar.

Design: Nationally representative cross-sectional study of births

Setting: France in 2010

Participants: Live singleton births (N=14 326)

Primary and secondary outcome measures: Preterm and early term birth rates overall and by mode of delivery (spontaneous and indicated). Risk factors were maternal sociodemographic characteristics, previous preterm birth, height, pre-pregnancy body mass index (BMI) and smoking, assessed using multinomial regression models with full term births 39 weeks and over as the reference group.

Results: There were 5.5% preterm and 22.5% early term births. Common risk factors were: a previous preterm delivery (adjusted relative risk ratio aRRR=8.2 [95% CI: 6.2-10.7] and aRRR=2.4 [95% CI: 2.0-3.0] respectively), short stature, underweight (overall and in spontaneous deliveries), obesity (in indicated deliveries only), a low educational level, and Sub Saharan African origin. In contrast, primiparity was a risk factor only for preterm birth, aRRR=1.8 [95% CI: 1.5-2.2], while higher parity was associated with greater risk of early term birth.

Conclusions: Most population-level risk factors were common to both preterm and early term birth with the exception of primiparity, and BMI which differed by mode of onset of delivery. Our results suggest that preterm and early term birth share similar etiologies and thus potentially common strategies for prevention.

<u>Strengths and limitations of this study:</u>

- We had detailed information on prenatal social and demographic characteristics collected using a standardized maternal interview in a representative sample of births in France.
- We had few missing data for which we corrected using multiple imputation.
- We used multinomial regression to estimate preterm and early term birth adjusted relative risk ratios and their 95% confidence intervals by maternal characteristics using births reaching full term (i.e. births 39 weeks and over) as the reference.
- Because very preterm births represented 0.6% of births in our sample, we do not report associations by preterm GA subgroups.
- Our sample size may have been too small to detect low to moderate associations in less prevalent sub groups of women, such as heavy smokers, for instance.

Funding:

This work was supported by Paris Descartes University, Paris, France.

The French National Perinatal Survey 2010 was funded by the French Ministry of Health.

The funding agencies were not involved in the study.

Competing interests: No competing interests

Introduction

Preterm birth, defined as birth before 37 weeks of gestation, is a leading cause of perinatal mortality and morbidity. In Europe, preterm infants represent 75% of all neonatal deaths and 60% of all infant deaths (1). They are at risk of short and long-term neurocognitive and motor impairments, and display higher rates of chronic disease and premature death compared to term infants (1, 2). The prevention of preterm birth is a global priority, however preterm births are not the only gestational age subgroup at risk of adverse health outcomes (3, 4). Compared to being born full term, defined as between 39 and 41 weeks, early term birth at 37 and 38 weeks is associated with higher risks of neonatal mortality, more intensive care unit admissions (4), and higher health-related costs well into childhood for obstructive airway diseases, visual and motor disabilities (5).

There are large differences in rates and trends of preterm and early term births among countries with similar levels of development (1, 6-7). In Europe in 2010, preterm birth rates ranged between 4.1% and 8.2% while early term rates ranged between 15.6% and 30.8% (1); such heterogeneity across countries suggests that rate reductions may be possible. However, despite the significant public health burden (4, 8-10), little progress has been made in decreasing the number of these early births (6, 11, 12). The latest French recommendations for the prevention of spontaneous preterm birth focus on smoking cessation and on interventions for women with high risk pregnancies (i.e. cerclage, progesterone), but conclude that high quality evidence does not exist for other preventive strategies (13); this is partially due to the low predictive accuracy of diagnostic tools (11). As for early term birth, prevention efforts are recent, with a focus by professional societies in the United States on the reduction of indicated early term deliveries for non-medical reasons (14).

More research on the etiology of early delivery is required to orient prevention efforts and practice. There is recent evidence that in high-income countries, moderate and late preterm birth rates are associated with rates of early term birth (15). Positive associations between preterm and early term birth country rates suggest that common population-level determinants could underpin shifts in the gestational age distribution towards early delivery. Known maternal characteristics that contribute significantly to preterm birth rates and trends within countries include maternal age, underweight, obesity, and socioeconomic status (16). Early term and late preterm births also have worse neonatal outcomes compared to full term births (17). However, what is not known is which maternal characteristics related to preterm birth risk (1, 11, 16, 18) could also relate to early term birth (19). Thus in this study we aimed to identify maternal population determinants of preterm and early term birth overall and by mode of onset of delivery, i.e. spontaneous or indicated, using nationally representative data from the French National Perinatal Survey in 2010.

Materials and Methods

The French National Perinatal Survey 2010 (*Enquête Nationale Périnatale*, ENP) is based on a representative sample of births in Metropolitan France. The National Perinatal Surveys have been conducted periodically since 1995 and constitute part of the routine health information system for the surveillance of mothers and newborns in France (20). Data are collected on all live and stillbirths starting at 22 weeks of gestation or weighing at least 500g over the course of one week in all public and private maternity units. In 2010, there were 535 maternity units operating in metropolitan France of which one refused to participate (20) . For this study, we included singleton pregnancies ending in a live birth with a gestational age of 22 weeks or over (N=14,326 pregnant women). Multifetal pregnancies and stillbirths were excluded because of differences in delivery practices and etiology for these births.

