Original Article

Feedback from a point-of-care test for nicotine intake to reduce smoking during pregnancy

Graham F Cope[1], Pamela Nayyar[2] and Roger Holder[2]

Addresses
[1]Wolfson Applied Technology Laboratory
University of Birmingham
Queen Elizabeth Medical Centre
Egbaston, Birmingham B15 2TH, UK
[2]Department of Mathematics and Statistics
University of Birmingham
Birmingham, UK

Correspondence
Dr GF Cope
Institute of Research and Development
Birmingham Research Park
Birmingham B15 2SQ, UK
E-mail: g.cope.mermaid@ukonline.co.uk

Abstract

Background Smoking is the most important modifiable risk factor for adverse pregnancy outcome in the UK. New tools are needed to improve smoking cessation advice. The aim was to investigate a point-of-care urine test for smoking, to provide feedback to women, to improve awareness about the effects of smoking during pregnancy and to relate the test results to pregnancy outcome.

Methods A cross-sectional randomized controlled trial involving 856 pregnant women. All intervention patients were interviewed at their initial visit and tested for smoking. The test provided visual and numerical feedback. Smokers were followed up and retested at subsequent visits. The control group received anti-smoking counselling as part of routine care, but their smoking was monitored using the test. Both groups were interviewed and retested at 36 weeks' gestation.

Results Self-reported cigarette consumption fell significantly ($P<0.001$) in the intervention group, with 16.2% giving up and 33.3% significantly reducing their cigarette consumption. There was a significant fall in test results from 'booking' to 36 weeks' gestation ($P<0.0001$). In the control group, only 8% reported stopping and 23% reducing their cigarette consumption. Combined smoking test results at 36 weeks correlated significantly with birth weight ($P=0.006$) and body length ($P=0.011$).

Conclusions Point-of-care testing and feedback coupled with counselling can significantly reduce smoking during pregnancy and increase birthweight.

Ann Clin Biochem 2003; **40**: 674–679

Introduction

Smoking is the foremost modifiable risk factor for adverse pregnancy outcome in the UK,[1] being responsible for low birthweight as a result of intrauterine growth retardation.[2] At least a third of women who smoke will continue to do so during pregnancy, despite knowing many of the risks involved. Routine advice is clearly inadequate, and new strategies, with a co-ordinated and consistent effort from the medical profession, are urgently needed.[3]

Pregnant women who smoke are often pressurized to reduce or stop smoking and the incentive to misreport may be greater than in the past.[4] Furthermore, the assessment of smoking behaviour is far more complex than merely asking about cigarette consumption, as this does not take into account: the yield of cigarettes smoked, the method of smoking (puff topography), depth of inhalation, efficiency of absorption and metabolism.[5] Because of these difficulties, smoking cessation interventions in pregnancy are turning towards biochemical measurements to verify self-report and to quantify tobacco intake. A US study which measured serum cotinine (a major metabolite of nicotine) found that non-disclosure varied from 28% at enrolment to 35% at 36 weeks' gestation. This may reflect the fact that some patients react to interventions by providing the desired response to questions at follow-up.[6] This, and a number of studies, have found a closer dose–effect relationship between birthweight deficits and nicotine metabolite levels in serum and urine than with self-reported cigarette consumption.[7,8] Serum cotinine concentration at 16 weeks' gestation was also found to have a high positive predictive value for small-for-gestational age deliveries, which was double that for self-reported smoking habit and independent of associated maternal characteristics.[9] This led to the recommendation that

biochemical verification of self-reported quitting is essential to the evaluation of smoking cessation interventions and may be a useful predictor of poor pregnancy outcome.[6,9]

Biochemical testing for smoking is currently of little value to the patient. The laboratory tests are time-consuming for the midwives, and the impact is reduced because of the delay in obtaining the result. Point-of-care testing is an increasingly common mode of providing biomedical information to patients, and various approaches have been shown to be effective in changing patients' smoking behaviour.[10] Feedback is thought to offer important information, to create a sense of caring, to increase engagement in educational materials, to boost motivation and to provide comparisons and norms.[11,12]

We have developed a simple-to-use, point-of-care test that measures nicotine and its breakdown products, including cotinine, in urine.[13] Our aim was to investigate, for the first time, the clinical use of this test by assessing its effectiveness at reducing smoking during pregnancy and to determine any resultant improvement in birthweight and other birth parameters, the assumptions being that benefits could be derived from feedback and monitoring change.

