

Active and passive smoking and fecundability in Danish pregnancy planners

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Objective: To investigate the extent to which fecundability is associated with active smoking, time since smoking cessation, and passive smoking.

Design: Prospective cohort study.

Setting: Denmark, 2007–2011.

Patient(s): A total of 3,773 female pregnancy planners aged 18–40 years.

Intervention(s): None.

Main Outcome Measure(s): Self-reported pregnancy. Fecundability ratios (FRs) and 95% confidence intervals (CIs) were estimated using a proportional probabilities model that adjusted for menstrual cycle at risk and potential confounders.

Result(s): Among current smokers, smoking duration of ≥ 10 years was associated with reduced fecundability compared with never smokers (FR, 0.85, 95% CI 0.72–1.00). Former smokers who had smoked ≥ 10 pack-years had reduced fecundability regardless of when they quit smoking (1–1.9 years FR, 0.83, 95% CI 0.54–1.27; ≥ 2 years FR, 0.73, 95% CI 0.53–1.02). Among never smokers, the FRs were 1.04 (95% CI 0.89–1.21) for passive smoking in early life and 0.92 (95% CI 0.82–1.03) for passive smoking in adulthood.

Conclusion(s): Among Danish pregnancy planners, cumulative exposure to active cigarette smoking was associated with delayed conception among current and former smokers. Time since smoking cessation and passive smoking were not appreciably associated with fecundability. (Fertil Steril® 2014; ■:■–■. ©2014 by American Society for Reproductive Medicine.)

Key Words: Fecundability, fertility, cigarette smoking, tobacco smoke pollution, cohort study

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Tobacco smoke constituents demonstrate acute effects on female reproductive physiology, including damaging the oocyte (1, 2) and altering concentrations of endogenous hormones (3–9). In addition, smoking may have persistent

effects (10–13) by depleting the ovarian reserve (14, 15) and increasing susceptibility to sexually transmitted infection (16–18).

Epidemiologic studies have consistently shown an inverse association between intensity of current smoking and

fecundability (19), defined as the cycle-specific probability of conception among noncontracepting couples. Studies of former smokers have not found reduced fecundability (20–22) or an increased risk of infertility (16, 23) relative to never smokers, implying that the effect of smoking on fecundability does not persist. However, these studies did not use information on the amount or duration of smoking among the former smokers, which may have obscured possible tobacco effects with high cumulative levels of exposure (19, 24). With regard to prenatal exposure to tobacco smoke, studies of fecundability in relation to in utero

Received January 9, 2014; revised February 26, 2014; accepted March 11, 2014.

R.G.R. has nothing to disclose. E.E.H. has nothing to disclose. K.J.R. has nothing to disclose. E.M.M. has nothing to disclose. H.T.S. has nothing to disclose. A.H.R. has nothing to disclose. L.A.W. has nothing to disclose.

Supported by the National Institute of Child Health and Human Development (NICHD) (R21-050264) and the Danish Medical Research Council (271-07-0338). R.G.R. received support from NICHD training grant T32-HD052458. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Fertility and Sterility® Vol. ■, No. ■, ■ 2014 0015-0282/\$36.00

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<http://dx.doi.org/10.1016/j.fertnstert.2014.03.018>

exposure to maternal smoking are mixed, with some showing an inverse association (22, 25, 26) and others showing little association (27–29).

We examined the association of cumulative exposure to active smoking with fecundability among both current and former smokers in a prospective cohort study of pregnancy planners in Denmark. In addition, we assessed the association between cumulative exposure to smoking and fecundability among former smokers in groups of time since cessation. Among never smokers, we assessed the extent to which exposure to passive smoking during various life stages (in utero or in childhood; adolescence; and adulthood) was associated with reduced fecundability.

MATERIALS AND METHODS

Study Population

The Snart Gravid study enrolled women in Denmark aged 18–40 years who were planning a pregnancy during 2007–2011. Eligible participants were in a stable relationship with a male partner, not using fertility treatments, and willing to provide their identification number from the Danish Civil Registration System and e-mail address (30). The study used Internet-based questionnaires to obtain informed consent and self-reported exposure and outcome data (31). The study protocol was approved by the ethical review boards of Boston University Medical Center and the Danish Data Protection Board (J. no. 2010-41-4345).

