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BMJ Open Do smoking abstinence periods among pregnant smokers improve birth weight? A secondary analysis of a randomised, controlled trial

Ivan Berlin ¹, Leontine Goldzahl,² Florence Jusot,³ Noemi Berlin⁴

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¹Département de Pharmacologie Médicale, Hôpitaux Universitaires Pitié Salpêtrière – Charles Foix, Paris, France
²ISEG School of Management, Université de Lille, Lille, France
³Paris Dauphine University, Paris, France
⁴CNRS, EconomiX, Université Paris Nanterre, Nanterre, France

Correspondence to
Dr Ivan Berlin;
ivan.berlin@aphp.fr

ABSTRACT

Objectives Maternal smoking during pregnancy is associated with low birth weight (LBW). Reduction of cigarette consumption does not seem to improve birth weight but it is not known whether implementation of periods of smoking abstinence improves it. We assessed whether the number of 7-day periods of smoking abstinence during pregnancy may help reduce the number of newborns with LBW.

Design and setting Secondary analysis of a randomised, controlled, multicentre, smoking cessation trial among pregnant smokers.

Participants Pregnant women were included at <18 weeks of gestational age and assessed at face-to-face, monthly visits. Data of 407 singleton live births were analysed.

Primary outcome measure Newborns with low birth weight.

Results 40 and 367 newborns were born with and without LBW, respectively. Adjusted for all available confounders, 3 or more periods of at least 7 days' smoking abstinence during pregnancy was associated with reduced likelihood of LBW compared with no abstinence periods (OR = 0.124, 95% CI 0.03 to 0.53, $p = 0.005$). Reduction of smoking intensity by at least 50% was not associated with birth weight.

Conclusion Aiming for several periods of smoking abstinence among pregnant smokers unable to remain continuously abstinent from smoking may be a better strategy to improve birth weight than reducing cigarette consumption.

Trial registration number ClinicalTrials.gov NCT02606227.

INTRODUCTION

The global prevalence of smoking during pregnancy has been estimated to be 1.7% in 2018 (95% CI 0 to 4.5) but shows large country specific and regional variations, the highest being in Ireland (38.4%, 95% CI 25.4 to 44.8) and in the European Region (8.1%, 95% CI 4.0 to 12.2), and the lowest in Tanzania (0.2%, 95% CI 0.0 to 0.6) and in the African Region (0.8%, 95% CI 0.0 to 2.2).¹ Smoking during pregnancy is associated with

STRENGTH AND LIMITATIONS OF THIS STUDY

- ⇒ This study assessed the association between smoking abstinence periods and birth weight in a sample of 407 mother–newborn dyads.
- ⇒ This was a secondary analysis of a randomised, controlled, smoking cessation trial among pregnant smokers.
- ⇒ Smoking abstinence was assessed by self-reports and expired air carbon monoxide determinations during face-to-face visits.
- ⇒ Limitations include the fact that this was a secondary, post hoc, exploratory analysis without a priori sample size determination.
- ⇒ The results should be confirmed by future trials.

150–250 g reduction in birth weight² and low birth weight (LBW) is a risk factor for perinatal morbidity and mortality. Smoking cessation in pregnancy is associated with substantial improvement in birth outcomes including increased birth weight.² Previous data have shown that smoking is fluctuating during pregnancy³ probably because pregnant women are aware of the negative health consequences of smoking during pregnancy, and make attempts to reduce their consumption or try to implement alternate periods of smoking abstinence and smoking.