Subjects and methods

Point-of-care test

We developed a 6-min, disposable point-of-care test that measured nicotine and its breakdown products, including cotinine, in urine (SmokeScreen®, Mermaid Diagnostics Limited, Birmingham, UK). A 2-mL urine sample added to dried chemicals contained within a patented testing device produced a concentration-dependent pink/orange derivative. The absorbance change at 510 nm was monitored by a portable colorimeter. The test was quantitative by comparison with a cotinine standard, and included a compensation factor for urine dilution. The assay detected the presence of a pyridine ring, a common biochemical feature of nicotine metabolites. Collectively, compared with a cotinine standard curve, the concentration of metabolites was referred to as cotinine equivalents (mg/L). The urine concentration was monitored by light absorption to assess the concentration of urine chromophores and referred to as urine absorbance. The test result was expressed as cotinine equivalent concentration/urine absorbance ratio.

The results ranged from 0 to 275, with a baseline of 10 taken to indicate an active smoker. The results correlated with self-reported cigarette consumption ($r = 0.69$, $P < 0.0001$) and nicotine yield of cigarettes smoked ($r = 0.14$, $P < 0.001$), and independent cotinine measurements by gas chromatography ($r = 0.89$, $P < 0.001$). The test had a sensitivity of 89.9% and specificity of 98.9%.[13]

Subjects

New referrals to three large inner-city hospital antenatal clinics were randomized on the basis of their allocated hospital unit number, even numbers being placed in the case or intervention group, or those who were provided with feedback from the smoking test at point of care. Initially, a pilot study was undertaken to assess the attitude of intervention smokers to the test, and determine whether the result and feedback did have any effect on smoking behaviour. After encouraging results, the pilot study was extended with a revised protocol.

Intervention

The intervention group, smokers and non-smokers alike, were seen at their initial visit and given a brief verbal explanation of the test and the aims of the research (*see* Fig. 1). Each was asked to give verbal consent for inclusion in the study. After agreeing, they were asked for a sample of urine, which they usually had brought with them to clinic, for routine testing. The 6-min test was carried out in their presence, during which time the patient was asked about current and previous smoking habit, and other social and demographic details, which were entered onto a short questionnaire.

On completion, the women were shown the resultant colour of the test and told the numerical result. This was illustrated as a point on a graph showing a previously compiled wide range of smoking test results against reported daily cigarette consumption (*see* Fig. 2). This distribution is similar for any biochemical measure of smoking and to a great extent represents the variations in smoking behaviour and nicotine metabolism. Current smokers and those with a positive result were enrolled in the study. All non-smokers with a negative result were further excluded.

A specific 'quit date', usually within the next 14 days, was chosen by mutual agreement, and this was written on the test result sheet. The women were given a printed leaflet containing practical advice on how to reduce their smoking and invited to return for measurement at their next and subsequent visits. A positive, friendly attitude was taken to smoking, with emphasis on trying to empower the smoker, with information, feedback and encouragement, to change her smoking behaviour. This protocol was repeated whenever the patient returned to the clinic, up to and including the 36-week visit, with measurement, questioning about changes in smoking, specific events on the 'quit date' and reinforcement of advice.