Survey items on mothers' demographic characteristics (e.g. maternal age, parity), socioeconomic status (e.g. level of education), prenatal care and behaviors were collected during interviews with midwives or nurses in the postpartum ward. Other data on the delivery and newborn health were abstracted from the medical records by medical staff, and include information on the mode of onset of delivery, pre-existing maternal medical conditions (hypertension, diabetes), as well as routine indicators of neonatal health at birth(20). We defined indicated deliveries as those with a provider-initiated mode of onset, i.e. either induction of labor or prelabor cesarean section. Although there may have been differences in the distribution of maternal characteristics by region, our total sample size precluded us carrying out more detailed analyses (24 regions in total, N min=58 and N max= 1312 live singleton births).

Our main outcomes were preterm and early term birth. These were defined respectively as births 22-36 completed weeks of gestation and 37-38 completed weeks overall and by mode of onset (spontaneous or indicated). Gestational age was based on the best obstetrical estimate. In France, nearly all women have a first trimester ultrasound for dating the pregnancy (20). The upper limit of gestational age included in the sample was 44 weeks, but very few deliveries were postterm (N=49, 0.4% at 42 weeks and over). We also do not report associations by preterm GA subgroups, in particular for very preterm births (N=122, 0.9%)

We selected risk factors based on a scoping review of the scientific literature, including recent research on preterm birth risk factors in France (18, 21). Some preterm birth exposures that were available in the French National Perinatal Survey were omitted from our study because of their low prevalence in the sample (i.e. use of fertility treatments: <4%, diabetes: <2%, and chronic hypertension: 2%), women with these conditions however were not excluded from the study.

We included the following variables in our analysis: maternal age (<20, 20-24, 25-29, 30-34, >=35 years old), parity (1,2-3,4+), previous preterm birth, nationality (French, Other European, North African, Sub-Saharan African, Other), maternal height presented in quartiles

(Q1: 100-160cm, Q2: 161-165cm, Q3: 166-168cm, Q4:169-190cm), pre-pregnancy body mass index (BMI), defined as underweight, normal, overweight, and obese women for BMIs <18.5, 18.5-24.9, 25-29.9, ≥30 respectively, level of education, and smoking during the third trimester. Level of completed education was defined based on the ISCED 2011 classification: low educational level ISCED 0-2 (i.e. up to lower secondary education completed), medium educational level ISCED 3-5 (i.e. upper secondary education or short cycle tertiary education completed), high educational level ISCED 6-7 (Bachelors' equivalent or higher). BMI is a measure of body mass that is independent of height in adults; therefore both variables were included in the study (22).

The National Council on Statistical Information (Comité du Label) and the French Commission on Information Technology and Liberties (CNIL) approved the French National Perinatal Surveys (Enquête Nationale Périnatale 2010)

<u>Analysis strategy</u>

We first compared the distributions of preterm and early term births by maternal characteristics. We included all maternal exposures hypothesized to be associated with preterm delivery in the multivariable analyses (18). We used multinomial regression to estimate preterm and early term birth adjusted relative risk ratios (aRRR) and their 95% confidence intervals by maternal characteristics using births reaching full term (i.e. births 39 weeks and over) as the reference. Adjusted relative risk ratios are similar to adjusted odds ratios in binary logistic regression.

In the mode of onset analyses, we computed relative risk ratios of spontaneous and indicated preterm and early delivery using the same full term reference population (i.e. all births 39 weeks and over, regardless of mode of onset). We used this reference population as we considered spontaneous and indicated births as two sub-types of our outcome (early delivery). Indicated deliveries at full term are principally for prolonged pregnancy, previous cesarean section and can be based on maternal request, indications which are much less common before 39 weeks (23, 24). Data were analysed using STATA 13.0 software (StataCorp LP, College Station, TX, USA).

There were 14 326 live singleton births in the survey of which 65 were missing GA data. We had less than 1% missing data on mode of onset of labor (i.e. spontaneous or provider-initiated delivery) and less than 5% missing sociodemographic data (i.e. nationality and level of education). There were 4% missing data on previous preterm birth and 6% missing on anthropometric characteristics (i.e. height or BMI). Although individual proportions of missing data were low, complete cases were only 86% of the total and therefore we imputed missing values (except the outcome) using multivariate imputation by chained equations. We performed 100 imputations using all available covariates (25). Descriptive and multivariate analyses were done on the imputed dataset. Because data were imputed, we used F-tests to look at differences in the distributions of maternal characteristics by GA subgroup (26).

Results

Table 1 provides descriptive statistics on our sample. We included 14 261 live singleton pregnancies with GA data available. The overall rate of preterm birth was 5.5% and early term birth was 22.6%. In the reference population of women with a full term birth, 2.4% were aged under 20 and 18.3% over 35 years of age; 44.1% were primiparous and 6.9% were parity 4 or more; 2.2% had a previous preterm birth, 7.8% were underweight, 9.4% were overweight and 16.4% smoked in the 3rd trimester of pregnancy. The risk profiles of mothers with a preterm and early term infant were different. These mothers were more likely to be older, have a previous preterm birth, be of shorter stature, with a lower level of education, and smoke. Mothers with a preterm birth were more likely to be primipara whereas mothers with an early term birth were more likely to be multipara, compared to mothers with a term birth.