Reduction in birth weight is linearly associated with cigarette consumption per day (cpd) up to 11–12 cpd, a further increase in cpd above this threshold has little or no further effect on birth weight.⁴ Reducing cpd does not improve the negative effect of smoking on birth weight and even low, 1–4 cpd is associated with reduced birth weight compared with continuous smoking abstinence during pregnancy.⁵

If reduced tobacco consumption during pregnancy does not improve birth weight, the question arises whether periods of smoking abstinence may help reduce the toxic effect of smoking on birth weight. In practice, the

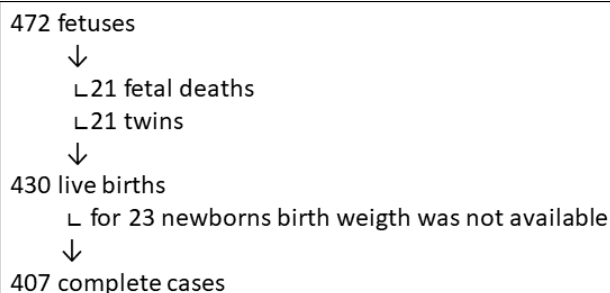


Figure 1 Flow chart of the number of foetuses, foetal deaths, twins and missing birth weight data.

question is whether the number of prenatal healthcare/smoking cessation visits during pregnancy at which women are abstinent is associated or not with the likelihood of LBW. If the increased frequency of periodic abstinence is associated with reduced likelihood of LBW, assessed as 7 days point prevalence abstinence, then healthcare professionals could suggest to pregnant smokers who are unable to maintain continuous abstinence from smoking, to increase the number of smoking abstinence periods with the aims of reducing the likelihood of LBW.

To answer this question, we analysed data of a randomised controlled trial assessing the efficacy of financial incentives (FI) in helping pregnant smokers quit.⁶ The aims of this secondary analysis were to assess: (a) the association between smoking abstinence periods during pregnancy and LBW; and (b) the association between reduction of smoking by 50% and LBW.

METHODS

The FISCP trial (Financial Incentives for Smoking Cessation in Pregnancy) was a randomised controlled trial run in 18 maternity wards in France.⁶ The control group received a €20 vouchers per visit for show up but participants were not rewarded for smoking abstinence. In the FI group, in addition to a €20 vouchers per visit for show up, participants received €20 vouchers on a progressively increasing way to reward smoking abstinence and incentivise the duration of smoking abstinence.⁶ 231 pregnant smokers were randomised in the FI and 229 in the control group. Participants were followed up from the first trimester to delivery. Participants were randomised at a gestational age of <18 weeks (visit 1) and could have

up to 5 monthly face-to-face visits during their pregnancy at which counselling and the vouchers were delivered. Smoking abstinence was defined as a self-report of no smoking during the past 7 days with an expired air carbon monoxide concentration ≤ 8 ppm. LBW was defined according to the WHO definition as birth weight less than 2500 g.⁷

Abstinence periods occurred also in the control group and the current report took into account all participants' abstinence/non-abstinence periods independently of the randomisation. The frequency of smoking abstinence periods during pregnancy was categorised as no abstinence; 1–2 abstinence periods; 3–4 abstinence periods; 5 abstinence periods. Five abstinence periods implied continuous abstinence throughout the FISCP trial.

Birth weight data were collected after birth. Investigators contacted the participants after delivery and checked, if available, the babies Health Booklet that usually contains birth weight. They were unable to record it for 23 babies. Checking missing birth weight data showed that missings were not associated with centres (maternity wards), with pregnancy or pregnancy outcomes but with other, external factors such as no recording of birth weight in the Health Booklet, having forgotten to contact the participant after delivery or the participant could not be reached because of change in contact information.

50% reduction in cigarette consumption was defined as follows:

Variation rate of cigarette consumption = (weekly number of cigarettes smoked at inclusion – average number of weekly cigarettes during the study) / weekly number of cigarettes smoked at inclusion $\times 100$. A reduction of 50% was coded 1 if the variation rate of cigarette consumption was >49.9 ; a reduction of 50% was coded 0 if the variation rate of cigarette consumption was ≤ 49.9 . In case of missing the weekly number of cigarettes smoked, the last recorded number was carried forward. Participants who were continuous abstainers were included in the group of 50% reduction.