By comparison, the women assigned to the control group were not seen at their initial visit, but had their urine measured. They therefore did not have the

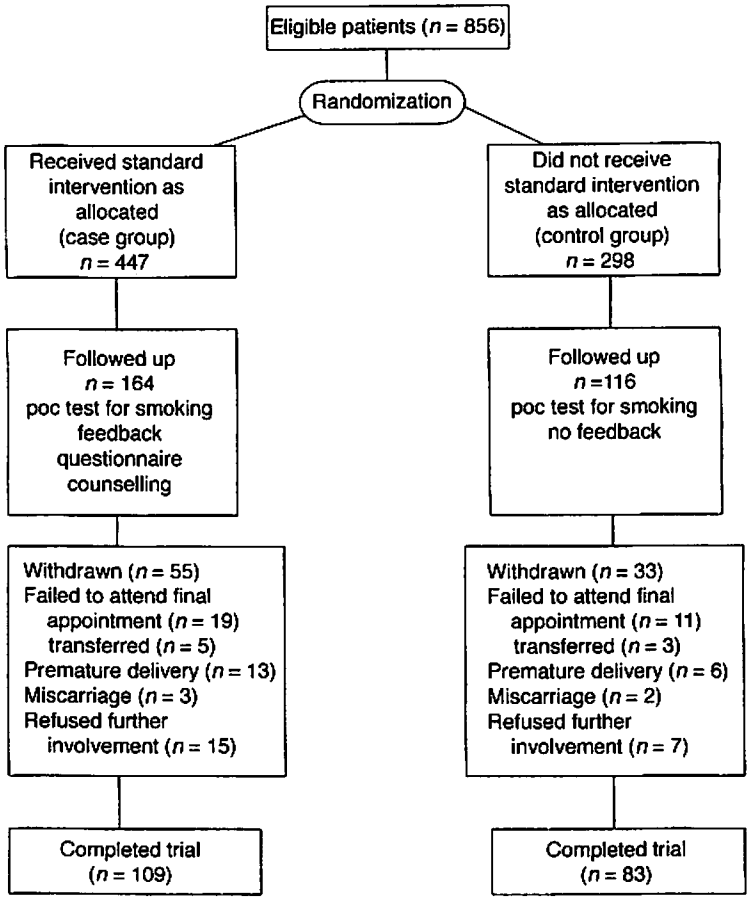

Figure 1. *Flow diagram showing methodology, including patient randomization and treatment during the intervention for case and control patients. poc, point-of-care.*

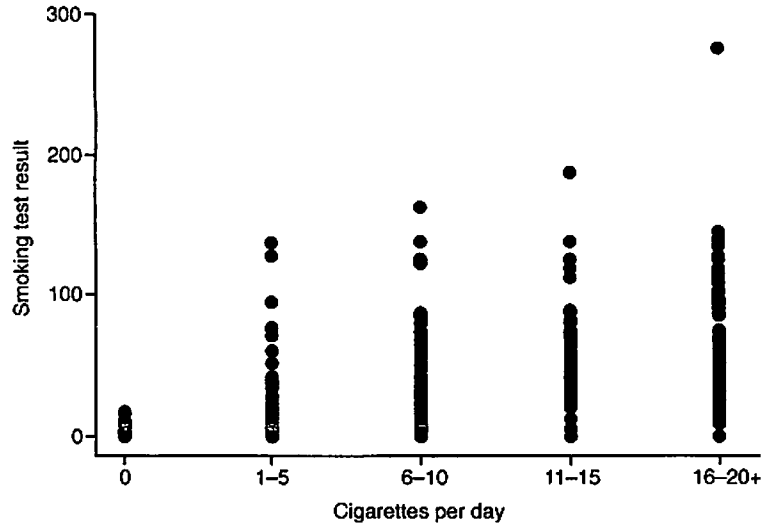

Figure 2. *The range of smoking test results against different categories of self-reported daily cigarette consumption. The broad range of results in each category reflects, in part, the variability of smoking behaviour in relation to brand of cigarettes smoked, puff topography, depth of inhalation, absorption and nicotine metabolism.*

benefit of seeing the test or its result. They received counselling about smoking in pregnancy from their hospital midwife and from the obstetrician as part of usual care. Control patients were traced throughout pregnancy and interviewed at their 36-week visit. Like the intervention women, they were interviewed and the nature of the study explained. The fact that their urine had been previously tested was also made clear and at this point verbal consent was obtained. They were asked about changes to their smoking throughout pregnancy, and about the frequency and source of any anti-smoking advice.