In multinomial multivariable models, most of these associations persisted; common population determinants for preterm and early term birth were: a previous preterm birth, shorter stature, underweight, sub-Saharan nationality, and a low level of education. There were some differences in the impact of these risk factors: a previous preterm birth was a stronger risk factor for preterm birth than early term birth (aRRR 8.2 vs. 2.4 respectively); maternal underweight and Sub-Saharan nationality were also stronger risk factors for preterm compared to early term birth. Primipara were at risk for preterm birth only (aRRR 1.8 [1.5-2.2]), whereas grand multipara (parity 4+) were at higher risk of early term birth. After adjustment, advanced maternal age, and smoking during the third trimester were no longer associated with increased risks of delivery before 39 weeks.

In Table 2, we display the associations between spontaneous preterm, and early term births by maternal characteristics. Out of all births, 2.8% were spontaneous preterm births and 13.6% were spontaneous early term births. Common risk factors were: a previous preterm birth, short stature, maternal underweight, foreign nationality (i.e. Other European), and a low level of education. There were some differences in the impact of these risk factors. Underweight was a stronger risk factor for spontaneous preterm than early term birth: aRRR 1.9[1.4-2.6] vs aRRR 1.3[1.1-1.5] respectively, and overweight women displayed a reduced risk of spontaneous early term delivery. Primipara were at risk of preterm birth but not early term birth. Smoking during the third trimester was associated with a moderately increased risk of spontaneous preterm delivery, although the confidence interval included 1: aRRR 1.5[1.0-2.2]. The aRRR was lower and non-significant for early term birth: 1.2[0.9-1.5].

In Table 3, we display the associations between indicated preterm and early term birth by maternal characteristics. Out of all births, 2.6% were indicated preterm deliveries and 8.8% were indicated early term deliveries. Most risk factors were common to indicated preterm and early term birth including: advanced maternal age, a previous preterm birth, short stature, obesity (aRRR 1.6(1.1-2.2] preterm, and aRRR 1.7[1.4-2.0] early term), sub-Saharan African origin (aRRR 2.2[1.4-3.5] preterm, and aRRR 1.6[1.2-2.2] for early term), and a low level of education, after adjusting on all other covariates. Primipara were only at risk for indicated preterm birth, aRRR=2.1[1.6-2.7]; while parity 4+ was associated with greater risk of indicated early term birth aRRR= 1.3 [1.1-1.6].

When we compare findings from our mode of onset analyses, Table 2 and 3 show that risk factors for delivery before 39 weeks are the same in spontaneous preterm and early term deliveries, and indicated preterm and early term deliveries - with the exception of BMI. Underweight was a risk factor for spontaneous delivery before 39 weeks (aRRR 1.9[1.4-2.6] for preterm and aRRR 1.3[1.1-1.5] for early term), whereas overweight was a risk factor for indicated delivery before 39 weeks (aRRR 1.6(1.1-2.2] preterm, and aRRR 1.7[1.4-2.0] early term).

Discussion

Our study provides new insight into the population determinants of preterm and early term birth by mode of onset of delivery. We identified shared risk factors for delivery before 39 weeks which were: a previous preterm birth, short stature, a low level of education, underweight (overall and in spontaneous deliveries), obesity (in indicated deliveries only), and foreign origin (for other European and sub-Saharan nationals). The impact of most risk factors was greater for preterm birth compared to early term birth, and primiparity was a risk factor for preterm birth but not early term birth.

A strength of our study is the availability of detailed population-based information on prenatal, social and demographic characteristics collected using a standardized maternal interview in a representative sample of births in France. We had few missing data for which we corrected using multiple imputation. In this study, we focused on the broader population determinants of early delivery that contribute to overall rates of preterm and early term birth in France. We conducted analyses for spontaneous and indicated deliveries separately to highlight potential differences in risk factors between these subtypes of preterm birth for which some medical maternal and fetal factors differ (27). We did not include pregnancy complications in our analyses as these constitute intermediate variables between population characteristics and the risk of preterm and early term deliveries (28, 29).

Our study also has some limitations. Our sample size may have been too small to detect low to moderate associations in less prevalent subgroups of women, such as heavy smokers, for instance. Similarly, we did not analyze some risk factors available in our dataset which had a low prevalence (i.e. preexisting medical conditions: diabetes, hypertension), or carry out analyses by region although there may have been differences in the distribution of maternal characteristics. We did not carry out separate analyses for very preterm births, and risk factors for this vulnerable subpopulation may differ from those for moderate and late preterm births at 32-36 weeks of gestation. Finally, we did not correct for multiple comparisons to maintain adequate power to carry out the study (30).

The strongest single predictor of both preterm and early term delivery was a previous preterm birth (overall and by mode of onset of delivery), as confirmed in other population-based studies (31, 32) and a recent systematic review which showed a 30% risk of recurrent spontaneous preterm birth (sPTB) following sPTB in singleton pregnancies (33) . In contrast, first-time mothers were more likely to deliver preterm, but not early term indicating that the shape of the risk distribution for early delivery in primipara may slightly differ from the overall GA distribution which peaks around 38-40 weeks of gestation. Fertility trends determining the proportion of primiparous women may therefore contribute to differences in preterm and early term birth rates across countries.

Socio-demographic characteristics, measured by a lower level of education and mother's country of birth, were also associated with earlier delivery overall and by mode of onset of delivery. Maternal educational level is a well-documented risk factor for preterm birth risk and recent findings from Canada have shown an association with early term birth (34-36). Exposures related to mothers' general quality of life and well-being (i.e. living and employment conditions, air pollution, exposure to stress) could mediate the association with social status via physiological pathways (37-41). In France, Prunet et al. showed that social status was associated with preterm birth risk independently of use of medical care during pregnancy (18). As for the association with foreign origin, our results are consistent with the literature showing higher risks of preterm birth among women from Sub-Saharan Africa (42).

