J. biosoc. Sci. (2002) **34**, 65–73
© 2002 Cambridge University Press Printed in the United Kingdom

DOES CIGARETTE SMOKING INCREASE TIME TO CONCEPTION?

MARCUS MUNAFÒ, MICHAEL MURPHY, DAVID WHITEMAN AND KATE HEY

Institute of Health Sciences, University of Oxford, Oxford

Summary. Data are reported on the relationship between cigarette smoking and other health-related behaviours and time to conception in a population-based sample of women who acted as a control group in a case-control study of twinning. Women who continued to smoke close to the time of conception took significantly longer to become pregnant than women who never smoked or stopped smoking before the year during which they attempted to conceive. A hierarchical regression analysis performed on time-to-conception data in women who continued to smoke in the year before conception provided weak evidence for a dose–response relationship between time to conception and number of cigarettes smoked per day. No significant relationships were found between time to conception and other health-related behaviours.

Introduction

Subfertility may be caused by factors present in either the mother or the father. Female subfertility is usually classified as being due to hormonal, mechanical or unexplained causes. The absolute or relative barriers to conception, however, remain poorly understood, and the area is under-researched. One measure of subfertility is an increased time to conception, although a number of other measures have been used.

Apart from certain demographic characteristics, such as maternal age, a number of health-related behaviours have been associated with subfertility. Vessey *et al.* (1978), for example, reported reduced fertility in women for up to 42 months following cessation of oral contraceptive use. The effects of vigorous exercise, and possibly moderate exercise, are also reported to be related to menstrual cycle characteristics and fertility (Bernstein *et al.*, 1987). The consumption of social drugs such as alcohol (Jensen *et al.*, 1998) and caffeine (Grodstein *et al.*, 1993) has also been reported to be related to subfertility, although there is as yet little consensus regarding the strength, or even existence, of these relationships.

Another health-related behaviour for which there is evidence of an association with subfertility is cigarette smoking (Howe *et al.*, 1985). Several studies have reported

https://doi.org/10.1017/S0021932002000652 Published online by Cambridge University Press

that women who smoke take longer to conceive than women who don't smoke, during both natural and assisted conception attempts. For example, Joesoef *et al.* (1993) reported an increase in average time to conception in women who were current smokers compared with never-smokers and ex-smokers. Similar results have been reported elsewhere (Hughes & Brennan, 1996; Stanton & Gray, 1995, Alderete, Eskenazi & Sholtm, 1995). While several mechanisms have been proposed to explain these data, such as the effect of smoking on ovarian or oocyte function (Shiverick & Salafia, 1999; Zenzes, Wang & Casper, 1995), it remains unclear whether lifetime smoking or current smoking (or both) are related to time to conception. It also remains to be determined whether any relationship between smoking and time to conception is dose-dependent.

The public health messages regarding the risks of smoking during pregnancy tend to focus on the potential harm to the fetus. The evidence that cigarette smoking may decrease a woman's chances of conceiving might form the basis of another important public health message.

This study sought to determine whether cigarette smoking affects time to conception among women in southern England.

Methods

The current study reports data from the control group in a study of factors affecting twinning in Oxfordshire and West Berkshire. The data provide information regarding the demographic characteristics of the mother and the father, oral contraceptive use, certain health-related behaviours (exercise, alcohol consumption, caffeine consumption and cigarette consumption) and self-reported time to conception. These data are used in the present study to investigate the relationship between health-related behaviours and time to conception, in particular smoking behaviour.

The Central Oxford Research Ethics Committee (COREC) and West Berkshire Ethics Committee granted ethical approval for the study. With the agreement of their general practitioners, a population-based sample of women who gave birth in the Horton, John Radcliffe and Royal Berkshire hospitals in the years 1994, 1995 and 1996, for participation in a case-control study of twinning, were approached. The few pairs in which stillbirths and neonatal deaths occurred were excluded ($n=37$). Women who gave birth to twins comprised the cases, while controls were randomly sampled from among women giving birth to singletons. The study was described to potential participants as one examining factors affecting fertility. Only participants from the control sample (i.e. women who gave birth to singletons) are included in this analysis.

The women were approached by letter and requested to complete a postal questionnaire. Non-responders were followed up at least twice, either by letter or by telephone. This generated a response rate of 82% among controls (who represent the sample on which data are reported here).