Data analysis

Birth details, including gender, birthweight, length and head circumference, together with gestation, type of delivery and Apgar scores at 1 and 5 min, were collected post-partum from the medical records. All

data were entered into a database and analysed with Minitab® statistical software. ANOVA, ANCOVA and Wilcoxon sign rank test were used for analysis of quantitative smoking test device results, with $P<0.05$ taken as statistically significant.

Results

The initial recruitment of women in the intervention group was 447. Of these, 164 (36.7%) reported being current smokers, with an average consumption of 11.8 cigarettes per day; 43 (9.6%) reported quitting during pregnancy, but before their first hospital visit; and two (0.4%) quit within the previous 12 months, but before conception. The remainder (53.2%) had never smoked or were long-term ex-smokers. In the control group we recruited 409, of which 116 (38.9%) had a positive smoking test device result and were therefore classified as current smokers; 34 (11.4%) were subsequently found to have quit before their first antenatal visit; 12 (4%) quit within the previous 12 months. This left 45.7% as long-term ex-smokers or never smokers.

During the course of the investigation we followed through to delivery 109 smokers in the intervention group and 83 smokers in the control group. The reasons for exclusion or loss to follow-up at 36 weeks in the intervention group ($n=55$) were: 27.7% failed to attend their final appointment, were lost, moved or could not be located, 6.2% were referred to another care provider, 21.5% had premature delivery prior to 36 weeks, 3.1% had a suspected miscarriage, and 26.2% refused to take further part in the study. The reasons for loss to follow-up in the control group ($n=33$) were: 12.3% had false positive test results, 29.8% failed to attend final appointment, were lost, moved or were unable to be located, 10.5% were referred to another care provider, 19.3% had a premature delivery, 7% had a suspected miscarriage and 21.1% refused to take further part in the study. The remainder dropped out for unknown reasons.

With respect to self-reported smoking at 36 weeks, in the intervention group 16 (16.2%) stopped smoking, 33 (33.3%) significantly reduced their cigarette consumption, leaving 50.5% who reported being unable to change and were maintaining their usual smoking habit. By comparison, in the control group, none reported quitting during the period of the study, 30 (47.6%) reported cutting down and 33 (52.4%) reported maintaining their usual habit.

Collectively, there was a highly significant fall in smoking test results in the intervention group from 'booking' (median ratio 42.5) to 36 weeks' gestation (median 27.6, $P<0.0001$), whereas in the control group there was no significant difference between the two points. The smoking test results in the intervention group at 36 weeks were significantly lower than in the control group (median 37.6, $P<0.003$).

Smoking test data on smokers, measured both at the beginning and end of the intervention (*see* Table 1), showed that at 36 weeks in the intervention group 22.2% had a negative smoking test, 5.1% had a positive but very low result (indicating exposure to environmental tobacco smoke or occasional cigarette use), 42.4% had a significantly lower test result than at 'booking', and 11.1% had elevated values, including three women in whom the result was more than double their initial result. The changes in the control group were: 6.8% having a negative result and 33.9% significantly reduced their result. However, the greatest differences were that 45.7% increased their initial value, with 17 women more than doubling their result.

While self-reported cigarette consumption at recruitment was no predictor of changes to smoking, the smoking test results showed trends in which women with high results reduced their nicotine intake, while some with a low initial result, because they had previously reduced their cigarette consumption, tended to increase their nicotine intake. Women who quit included both those with low results who were long-term light smokers and women with high results who were shocked by the result and took a decision to stop.