There were common anthropometric determinants of delivery before 39 weeks overall, although there were differences by mode of onset of delivery. Our findings confirm previous research on the association between preterm birth and short stature (43, 44) and we provide new evidence on the association with early term birth. Thinness is often associated with spontaneous preterm birth but the association between GA and overweight is less clear (45-47). A greater prevalence of comorbities in obese women could contribute to the excess in indicated delivery (48), which we observed. In contrast, the decreased risk of spontaneous preterm and early term delivery in women with BMIs over 30 could be due to specific delivery practices, and greater levels of obstetrical interventions for obese women in general (49).

Finally, smoking and advanced maternal age are traditionally cited as preterm birth risk factors (50, 51); while there was an increased risk for spontaneous preterm birth in heavy smokers, and an increased risk for indicated preterm and early term delivery in mothers over 35, associations with either variable in the overall analyses were not statistically significant.

Previous data from France, also showed a limited impact of smoking on overall preterm birth risk whereas associations were stronger in studies from other countries (20, 21).

Our findings showing common risk patterns for preterm and early term births suggest a shared etiology for these births overall, with some exceptions for primiparous women and by mode of onset of delivery for BMI. These results raise questions about the appropriate definition of preterm birth, and the GA thresholds which should be used (52). Our findings by mode of onset of delivery are also consistent with two reports documenting shared pregnancy complications for spontaneous preterm and early term deliveries (28, 29). Delivery following spontaneous labour even close to full term may be a result of pathological processes (28), with a slightly more heterogeneous etiology for medically indicated late preterm and early term phenotypes (i.e. anemia and gastrointestinal disease were associated with late preterm but not early term delivery) (29). Future research associating maternal exposures with pregnancy complications such as: diabetes mellitus, infection and inflammation, placental ischemia, polyhydramnios and oligohydramnios, which are related to spontaneous and indicated preterm and early term births could provide insight into the mechanisms underpinning early delivery (28).

In conclusion, our population-based study shows that there are several shared maternal prenatal and socio-demographic risk factors for delivery before full term (i.e. 39 weeks and over). Because strategies to reduce individual risk of preterm birth have had a limited impact on overall rate reductions (11), investing in broader population-based interventions may be justified, including those targeting maternal pre-pregnancy BMI and social inequalities in health (48). Moreover, due to the large volume of births at 37-38 weeks, even small point percentage reductions are likely to impact on health and needs for educational and social services. Each additional week of gestation after 35 weeks reduces specific delays in communication, personal-social, fine-motor, and problem-solving skills up until 24 months of age, and the population attributable fraction for poor achievement in school is highest among early term births (53, 54). The existence of shared risk factors for both gestational age subgroups and the greater number of early term births compared to preterm births provides greater power to investigate the mechanisms leading to early delivery, and supports the use of a broader research paradigm for preterm birth prevention.

Contributions: MD, BB and JZ contributed to the study design, and interpretation of the data. MD, BB, and CP participated in the data collection and analysis. MD and JZ drafted the manuscript, BB provided critical revisions. All authors have read and approved the final version of the manuscript.

Data sharing statement: Instructions for applying for public access data from the French National Perinatal Survey are available upon request from the authors.

References

1. Euro-Peristat project with SCPE and EUROCAT, European Perinatal Health Report. The health and care of pregnant women and babies in Europe in 2010. 2013 May 2013. Report No.
2. Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller AB, et al. Born too soon: the global epidemiology of 15 million preterm births. Reproductive health. 2013;10 Suppl 1:S
3. Zhang X, Kramer MS. Variations in mortality and morbidity by gestational age among infants born at term. The Journal of pediatrics. 2009;154(3):358-62, 62 e1.
4. Sengupta S, Carrion V, Shelton J, Wynn RJ, Ryan RM, Singhal K, et al. Adverse neonatal outcomes associated with early-term birth. JAMA pediatrics. 2013;167(11):1053-9
5. Helle E, Andersson S, Hakkinen U, Jarvelin J, Eskelinen J, Kajantie E. Morbidity and Health Care Costs After Early Term Birth. Paediatric and perinatal epidemiology. 2016;30(6):533-40.
6. Richards JL, Kramer MS, Deb-Rinker P, Rouleau J, Mortensen L, Gissler M, et al. Temporal Trends in Late Preterm and Early Term Birth Rates in 6 High-Income Countries in North America and Europe and Association With Clinician-Initiated Obstetric Interventions. JAMA. 2016;316(4):410-9.
7. Zeitlin J, Szamotulska K, Drewniak N, Mohangoo AD, Chalmers J, Sakkeus L, et al. Preterm birth time trends in Europe: a study of 19 countries. BJOG. 2013;120(11):1356-65.
8. Jacob J, Lehne M, Mischker A, Klinger N, Zickermann C, Walker J. Cost effects of preterm birth: a comparison of health care costs associated with early preterm, late preterm, and full-term birth in the first 3 years after birth. The European journal of health economics : HEPAC : health economics in prevention and care. 2016.
9. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. Lancet. 2008;371(9608):261-9.
10. Crump C, Sundquist K, Winkleby MA, Sundquist J. Early-term birth (37-38 weeks) and mortality in young adulthood. Epidemiology. 2013;24(2):270-6.
11. Chang HH, Larson J, Blencowe H, Spong CY, Howson CP, Cairns-Smith S, et al. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. Lancet. 2013;381(9862):223-34.