The fertility questionnaire covered participants' fertility characteristics and their general health and behaviours that might be related to fertility or hormone levels. Questions were of the form 'Have you ever smoked cigarettes regularly, that is, one a week or more?', which required a 'Yes' or 'No' answer, or of the form 'On average, how many cigarettes per day?', which required a numeric answer e.g. '*x*

https://doi.org/10.1017/S0021932002000652 Published online by Cambridge University Press

per day'. Respondents were also asked to provide information regarding the number of years that they had smoked before they became pregnant, the number of cigarettes smoked per day during this time, whether they smoked in the 12 months before becoming pregnant and, if so, the number of cigarettes smoked per day in this 12-month period.

From the 843 controls who responded, women undergoing treatment for infertility, women whose partners were undergoing treatment for infertility and women who did not report actively attempting to conceive (including women who conceived while taking the oral contraceptive pill) were excluded, leaving 569 women.

Respondents were classified as current smokers ($n=114$, those reporting smoking in the year before conception), ex-smokers ($n=94$, those reporting not smoking in the year before conception but with a previous history of smoking) and never-smokers ($n=361$, those reporting no history of smoking). These figures are typical of smoking prevalence in the population from which the sample was drawn (Petersen, Stewart-Brown & Peto, 1998).

A comparison of mean time to conception (in months) across the groups current smokers, ex-smokers and never-smokers was performed to test the null hypothesis that smoking status is not related to time to conception.

A series of hierarchical regression analyses were performed on the time-to-conception data. These data were analysed together in the first instance and then stratified by smoking status. Separate analyses are presented for these groups (never-smokers, ex-smokers and current smokers). Variables were entered in the order: physical characteristics of the mother (weight [kg], height [cm], age [years]), father's age (father's age [years]), lifetime oral contraceptive use to index year (OC use [months]), oral contraceptive use in the year preceding conception (OC use in index year ['yes' or 'no']) and health behaviours of the mother (alcohol consumption [units/month], caffeine consumption [mg/week], moderate exercise [hours/week], vigorous exercise [hours/week], lifetime smoking [pack years], index year smoking [cigarettes/day]). Moderate exercise was defined by example (e.g. cycling, walking, heavy housework), as was vigorous exercise (where you work up a sweat e.g. running, dance/exercise class, digging). Pack years was defined as the product of the self-reported daily consumption of cigarettes over the course of the smoking lifetime and the number of years smoking, to give an overall measure of exposure. That is: pack years = ([cigarettes per day/20]365)number of years smoking.

A variable was excluded if the p value for the Beta coefficient was greater than 0·2, and the analysis performed again. All analyses were performed using SPSS version 10·0.

Results

The mean age of the women in the study sample was 29 years 8 months (SD 4 years 5 months). A one-way analysis of variance suggested that age differed significantly across the groups current smokers (mean = 28 years, SD = 4 years 7 months), ex-smokers (mean = 30 years, SD = 4 years 5 months) and non-smokers (mean = 30 years 2 months, SD = 4 years 2 months) ($F=11·659$, df = 2, $p<0·001$). A post-hoc comparison

https://doi.org/10.1017/S0021932002000652 Published online by Cambridge University Press