When asked to subjectively evaluate the influence of the smoking test on changes in their smoking behaviour, a majority thought the test was a good idea and had helped them to appreciate more about their smoking. The control group were asked to recall any questions or advice they were given by hospital staff while attending the hospital. A majority (66.7%) could not recall any questions or information being given, even though questions were routinely included as part of the 'booking' procedure.

Analysis of available birth parameters and smoking test results showed that in the intervention group ($n=78$) test results at 'booking' were not related to any post-partum parameters or other delivery assessments, while results at 36 weeks correlated with birthweight

Table 1. *Results showing changes in smoking habit in intervention and control women as determined by the smoking test device*

	Intervention		Control	
	n	%	*n*	%
Quit smoking (>10 to <10)	22	22.2	4	6.8
Reduced (<20%)	5	5.1	0	0.0
Reduced (21% to 80%)	42	42.4	20	33.9
Remained the same (81% to 120%)	19	19.2	8	13.6
Increased (121% to 200%)	8	8.1	10	16.9
Increased (>200%)	3	3.0	17	28.8

Tests positive for nicotine metabolites have a result greater than 10. Results are those at 36 weeks compared with initial results at 'booking'.

($r = -0.23$, $P = 0.04$) and infant length ($r = -0.24$, $P = 0.04$). Combination with the control group provided a larger group for analysis ($n = 158$). Nicotine intake, as measured by the smoking test, was related to birthweight ($r = -0.22$, $P = 0.006$) and body length ($r = -0.20$, $P = 0.011$), and its relationship with head circumference approached significance ($r = -0.154$, $P = 0.056$). There was no significant relationship between the smoking test result and gender, gestation, type of delivery or Apgar scores.

Adjustment for nicotine metabolite results in the two groups using ANCOVA revealed a significant difference in birthweight between the intervention group (3.26 kg) and the control group (3.08 kg, $P < 0.03$). This would suggest that the intervention had an overall effect of improving birthweight irrespective of nicotine metabolite values.

Discussion

Biochemical measurement of smoking, by the laboratory assessment of nicotinic metabolites such as cotinine, is increasingly used in the research antreatment of smoking-related conditions, in particular smoking during pregnancy.[6] Such measurements are of little value to the patients because of time delays in returning the result. We developed a 6-min point-of-care test for smoking, measuring nicotine and all its metabolites, based on a colorimetric assay in urine to provide immediate feedback about smoking habit.

This randomized controlled trial of the use of the smoking test provided both visual and numerical feedback to both patient and investigator and formed the basis for counselling which took into account the individual's smoking behaviour. An encouraging and non-judgemental approach improved the quit rate, and resulted in a reduction in cigarette consumption compared with the control group. The smoking test results demonstrated a highly significant reduction in nicotine intake, not only among those who quit or cut down, but also in a proportion of women who reported maintaining their smoking habit. Discussions with this group suggested that changes in cigarette use were evident, despite cigarette consumption remaining the same.

In the control group, only a few women remembered receiving any advice about smoking in pregnancy, except perhaps the generalized statement that they should stop. All agreed this had little or no effect on their smoking behaviour, particularly as no further advice on how the women might achieve this was offered.

Analysis of birth parameters showed that the test result at 36 weeks was related to birthweight and body length and to a lesser extent head circumference, and we found that quitters had significantly heavier and larger babies than those who continued to smoke. Adjustment for smoking test results showed a significant difference in birthweight between both groups, implying that the provision of tailored advice coupled with friendly practical guidance from a dedicated counsellor improved the pregnancy outcome.

Our approach was based on a number of previous studies, one of which advocated the use of designated counsellors who taught specific cessation skills and reinforced advice with follow-up contact and printed material specifically for the pregnant smoker.[14] A study by Haddow *et al.*[15] verified self-reported smoking by serum cotinine measurement using a laboratory method, and sent the results to the woman's physician, along with an interpretation of its meaning and an estimate of her relative risk due to smoking. This intervention led to a significant reduction in smoking and an increase in birthweight.[15] We concurred with recommendations that immediate and complete cessation is too demanding for most smokers, and that cessation must be viewed as a process of stages of change, in order to understand the smoker's point of view, to motivate her progress and to respond to the patient's needs.[14,16]

A recent study by Moore *et al.*[17] to evaluate the effectiveness of a self-help approach to smoking cessation found that specifically designed booklets given or sent out at particular times during pregnancy were ineffective. The cotinine-validated rates of cessation were substantially lower than self-reported rates.[17] This study lends weight to the theory that individually tailored advice and feedback about smoking levels could be a better approach.