12. Lawn JE, Kinney MV, Belizan JM, Mason EM, McDougall L, Larson J, et al. Born too soon: accelerating actions for prevention and care of 15 million newborns born too soon. Reproductive health. 2013;10 Suppl 1:S6.
13. Sentilhes L, Senat MV, Ancel PY, Azria E, Benoist G, Blanc J, et al. Prevention of spontaneous preterm birth: Guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). European journal of obstetrics, gynecology, and reproductive biology. 2017;210:217-24.
14. ACOG Committee Opinion No 579: Definition of term pregnancy. Obstetrics and gynecology. 2013;122(5):1139-40.
15. Delnord M, Mortensen L, Hindori-Mohangoo AD, Blondel B, Gissler M, Kramer MR, et al. International variations in the gestational age distribution of births: an ecological study in 34 high-income countries. The European Journal of Public Health. 2017:ckx131.
16. Delnord M, Blondel B, Zeitlin J. What contributes to disparities in the preterm birth rate in European countries? Current opinion in obstetrics & gynecology. 2015;27(2):133-42.
17. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Neonatal morbidity associated with late preterm and early term birth: the roles of gestational age and biological determinants of preterm birth. International journal of epidemiology. 2014;43(3):802-14.
18. Prunet C, Delnord M, Saurel-Cubizolles MJ, Goffinet F, Blondel B. Risk factors of preterm birth in France in 2010 and changes since 1995: Results from the French National Perinatal Surveys. Journal de gynecologie, obstetrique et biologie de la reproduction. 2016.
19. Raju TN. Moderately preterm, late preterm and early term infants: research needs. Clinics in perinatology. 2013;40(4):791-7.
20. Blondel B, Lelong N, Kermarrec M, Goffinet F, National Coordination Group of the National Perinatal S. Trends in perinatal health in France from 1995 to 2010. Results from the French National Perinatal Surveys. Journal de gynecologie, obstetrique et biologie de la reproduction. 2012;41(4):e1-e15.
21. Prunet C, Delnord M, Saurel-Cubizolles MJ, Goffinet F, Blondel B. Risk factors of preterm birth in France in 2010 and changes since 1995: Results from the French National Perinatal Surveys. Journal of gynecology obstetrics and human reproduction. 2017;46(1):19-28.
22. Heymsfield SB, Heo M, Thomas D, Pietrobelli A. Scaling of body composition to height: relevance to height-normalized indexes. The American journal of clinical nutrition. 2011;93(4):736-40.
23. Roman H, Blondel B, Breart G, Goffinet F. Do risk factors for elective cesarean section differ from those of cesarean section during labor in low risk pregnancies? Journal of perinatal medicine. 2008;36(4):297-305.
24. Coulm B, Blondel B, Alexander S, Boulvain M, Le Ray C. Elective induction of labour and maternal request: a national population-based study. BJOG : an international journal of obstetrics and gynaecology. 2016;123(13):2191-7.
25. Graham JW, Olchowski AE, Gilreath TD. How many imputations are really needed? Some practical clarifications of multiple imputation theory. Prevention science : the official journal of the Society for Prevention Research. 2007;8(3):206-13.
26. van Ginkel JR, Kroonenberg PM. Analysis of Variance of Multiply Imputed Data. Multivariate behavioral research. 2014;49(1):78-91.
27. Savitz DA, Dole N, Herring AH, Kaczor D, Murphy J, Siega-Riz AM, et al. Should spontaneous and medically indicated preterm births be separated for studying aetiology? Paediatric and perinatal epidemiology. 2005;19(2):97-105.
28. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Biological determinants of spontaneous late preterm and early term birth: a retrospective cohort study. BJOG : an international journal of obstetrics and gynaecology. 2015;122(4):491-9.
29. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Maternal, fetal, and placental conditions associated with medically indicated late preterm and early term delivery: a retrospective study. BJOG : an international journal of obstetrics and gynaecology. 2016;123(5):763-70.