Statistical analysis

Ordinary least square regression (linear probability model) analysis was used to assess the probability of LBW according to the number of smoking abstinence periods during pregnancy. Univariate analyses were used to assess the association of potential known predictors with LBW such as partners' smoking, alcohol consumption, cannabis use, maternal age, previous history of medical, psychiatric or obstetrical disorders, pre-pregnancy body mass index, and the newborn's sex and treatment arm. Frequencies were compared by the χ^2 test, continuous variables by the Mann–Whitney non-parametric test. Variables showing an association with LBW at $p \leq 0.10$ were included in the multivariable stepwise logistic regression. Prematurity or gestational age were not included in the logistic regression: smoking is a known risk factor for prematurity or reduced gestational age and both are strongly correlated with birth weight. Gestational age is often mislabelled as

Table 1 Number (%) of newborns with (<2500 g) or without low birth weight (≥ 2500 g) according to the number of pregnancy visits at which the pregnant women had at least 7 days smoking abstinence

Birth weight	<2500 g, n = 40	≥ 2500 g, n = 367
0 visit with abstinence	34 (85.0)	218 (59.4)
1–2 visits with abstinence	4 (10.0)	37 (10.1)
3–4 visits with abstinence	1 (2.5)	62 (16.9)
5 visits with abstinence	1 (2.5)	50 (13.6)

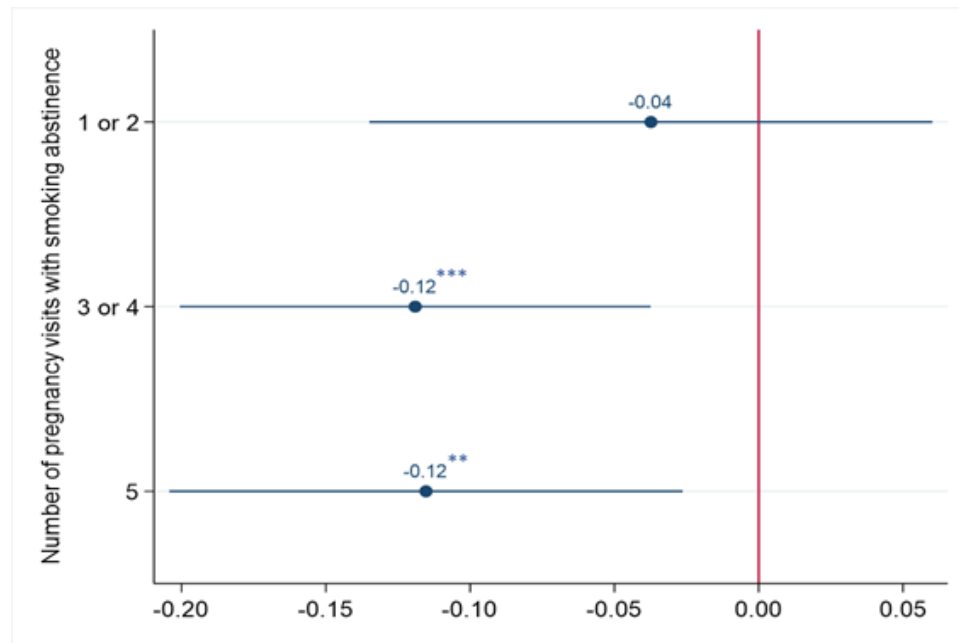


Figure 2 Probability of low birth weight (<2500g) as a function of the number of pregnancy visits at which 7 days, biochemically verified smoking abstinence was observed. Comparator: no abstinence at visits. Horizontal bars: 95% CI. X-axis coefficients from the OLS (ordinary least squares) regression (linear probability model). Negative values on the X axis indicate reduced probabilities. *** $p < 0.01$; ** $p < 0.05$.

a confounder but it is, in fact, an intermediate variable.⁸ Adjustment for gestational age (or prematurity) would lead to overadjustment defined as an intermediate that lies on a causal pathway from exposure (smoking) to outcome (birth weight).⁸ An overadjustment bias reduces the precision of the estimate.⁹

Only singleton births were included. Adverse pregnancy events/outcomes, adverse infant birth outcomes and poorer infant development are strongly associated with multiple pregnancies. Therefore, analysing multiple and singleton pregnancies together renders the findings difficult to interpret.¹⁰

Patient and public involvement

Participants were not involved in setting the research question or the outcome measures, nor were they involved in developing plans for recruitment, design or implementation of the study. Participants were not asked to advise on interpretation or writing up of results.