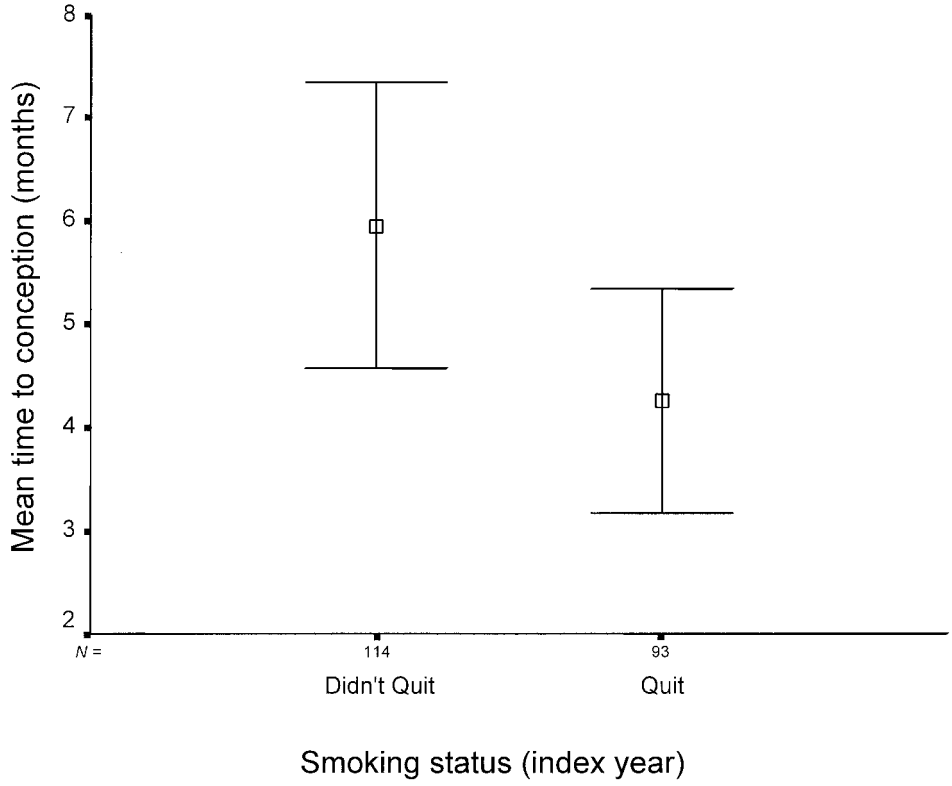


Fig. 1. Time to conception among women smokers in Oxfordshire and West Berkshire (1994–1996).

of means (Tukey) indicated that current smokers were significantly younger than ex-smokers ($p = 0.002$) and non-smokers ($p < 0{\cdot}001$). The mean age of ex-smokers and non-smokers did not differ significantly ($p = 0.946$).

Time to conception by smoking status

A Kruskal–Wallis one-way analysis of variance was performed on the time-to-conception data, grouped by smoking status (current smoker, ex-smoker, never-smoker). This suggested a main effect of smoking status on time to conception that approached significance ($\chi^2 = 5.849$, df = 2, $p = 0.054$).

A post-hoc Mann–Whitney *U* test suggested no difference in time to conception between women who had ever smoked (current smokers and ex-smokers) compared with never-smokers ($Z = 0.126$, $p = 0.207$). However, women who continued to smoke in the year prior to conception took longer to conceive than women who stopped smoking during this time ($Z = 1.997$, $p = 0.046$). This effect was in the predicted direction, with women who continued to smoke while attempting to become pregnant taking, on average, almost 2 months longer to conceive than women who ceased smoking while attempting to become pregnant. This is illustrated in Fig. 1.

https://doi.org/10.1017/S0021932002000652 Published online by Cambridge University Press

Table 1. Means and standard deviations (in parentheses) of variables included in regression models, grouped by smoking status

	All women	Non-smokers	Ex-smokers	Current smokers
Age (years)	29·67 (4·41)	30·14 (4·21)	29·98 (4·41)	27·92 (4·64)
Weight (kg)	63·04 (11·65)	63·08 (11·13)	63·63 (11·60)	62·40 (13·23)
Oral contraceptive (months)	75·05 (51·64)	74·09 (50·45)	83·54 (51·72)	70·75 (55·11)
Alcohol consumption (units/month)	19·86 (30·96)	16·37 (24·61)	28·16 (37·60)	24·14 (40·30)
Vigorous exercise (hours/week)	2·44 (4·21)	2·20 (3·90)	2·86 (5·05)	2·86 (4·39)
Lifetime smoking (pack years)	na	na	3·86 (4·15)	6·22 (5·23)
Index year smoking (cigarettes/day)	na	na	na	10·95 (6·04)

Linear regression: all participants

The final regression model included maternal age, maternal weight, lifetime oral contraceptive use, alcohol consumption, level of vigorous exercise, pack years and cigarettes smoked per day in the index year as predictor variables. This model accounted for 4% of the variance in time to conception, which was significant at the 0·001 level ($F_{(7, 390)} = 3.416$). Beta coefficients for the model for all women are presented in Table 2, indicating important, opposed effects of the two smoking variables that are both significant at the 0·01 level.

This model provided the basic regression model for subsequent analyses, so that terms for maternal age, maternal weight, oral contraceptive use, alcohol consumption and level of vigorous exercise were always included. The means and standard deviations of these variables, grouped by smoking status, are presented in Table 1.

Linear regression: never-smokers

The regression model described above accounted for 3% of the variance in time to conception in never-smokers, which was significant at the 0·05 level ($F_{(5, 300)} = 3.024$, $p = 0.011$). Beta coefficients for the model are presented in Table 2, with only lifetime oral contraceptive use individually significant at the 0·05 level.