Assessment of Exposure

Participants reported their current smoking habits and history of active and passive smoking exposure on the baseline questionnaire. Current smokers were categorized as regular smokers if they smoked at least one cigarette per day and occasional smokers if they smoked less. Regular smokers reported the current intensity in categories of cigarettes smoked per day (1–4, 5–9, 10–19, 20–29, and ≥ 30), the age they started, and the number of years they had abstained from smoking. Former smokers reported the average number of cigarettes smoked per day in the same categories, the ages when they started and stopped, and the duration of smoking in years. Participants reported their history of passive smoking exposure as the average number of hours per day during the following ages: 0–10, 11–20, 21–30, and 31–40 years. The questionnaire also asked participants about their exposure in utero: “Did your mother smoke cigarettes while she was pregnant with you?”

Assessment of Covariates

The baseline questionnaire included information on female age, height and weight, education, household income, occupation, reproductive and medical histories, and lifestyle habits such as frequency of intercourse, consumption of alcoholic and caffeinated beverages, and physical activity. Participants reported whether they had daily or near-daily exposure to the following environmental hazards at home or at work: agricultural pesticides; metal particulates or fumes; solvents, oil-based paints, or cleaning compounds; environments with

temperatures $>25^{\circ}\text{C}$; chemotherapeutic drugs; engine exhaust; chemicals for hair dyeing, straightening, or curling; chemicals for manicure and pedicure. Women also reported information on their male partner’s age, height and weight, smoking habits and history, and exposure to environmental hazards.

Assessment of Pregnancy and Cycles at Risk

On bimonthly follow-up questionnaires, participants reported whether they had conceived and, if so, whether the pregnancy was confirmed by a home pregnancy test and/or clinician. Total menstrual cycles at risk were calculated from participants’ reported number of months spent trying to conceive at the time of enrollment, date of last menstrual period (LMP) before enrollment, usual menstrual cycle length, and LMP date on each follow-up questionnaire (32). A participant contributed menstrual cycles from the time she enrolled until she reported a confirmed pregnancy or was censored. Censoring occurred if the woman initiated fertility treatment, was no longer attempting pregnancy, withdrew from the study, was lost to follow-up, or completed 12 cycles from the beginning of her attempt to conceive, whichever came first.

Exclusions

From June 2007 through December 2011, 5,921 eligible women enrolled. We excluded 297 women (5%) with incomplete or implausible information about their LMP date or the start date of their pregnancy attempt; 580 women (10%) who did not fill out a follow-up questionnaire; 1,153 women (20%) who had attempted pregnancy for >6 cycles at baseline; and 118 women (2%) who reported smoking cessation <1 year ago (because of uncertainty of the timing of smoking cessation with respect to the start of the pregnancy attempt). After these exclusions, 3,773 women were included in the present analysis. The 475 women (13%) subsequently lost to follow-up (mean follow-up time, 3.3 months) were on average younger (27.9 vs. 28.4 years), heavier (body mass index [BMI], 25.1 vs. 24.0 kg/m^2), less educated (≥ 4 years of vocational training: 50% vs. 59%), more likely to be parous (33% vs. 28%), regular smokers (18% vs. 11%), and exposed to passive smoking in adulthood (42% vs. 34%) than those not lost to follow-up. Similar proportions used oral contraceptives (OC) as their last form of birth control (61% vs. 61%).

Data Analysis

We analyzed exposure to smoking among current smokers in terms of duration and intensity, and among former smokers, in terms of duration, intensity, pack-years, and time since cessation. We also assessed joint categories of these variables where appropriate. Never smokers were the reference category for these analyses. Pack-years among current smokers depended greatly on the current intensity category. Because of the ambiguity of whether it captured current intensity of exposure or cumulative exposure, we did not analyze exposure among current smokers in terms of pack-years. We defined exposure to passive smoking as spending ≥ 1 hour per day in the same room with someone who was smoking.

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