30. Feise RJ. Do multiple outcome measures require p-value adjustment? BMC medical research methodology. 2002;2:8.
31. Yang J, Baer RJ, Berghella V, Chambers C, Chung P, Coker T, et al. Recurrence of Preterm Birth and Early Term Birth. Obstetrics and gynecology. 2016;128(2):364-72.
32. Ferrero DM, Larson J, Jacobsson B, Di Renzo GC, Norman JE, Martin JN, Jr., et al. Cross-Country Individual Participant Analysis of 4.1 Million Singleton Births in 5 Countries with Very High Human Development Index Confirms Known Associations but Provides No Biologic Explanation for 2/3 of All Preterm Births. PloS one. 2016;11(9):e0162506.
33. Phillips C, Velji Z, Hanly C, Metcalfe A. Risk of recurrent spontaneous preterm birth: a systematic review and meta-analysis. BMJ open. 2017;7(6):e015402.
34. Auger N, Leduc L, Naimi AI, Fraser WD. Delivery at Term: Impact of University Education by Week of Gestation. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC. 2016;38(2):118-24.
35. Oftedal AM, Busterud K, Irgens LM, Haug K, Rasmussen S. Socio-economic risk factors for preterm birth in Norway 1999-2009. Scandinavian journal of public health. 2016;44(6):587-92.
36. Poulsen G, Strandberg-Larsen K, Mortensen L, Barros H, Cordier S, Correia S, et al. Exploring educational disparities in risk of preterm delivery: a comparative study of 12 European birth cohorts. Paediatric and perinatal epidemiology. 2015;29(3):172-83.
37. Stieb DM, Chen L, Eshoul M, Judek S. Ambient air pollution, birth weight and preterm birth: a systematic review and meta-analysis. Environmental research. 2012;117:100-11.
38. Staneva A, Bogossian F, Pritchard M, Wittkowski A. The effects of maternal depression, anxiety, and perceived stress during pregnancy on preterm birth: A systematic review. Women and birth : journal of the Australian College of Midwives. 2015;28(3):179-93.
39. Ncube CN, Enquobahrie DA, Albert SM, Herrick AL, Burke JG. Association of neighborhood context with offspring risk of preterm birth and low birthweight: A systematic review and meta-analysis of population-based studies. Social science & medicine. 2016;153:156-64.
40. Zeitlin J, Combier E, Levaillant M, Lasbeur L, Pilkington H, Charreire H, et al. Neighbourhood socio-economic characteristics and the risk of preterm birth for migrant and non-migrant women: a study in a French district. Paediatric and perinatal epidemiology. 2011;25(4):347-56.
41. Sorbye IK, Daltveit AK, Sundby J, Vangen S. Preterm subtypes by immigrants' length of residence in Norway: a population-based study. BMC pregnancy and childbirth. 2014;14:239.
42. Gagnon AJ, Zimbeck M, Zeitlin J, Collaboration R, Alexander S, Blondel B, et al. Migration to western industrialised countries and perinatal health: a systematic review. Social science & medicine. 2009;69(6):934-46.
43. Derraik JG, Lundgren M, Cutfield WS, Ahlsson F. Maternal Height and Preterm Birth: A Study on 192,432 Swedish Women. PloS one. 2016;11(4):e0154304.
44. Han Z, Lutsiv O, Mulla S, McDonald SD. Maternal height and the risk of preterm birth and low birth weight: a systematic review and meta-analyses. J Obstet Gynaecol Can. 2012;34(8):721-46.
45. Cnattingius S, Villamor E, Johansson S, Edstedt Bonamy AK, Persson M, Wikstrom AK, et al. Maternal obesity and risk of preterm delivery. Jama. 2013;309(22):2362-70.
46. Torloni MR, Betran AP, Daher S, Widmer M, Dolan SM, Menon R, et al. Maternal BMI and preterm birth: a systematic review of the literature with meta-analysis. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2009;22(11):957-70.
47. Lynch AM, Hart JE, Agwu OC, Fisher BM, West NA, Gibbs RS. Association of extremes of prepregnancy BMI with the clinical presentations of preterm birth. American journal of obstetrics and gynecology. 2014;210(5):428 e1-9.
48. Gould JB, Mayo J, Shaw GM, Stevenson DK, March of Dimes Prematurity Research Center at Stanford University School of M. Swedish and American studies show that initiatives to decrease maternal obesity could play a key role in reducing preterm birth. Acta paediatrica. 2014;103(6):586-91.

49. Hermann M, Le Ray C, Blondel B, Goffinet F, Zeitlin J. The risk of prelabor and intrapartum cesarean delivery among overweight and obese women: possible preventive actions. American journal of obstetrics and gynecology. 2015;212(2):241 e1-9.
50. Savitz DA, Murnane P. Behavioral influences on preterm birth: a review. Epidemiology. 2010;21(3):291-9.
51. Luke B, Brown MB. Elevated risks of pregnancy complications and adverse outcomes with increasing maternal age. Human reproduction. 2007;22(5):1264-72.
52. Kirby RS, Wingate MS. Late preterm birth and neonatal outcome: is 37 weeks' gestation a threshold level or a road marker on the highway of perinatal risk? Birth. 2010;37(2):169-71.
53. Dueker G, Chen J, Cowling C, Haskin B. Early developmental outcomes predicted by gestational age from 35 to 41weeks. Early human development. 2016;103:85-90.
54. Searle AK, Smithers LG, Chittleborough CR, Gregory TA, Lynch JW. Gestational age and school achievement: a population study. Archives of disease in childhood Fetal and neonatal edition. 2017.

Table 1: Associations between maternal characteristics and risks of preterm (<37 weeks) and early term birth (37-38 weeks) using births reaching full term (i.e. 39 weeks and over) as the reference in a representative sample of births in France in 2010