Linear regression: ex-smokers

The final regression model for time to conception in ex-smokers included, in addition to the predictor variables described above, pack years as a predictor variable. This model accounted for 6% of the variance in time to conception. This was not statistically significant, although the effect approached significance ($F_{(6, 74)} = 1.897$, $p = 0.093$). Beta coefficients for the model are presented in Table 2, with that for age significant at the 0·05 level.

https://doi.org/10.1017/S0021932002000652 Published online by Cambridge University Press

Table 2. Regression coefficients for time to conception among women in Oxfordshire and West Berkshire (1994–1996)

Variable	Beta	*t*	*p*
All women			
Age	0·070	1·326	0·186
Weight	0·079	1·598	0·111
Oral contraceptive	− 0·083	− 1·643	0·101
Alcohol consumption	0·078	1·554	0·121
Vigorous exercise	− 0·077	− 1·562	0·119
Lifetime smoking	− 0·256	− 2·759	0·006
Index year smoking	0·347	3·689	0·000
Women who never smoked			
Age	0·107	1·825	0·069
Weight	0·097	1·710	0·088
Oral contraceptive	− 0·122	− 2·108	0·036
Alcohol consumption	− 0·073	− 1·271	0·205
Vigorous exercise	0·100	1·762	0·079
Women who stopped smoking			
Age	0·230	2·015	0·048
Weight	0·152	1·355	0·179
Oral contraceptive	− 0·100	− 0·875	0·384
Alcohol consumption	0·197	1·807	0·075
Vigorous exercise	0·097	0·864	0·390
Lifetime smoking	− 0·032	− 0·276	0·783
Women who continued to smoke			
Age	− 0·008	− 0·062	0·952
Weight	0·031	0·283	0·778
Oral contraceptive	0·030	0·274	0·784
Alcohol consumption	− 0·087	− 0·806	0·423
Vigorous exercise	0·014	0·131	0·896
Lifetime smoking	− 0·308	− 1·960	0·053
Index year smoking	0·285	1·995	0·049

Linear regression: current smokers

The final regression model for time to conception in current smokers included, in addition to the predictor variables described above, cigarettes smoked per day in the index year as a predictor variable. This model accounted for 7% of the variance in time to conception. This was not statistically significant at the 0·05 level ($F_{(7, 83)} = 0.95$, $p = 0.491$). Beta coefficients for the model are presented in Table 2, with that for smoking in the year preceding conception significant at the 0·05 level and that for lifetime smoking approaching significance (in the opposite direction).

https://doi.org/10.1017/S0021932002000652 Published online by Cambridge University Press

Discussion

The results presented above provide further support for the previously reported relationship between cigarette smoking and time to conception. Lifetime smoking appears not to delay time to conception if the woman stops smoking while attempting to become pregnant, but continuing to smoke while attempting to become pregnant results in increased time to conception compared with women who cease smoking while attempting to become pregnant.

Among women who never smoked, the only significant predictor of time to conception was lifetime oral contraceptive use. This is apparently inconsistent with previous findings that suggest that the use of oral contraceptives increases the time to conception for several months after they are no longer used. However, oral contraceptive use in the year preceding conception (a dichotomous variable) was not a significant predictor of time to conception in this or any of the other models. It is not clear why lifetime oral contraceptive use should show this relationship, and it is not significant in the other models reported. Variables such as age, weight and vigorous exercise were not significant in this model, although the relationships were in the predicted direction. The authors are unaware of other reported, relevant data regarding oral contraceptive use *other than* close to the time of conception.

Among ex-smokers, age was the only significant independent predictor of time to conception, although the effects of weight and alcohol consumption approached significance in the predicted directions. This suggests that past cigarette smoking has no residual effects on time to conception, and that the effect disappears within one year of quitting.

Among women who continued to smoke in the year before pregnancy, cigarette smoking in the year preceding conception (cigarettes/day) was a significant predictor of time to conception. No other independent predictors of time to conception reached significance, although the other smoking variable (lifetime consumption in pack years) approached significance. The relationship between cigarettes smoked per day in the year preceding conception (i.e. during the attempt to become pregnant) and time to conception was in the predicted direction, suggesting that increased daily cigarette consumption is associated with increased time to conception. Surprisingly, the lifetime exposure to cigarettes, as measured in pack years, was negatively related to time to conception, a relationship opposite to that predicted, and similar in size of effect to that of current smoking, although of borderline non-significance. The possibility of this being a confounder related to age is excluded by the inclusion of age itself as a (non-significant) predictor in this model. While it is possible that study participants were a biased group of parous women, this is an unlikely explanation for the inverse association between lifetime cigarette consumption and time to conception. Residual confounding by other, unmeasured factors might underlie this observation, about which little can necessarily be said. However, the small proportion of variance in time to conception accounted for by all the models reported does suggest that this is possible. Finally, it is possible that this may be a real effect, although the mechanism remains elusive. One might propose that cigarette smoking has both early and late effects on time to conception, perhaps mediated by both a chronic anti-oestrogenic action on ovulation and a more acute effect on the quality of oocytes or implantation.

