You snus you lose? The effect of Swedish snus on offspring birthweight: a quasi-experimental sibling analysis

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INTRODUCTION

Maternal smoking during pregnancy (SDP) is considered the most important single determinant on offspring’s birthweight reduction, 1-5 although the specific mechanism through which it occurs is not yet very well established. Some evidence suggests that nicotine obstructs oxygenation and decreases blood pressure circulation, which impairs the structure and function of the placenta,6 and is therefore responsible for many complications (among them birthweight reduction). Against this line of reasoning, some studies show that passive smoker mothers (i.e not exposed to nicotine) experience similar offspring’s birthweight reduction to smokers7, which suggests therefore that the association between SDP and birthweight may be mediated by its combustion and, consequently, that the mechanism involved does not operate throughout to hypoxia but to toxicity.

This paper aims at analyzing this intuition by studying the effect of maternal snus-use during pregnancy on offspring’s birthweight. Swedish snuff (snus), different from other kind of snuff products, is ground tobacco (mixed with salt, and sodium carbonate) without any toxic substance added, which provides us with the opportunity to isolate the effect of nicotine on birthweight. This study performs a quasi-experimental sibling analysis to account for unknown genetic and other maternal characteristics associated to both tobacco habits and offspring birthweight. This design has potential to study causal associations by studying, ceteris paribus the effects of different exposures (snus/non-snus) on the birthweight of individuals who are very similar (e.g siblings) 8. Sibling desing is increasingly used in epidemiology however, to our knowledge, it has never before been applied to the purpose of this study.
METHODS

Study population
We based our study on the Swedish Medical Birth Register (MBR) for the period 2002-2009. We selected all babies born in Sweden as singleton and at full term to native Swedish mothers ($n = 601,077$). Subsequently, for the purpose of the sibling analysis, we performed a further selection including only mothers with discordant snus-use habits between pregnancies (i.e., women who had at least one pregnancy during which they use snus and at least one other pregnancy during which they did not use snus). This procedure rendered 50,497 discordant siblings grouped within 23,443 mothers.

The study outcome variable was birthweight in grams (g.). Information on snus use during pregnancy was self-reported and assessed at the first antenatal visit (i.e., between gestational weeks 10 and 12) and at the third trimester (i.e., between gestational weeks 30-32). All models were adjusted for gestational age, smoking during pregnancy, birth order, sex, complications during pregnancy, mother’s age, and marital status.

Statistical analyses
We applied a conventional multiple linear regression to estimate the association between maternal SDP and offspring birthweight for the whole sample of singletons, and a multilevel linear regression with Markov Chain Monte Carlo (MCMC) and orthogonal parameterization with siblings at the first level and mothers at the second level. The purpose of this analysis was to obtain mother-specific regression coefficients. By including a random term for the mother, the multilevel regression analysis adjusted for unknown genetic and environmental factors related to each and every one of the mothers.

RESULTS

The socio-demographic and clinical characteristics of the whole population and of the subpopulation of siblings with contrast of exposure were very similar.

In the conventional multiple regression, we observed a reduction in birthweight in 15 g. for those who use snus throughout the pregnancy. This reduction is of 7 g. among those who quit
using snus after the first prenatal visit and, on the contrary, birthweight increases in 23 g. among those who relapsing snus use after the first trimester. The quasi-experimental sibling analysis does not show statistical significant differences in any category of using snus compared to mothers who never used snus.

DISCUSSION:
To some degree the conventional linear regression analysis suggested that using snus during pregnancy reduced the offspring’s birthweight. However, the use of a quasi-experimental sibling analysis evidences absence of any relevant birthweight reduction in babies exposed to maternal snus during pregnancy. Therefore, it appeared that the findings from the conventional analysis were confounded by unknown genetic and environmental characteristics of the mother.

Our results are in line with a previous conventional analysis which did not find any association between nicotine replacement therapy (i.e., patch, gum, inhaler) and offspring’s birthweight. However, our findings should not be interpreted as though the use of snus were a healthier alternative to smoking during pregnancy since the use of snus conveys its own harmful health consequences. Our results, however, are of particular importance in order to disentangle the mechanisms through which tobacco consumption influences birthweight. Based on a quasi-experimental sibling analysis our study gives support to the hypothesis that the adverse effect of smoking during pregnancy is not mediated by nicotine but possibly by toxic products related to tobacco combustion.
REFERENCES