RESULTS

The current secondary analysis included data of 407 singleton live births and whose birth weight was available (figure 1).

The mean age of the mothers whose baby was born with LBW was 30.4 (SD 5.5) and of those without LBW 29.2 (SD 5.4) years, respectively. The mean gestational age was 39.5 (1.5) and 35.7 (3.3) weeks at birth among babies born without LBW and with LBW, respectively ($p < 0.001$). The mean body mass index of the mothers before pregnancy was 24.69 (4.94) and 25.01 (6.31) kg/m^2 , respectively. The mean score at the CAGE questionnaire (Cutting down, Annoyance by criticism, Guilty feeling and Eye-openers)¹¹ was 0.38 (0.84) and 0.37 (0.84). Cannabis use at inclusion was reported by 30 (8.2%) and 2 (5%) mothers without or with LBW, respectively. Among them any cannabis use during pregnancy was reported by 17 (4.7%) mothers of newborns without LBW; none of the mothers whose baby was born with LBW reported any cannabis use during pregnancy. 170 (48.3%) and 17 (57.5%) mothers reported previous medical or psychiatric and 230 (63%) and 24 (60%) previous obstetrical history of babies without or with LBW, respectively. There were 20 (50%) girls and 20 (50%) boys born with LBW and 164 (44.7%) girls and 203 boys (55.3%) born without LBW. All p values of these comparisons were higher than 0.1. 87.50% of the partners of mothers delivering a baby with LBW smoked at inclusion (ie, first trimester) versus

Table 2 Variables associated with low birth weight. Final model of the stepwise multivariable logistic regression

	Estimate	SE	Wald statistic	OR	95% CI	p value
Partners' smoking at inclusion	0.89	0.50	3.24	2.44	0.92 to 6.48	0.07
More than two abstinence periods versus none or less than two abstinence periods	-2.08	0.73	8.03	0.124	0.03 to 0.53	0.005

72.75% of the partners of mothers delivering a baby with no LBW (OR = 2.62, 95% CI 0.99 to 6.88, $p = 0.05$). FI as compared with lack of FI (control group) were associated with somewhat greater numbers of abstinence periods (OR = 1.95, 95% CI 0.99 to 3.85, $p = 0.055$).

Table 1 shows the number of newborns with or without LBW by the number of pregnancy visits at which the pregnant women had at least 7 days smoking abstinence. A statistically significant association occurred between the number of abstinence periods and birth weight ($\chi^2 = 12.21$, ddl (degree of freedom) = 3 $p = 0.007$). Compared with no abstinence, being abstinent three or four times or five times was associated with a 12 percentage point decrease in the probability of having a LBW (figure 2). On the contrary, a 50% reduction in weekly cigarettes consumption during pregnancy had no influence on the frequency of LBW: LBW group: reduction by 50%: 27/49 (55.1%, 95% CI 41.2 to 69); no reduction by 50%: 22/49 (44.9%, 95% CI 31 to 58.8); no LBW group: reduction by 50%: 148/370 (40%, 95% CI 33.9 to 46.1); no reduction by 50%: 222/370 (60%, 95% CI 55.9 to 64.1, $p = 0.512$).

Partner's smoking and treatment allocation were included in the multivariable stepwise logistic regression analysis along with abstinence periods (univariate analysis: $p \leq 0.1$). More than two smoking abstinence periods were associated with reduced likelihood of LBW (OR = 0.124, 95% CI 0.03 to 0.53, $p = 0.005$) compared with none or less than two abstinence periods. Partners' smoking at inclusion showed a tendency to be associated with an increased likelihood of LBW (OR = 2.44, 95% CI 0.92 to 6.48, $p = 0.072$) (table 2). Treatment allocation was not associated with LBW in the final model (OR = 1.51, 95% CI 0.75 to 3.03, Wald statistic 1.32, $p = 0.25$).