		<37 weeks GA % N=782	37-38 weeks GA % N=3010	≥39 weeks GA % N=10269	p[a]	<37 weeks GA aRRRs[b]	<37 weeks GA 95% CI	37-38 weeks GA aRRRs[b]	37-38 weeks GA 95% CI
Maternal age									
<20 years	346	3.9	2.3	2.4	0.005	1.0	0.7-1.6	0.9	0.7-1.2
20-24 years	2078	16.3	14.5	14.5		0.9	0.8-1.2	1.0	0.9-1.2
25-29 years	4737	32.8	31.7	33.7		Ref.	-	Ref.	-
30-34 years	4380	27.9	30.1	31.1		1.0	0.8-1.2	1.0	0.9-1.1
>=35 years	2720	19.1	21.4	18.3		1.1	0.9-1.4	1.2	1.0-1.3
Parity					<0.001				
1	6165	49.8	38.9	44.1		1.8	1.5-2.2	0.9	0.8-1.0
2-3	6980	39.8	50.8	49.1		Ref.		Ref.	-
4+	1116	10.4	10.3	6.9		1.2	0.9-1.6	1.2	1.1-1.4
Previous preterm birth					<0.001				
No	13740	86.6	94.1	97.8		Ref.	-	Ref.	-
Yes	521	13.4	5.9	2.2		8.2	6.2-10.7	2.4	2.0-3.0
Maternal height					<0.001				
Q1: 100-160 cm	4365	37.7	34.6	28.8		1.4	1.1-1.7	1.4	1.2-1.6
Q2: 161-165 cm	4143	25.9	29.9	29.0		1.0	0.8-1.2	1.2	1.1-1.4
Q3: 166-168 cm	2440	15.2	15.2	17.9		0.9	0.7-1.2	1.0	0.9-1.2
Q4: 169-190 cm	3313	21.3	20.4	24.3		Ref.	-	Ref.	-
Pre-pregnancy BMI[c]					0.307				
<18.5	1177	12.9	8.5	7.8		1.7	1.3-2.2	1.1	1.0-1.3
18.5-25.9	9190	59.9	63.6	65.0		Ref.	-	Ref.	-
25-29.9	2472	15.5	16.6	17.7		0.9	0.7-1.1	0.9	0.8-1.0
>=30	1422	11.7	11.2	9.4		1.2	1.0-1.6	1.1	1.0-1.3
Nationality					0.043				
French	12360	84.0	86.3	87.0		Ref.	-	Ref.	-
Other European	470	4.2	3.3	3.2		1.2	0.8-1.8	1.0	0.8-1.2
North African	685	4.9	4.4	4.9		1.1	0.7-1.5	0.8	0.7-1.0
Sub-Saharan Africa	392	4.5	3.3	2.4		1.8	1.2-2.6	1.3	1.0-1.6
Other	354	2.5	2.7	2.4		1.0	0.6-1.6	1.1	0.8-1.4
Level of education[d]									
Low ISCED 0-2	4054	37.5	31.9	26.7	<0.001	1.7	1.3-2.1	1.2	1.1-1.4
Medium ISCED 3-5	5883	38.8	40.6	41.7		1.2	1.0-1.5	1.1	1.0-1.2
High ISCED 6+	4324	23.7	27.6	31.7		Ref.	-	Ref.	-
Smoking n° cigarettes/day during the 3[rd] trimester					<0.001				
0	11814	79.1	81.4	83.6		Ref.	-	Ref.	-
1-9	1757	13.9	12.8	12.1		1.0	0.8-1.3	1.0	0.9-1.2
>=10	690	7.0	5.8	4.4		1.3	0.9-1.8	1.1	0.9-1.4

Note: a. F-test b. Adjusted Relative Risk Ratio c. Body Mass Index: BMI d. ISCED 2011, International Standard Classification of Education 2011
Ref. indicates the reference category for each variable

Table 2: Associations between maternal characteristics and risks of spontaneous preterm (<37 weeks) and early term birth (37-38 weeks) using births reaching full term (i.e. 39 weeks and over, N=10269) as the reference in a representative sample of births in France in 2010

	<37 weeks GA % N=405	37-38 weeks GA % N=1949	p[a]	<37 weeks GA aRRRs[b]	95% CI	37-38 weeks GA aRRRs[b]	95% CI
Maternal age							
<20 years	3.7	2.5	0.002	1.0	0.6-1.8	1.0	0.7-1.4
20-24 years	19.1	16.2		1.1	0.8-1.5	1.1	0.9-1.3
25-29 years.	34.9	34.4		Ref.	-	Ref.	-
30-34 years	24.2	30.1		0.8	0.6-1.0	0.9	0.8-1.0
>=35 years	18.1	16.8		1.0	0.7-1.3	0.8	0.7-1.0
Parity							
1	48.4	40.5	0.004	1.6	1.3-2.1	0.9	0.8-1.0
2-3	40.8	51.1		Ref.	-	Ref.	
4	10.8	8.3		1.3	0.9-1.9	1.2	1.0-1.4
Previous preterm birth							
No	84.6	94.5	<0.001	Ref.	-	Ref.	-
Yes	15.4	5.5		9.3	6.6-13.0	2.4	1.9-3.1
Maternal height							
Q1: 100-160 cm	38.2	33.0	<0.001	1.4	1.1-1.9	1.3	1.1-1.5
Q2: 161-165 cm	26.4	30.1		1.0	0.8-1.4	1.2	1.0-1.4
Q3: 166-168 cm	14.5	15.7		0.9	0.6-1.3	1.0	0.9-1.2
Q4: 169-190 cm	21.0	21.1		Ref.	-	Ref.	-
Pre-pregnancy BMI[c]							
<18.5	15.3	10.4	<0.001	1.9	1.4-2.6	1.3	1.1-1.5
18.5-24.9	61.9	67.1		Ref.	-	Ref.	-
25-29.9	13.6	14.7		0.8	0.6-1.0	0.8	0.7-0.9
>=30	9.3	7.8		0.9	0.6-1.3	0.7	0.6-0.9
Nationality							
French	83.7	87.1	0.6213	Ref.	-	Ref.	-
Other Europe	5.4	3.7		1.5	1.0-2.5	1.1	0.8-1.4
North African	5.7	3.9		1.2	0.8-2.0	0.8	0.6-1.0
Sub-Saharan Africa	3.1	2.5		1.2	0.7-2.3	1.0	0.7-1.4
Other	2.1	2.8		0.8	0.4-1.7	1.1	0.8-1.5
Level of education[d]							
Low ISCED 0-2	37.1	30.4	<0.001	1.4	1.0-1.9	1.1	0.9-1.3
Medium ISCED 3-5	38.4	39.7		1.1	0.8-1.4	1.0	0.9-1.1
High ISCED 6+	24.5	30.0		Ref.	-	Ref.	-
Smoking n° cigarettes/day during the 3rd trimester							
0	78.0	82.2	<0.001	Ref.	-	Ref.	-
1-9	13.5	11.9		1.0	0.7-1.3	0.9	0.8-1.1
>=10	8.5	5.9		1.5	1.0-2.2	1.2	0.9-1.5