https://doi.org/10.1017/S0021932002000652 Published online by Cambridge University Press

One strength of this study is that the sample is likely to be representative of the population from which it was drawn, given the random selection of patients approached to participate, and the high levels of participation. Another strength is the relative completeness of the data set, with missing items accounting for fewer than 1·5% of responses.

Nevertheless, certain weaknesses can be identified. The data were provided by self-report, with behaviour being reported retrospectively. The questionnaire instrument used was constructed for the purposes of the study and only elements of it have been validated and used elsewhere. Finally, the study had sufficient power to detect only relatively strong relationships between time to conception and smoking behaviours after controlling for confounding variables.

However, in the context of previous work this study provides further support for the view that smoking in women is associated with subfertility (measured as time to conception) when other confounding demographic variables and health behaviours are controlled for (Hughes & Brennan, 1996).

The growing body of evidence that continuing to smoke while attempting to become pregnant may increase time to conception suggests that greater emphasis on this public health message is warranted. Current opinion on smoking cessation favours total abstinence rather than gradual reduction as the most effective means of quitting and the best means of harm reduction. If a dose–response relationship does exist then strategies to enhance fertility based on this finding will also need debating.

Acknowledgments

This study was supported by Wellbeing Grant M3/95.

References

Alderete, E., Eskenazi, B. & Sholtm, R. (1995) Effect of cigarette smoking and coffee drinking on time to conception. *Epidemiology* **6**, 403–408.

Bernstein, L., Ross, R. K., Lobo, R. A., Hanisch, R., Krailo, M. D. & Henderson, B. E. (1987) The effects of moderate physical activity on menstrual cycle patterns in adolescence: Implications for breast cancer prevention. *Br. J. Cancer* **55**, 681–685.

Grodstein, F., Goldman, M. B., Ryan, L. & Cramer, D. W. (1993) Relation of female infertility to consumption of caffeinated beverages. *Am. J. Epidemiol.* **137**, 1353–1360.

Howe, G., Westhoff, C., Vessey, M. & Yeates, D. (1985) Effects of age, cigarette smoking, and other factors on fertility: Findings in a large prospective study. *Br. med. J.* **290**, 1697–1700.

Hughes, E. G. & Brennan, B. G. (1996) Does cigarette smoking impair natural or assisted fecundity? *Fert. Steril.* **66**, 679–689.

Jensen, T. K., Hjollund, N. H. I., Henriksen, T. B., Scheike, T., Kolstad, H., Giwercman, A., Ernst, E., Bonde, J. P., Skakkebaek, N. E. & Olsen, J. (1998) Does moderate alcohol consumption affect fertility? Follow up study among couples planning first pregnancy. *Br. med. J.* **317**, 505–510.

Joesoef, M. R., Beral, V., Aral, S. O., Rolfs, R. T. & Cramer, D. W. (1993) Fertility and use of cigarettes, alcohol, marijuana and cocaine. *Ann. Epidemiol.* **3**, 592–594.

https://doi.org/10.1017/S0021932002000652 Published online by Cambridge University Press

Petersen, S., Stewart-Brown, S. & Peto, V. (1998) *Health and Lifestyles in Four Counties: The Results of the Third Healthy Lifestyles Survey*. Health Services Research Unit, Oxford.

Shiverick, K. T. & Salafia, C. (1999) Cigarette smoking and pregnancy. *Placenta* **20**, 265–272.

Stanton, C. K. & Gray, R. H. (1995) Effects of caffeine consumption on delayed conception. *Am. J. Epidemiol.* **142**, 1322–1329.

Vessey, M. P., Wright, N. H., McPherson, K. & Wiggins, P. (1978) Fertility after stopping different methods of contraception. *Br. med. J.* **1**, 265–267.

Zenzes, M. T., Wang, P. & Casper, R. F. (1995) Cigarette smoking may affect meiotic maturation of human oocytes. *Hum. Reprod.* **10**, 3213–3217.

https://doi.org/10.1017/S0021932002000652 Published online by Cambridge University Press