DISCUSSION

This secondary analysis of a randomised controlled smoking cessation trial among pregnant smokers shows that the likelihood of LBW is lower when pregnant smokers are frequently abstinent during their pregnancy. Reduced cigarette consumption had no effect on birth weight. From a practical point of view, this means that healthcare professionals should propose pregnant smokers unable to remain continuously abstinent from smoking during the whole pregnancy to try introducing as many as possible 7 days smoking abstinence periods. This strategy to reduce the likelihood of LBW may be more promising than reducing the number of cigarettes per day smoked.

Prenatal tobacco exposure affects foetal growth, and maternal smoking during pregnancy is associated with reduced foetal growth if it occurs in the second or third trimester.¹² There is a non-linear exposure–response relationship between the number of cigarettes smoked by the pregnant women and the risk of LBW. Compared with those whose mothers did not smoke during pregnancy all levels of consumption increase the risk of LBW: (OR, 95% CI) 3 cpd: 1.46 (1.42–1.49), 5 cpd: 1.65 (1.60–1.70),

8 cpd: 1.84 (1.78–1.90), 15 cpd: 1.92 (1.85–2.00) and 25 cpd: 2.90 (2.62–3.22)¹³ confirming that even a low amount of cpd is associated with LBW. In line with the current results, longer period of no foetal exposure decreases the likelihood of LBW.¹³

Strength and limitations

The strength of this secondary analysis is that it draws attention, probably for the first time, to the positive effect of multiple smoking cessation periods during pregnancy on birth weight if the pregnant woman is unable to quit before or at the beginning of her pregnancy or remains continuously abstinent from smoking. Assessment of smoking abstinence included not only self-report but also the biochemical confirmation of no smoking by expired air carbon monoxide.⁶ The study's assessments were run by midwives and physicians specialised in smoking cessation and the visits were face-to-face with standardised smoking cessation counselling.⁶

Limitations include the fact that this was a secondary, post hoc, exploratory analysis whose power may be insufficient to conclude with confidence. The sample size of the LBW group is low and being a secondary analysis, the sample size was not a priori powered for the aims of this report. Therefore, its results should be confirmed by future trials. Baseline that is, early pregnancy smoking of the mothers' partners was significantly associated in the univariate analysis with LBW but the contribution of partners' smoking became non-significant in the multivariable-adjusted model. However, because of the reduced power of this study, this result should be interpreted with caution and further works should assess partners' smoking as a confounder of the effect of smoking abstinence periods on birth weight. Other substance uses than tobacco could also increase the likelihood of LBW and may confound or add to the beneficial effect of smoking cessation during pregnancy. However, the CAGE questionnaire score was very low indicating that alcohol use is unlikely to influence the results, and cannabis use at inclusion or during pregnancy was not associated with LBW.

CONCLUSIONS

Three or more periods of at least 7 days smoking abstinence during pregnancy were independently associated with reduced likelihood of LBW compared with no abstinence periods. Aiming for several periods of smoking abstinence among pregnant smokers who are unable to remain continuously abstinent from smoking may be a better strategy to improve birth weight than reducing cigarette consumption.

Contributors Conception of the work: IB, LG, FJ and NB. Data analysis: IB, LG and NB. Data interpretation: IB, LG, FJ and NB. First draft of the article: IB. Formation of figures and tables: IB, NB and LG. Critical revision of the article: IB, LG, FJ and NB. Final approval of the manuscript: IB, LG, FJ and NB. IB is the guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants and was approved by Comité de protection des personnes Ile de France. Approval on 17 April 2015. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request and with the agreement of the sponsor: Assistance publique-Hôpitaux de Paris.

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ORCID iD

Ivan Berlin <http://orcid.org/0000-0002-5928-5616>

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