Note: a. F-test b. Adjusted Relative Risk Ratio c. Body Mass Index: BMI d. ISCED 2011, International Standard Classification of Education 2011
Ref. indicates the reference category for each variable

Table 3: Associations between maternal characteristics and risks of indicated preterm (<37 weeks) and early term birth (37-38 weeks) using births reaching full term (i.e. 39 weeks and over, N=10269) as the reference in a representative sample of births in France in 2010

	<37 weeks GA % N=374	37-38 weeks GA % N=1259	p[a]	<37 weeks GA aRRRs[b]	95% CI	37-38 weeks GA aRRRs[b]	95% CI
Maternal age							
<20 years	4.1	1.9	0.0000	1.1	0.6-2.0	0.9	0.6-1.4
20-24 years	13.5	11.9		0.8	0.6-1.1	0.9	0.8-1.2
25-29 years	30.5	27.6		Ref.	-	Ref.	-
30-34 years	31.6	30.1		1.3	1.0-1.7	1.2	1.0-1.4
>=35 years	20.3	28.4		1.4	1.0-1.9	1.8	1.5-2.1
Parity							
1	51.5	36.6	0.0000	2.1	1.6-2.7	1.0	0.9-1.2
2-3	38.8	50.3		Ref.	-	Ref.	-
4	9.7	13.2		1.1	0.7-1.6	1.3	1.1-1.6
Previous preterm birth							
Yes	89.0	93.5	0.0000	6.6	4.5-9.7	2.5	1.9-3.3
No	11.0	6.5		Ref.	-	Ref.	-
Maternal height							
Q1: 100-160 cm	37.2	36.9	0.0000	1.3	1.0-1.8	1.5	1.3-1.8
Q2: 161-165 cm	25.2	29.3		1.0	0.7-1.3	1.2	1.0-1.5
Q3: 166-168 cm	15.9	14.4		1.0	0.7-1.4	1.0	0.8-1.3
Q4: 169-190 cm	21.6	19.3		Ref.	-	Ref.	-
Pre-pregnancy BMI[c]							
<18.5	10.4	5.6	0.0000	1.4	1.0-2.1	0.8	0.6-1.1
18.5-24.9	57.7	58.3		Ref.	-	Ref.	-
25-29.9	17.6	19.6		1.0	0.8-1.4	1.1	0.9-1.3
>=30	14.4	16.5		1.6	1.1-2.2	1.7	1.4-2.0
Nationality							
French	84.2	84.9	0.0044	Ref.	-	Ref.	-
Other Europe	2.9	2.8		0.8	0.4-1.6	0.8	0.6-1.2
North African	4.1	5.1		0.8	0.5-1.5	0.9	0.7-1.2
Sub-Saharan Africa	5.9	4.6		2.2	1.4-3.5	1.6	1.2-2.2
Other	2.9	2.6		1.2	0.6-2.2	1.1	0.8-1.6
Level of education[d]							
Low ISCED 0-2	38.0	34.2	0.0000	2.0	1.5-2.8	1.5	1.3-1.8
Medium ISCED 3-5	39.4	42.0		1.4	1.0-1.8	1.3	1.1-1.5
High ISCED 6+	22.7	23.8		Ref.	-	Ref.	-
Smoking n° cigarettes/day during the 3rd trimester							
0	80.5	80.3	0.0068	Ref.	-	Ref.	-
1-9	14.1	14.1		1.1	0.8-1.5	1.2	1.0-1.4
>=10	5.4	5.6		1.0	0.6-1.6	1.1	0.9-1.5

Note: a. F-test b. Adjusted Relative Risk Ratio c. Body Mass Index: BMI d. ISCED 2011, International Standard Classification of Education 2011
Ref. indicates the reference category for each variable

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	6

Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6-7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	Described in the response to reviewer 2 (see comment 2) and reviewer 3 (see comment 4)-Revision 1
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	NA

Outcome data	15*	Report numbers of outcome events or summary measures	8-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-10
		(*b*) Report category boundaries when continuous variables were categorized	6-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Described in the response to reviewer 2 (see comment 2) and reviewer 3 (see comment 4)- Revision 1
Discussion			
Key results	18	Summarise key results with reference to study objectives	9-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.