The advantages of using the smoking test are, firstly, that it correctly identifies the vast majority of smokers. Considering that denial is an important problem during antenatal care,[6] we observed a 10.3% denial rate of smoking to midwives during routine history-taking.[18] The visual and numerical feedback increased the smoker's awareness of her smoking, and repeat testing monitored any changes to smoking habit. Feedback has recently been described as offering important information to create a sense of a caring and helping relationship, to reach more directly decisional considerations, to increase engagement with the materials, to increase motivation, or to provide social comparison and norms.[11]

We emphasized to the patients that the test was not a 'lie detector' but merely an assessment of baseline smoking from which to progress, with advice, support and encouragement at all stages. The demonstration of the presence of smoke components in pregnant women in a clinic has previously been considered to be a valuable adjunct to cessation efforts.[15]

Our cessation rates in the intervention group of 22% compared with 7% in controls are similar to those achieved in other cotinine-validated interventions, but we were able to show that some women, although

consuming their usual amount of cigarettes, did alter their smoking habit by smoking less effectively. That is, not smoking the whole cigarette or inhaling less deeply following the initial 'hit'. A rise in nicotine metabolite levels observed in a control group towards the end of pregnancy had been noted previously, but the authors concluded that this rise was a manifestation of physiological changes during pregnancy.[8] Unfortunately, this study was not controlled, and a fall in the intervention group was not observed. A possible explanation for this is that smokers reduce their smoking at the onset of pregnancy, but in the last trimester, when anxiety, immobility and boredom are a problem, smoking increases, especially when smoking habit is not verified.

Recent studies have indicated that nicotine metabolism is altered in pregnancy, with the clearance of nicotine and cotinine being significantly higher in pregnant women and the half-life of cotinine being much shorter, 8.8 h compared with 16.6 h in the non-pregnant state.[1]

The present study evaluated a novel point-of-care test as a tool to reduce smoking in pregnancy. The test provided a simple-to-use, inexpensive means of correctly identifying the vast majority of smokers, assessing their baseline nicotine intake and monitoring adherence to anti-smoking advice. The programme of advice centred on the smoking test contributed to a significant improvement in smoking cessation, and reduced cigarette consumption. In women who reported maintaining their cigarette consumption, a third had significantly lower test results at their return visit, reflecting a decrease in nicotine intake despite consuming the same number of cigarettes. The study identified, for the first time, an increase in nicotine metabolite excretion towards the end of pregnancy in the control group, suggesting it to be a true reflection of an increase in smoking, probably due to enhanced anxiety and boredom, not as a physiological function of pregnancy, as was previously thought.[8]

Acknowledgements

We would like to thank Dr Roy Condie and Professor David Luesley of City Hospital NHS Trust and Mr Harry Gee of Birmingham's Women's Healthcare Trust for access to their patients. We acknowledge the midwives and clerical staff for their help and assistance throughout this project. We are indebted to the Department of Health for financial support. We would also like to thank the staff of Springfields Health Promotions Unit, Selly Oak Hospital, Birmingham, for supplying the Smoking in Pregnancy leaflet.

Conflict of interest

GFC is one of the joint inventors of SmokeScreen and is employed by Mermaid Diagnostics Limited, a company partially owned by the University of Birmingham, which now manufactures the test.

References

1 Dempsey D, Jacob P, Benowitz NL. Accelerated metabolism of nicotine and cotinine in pregnant smokers. *J Pharmacol Exp Ther* 2002; **301**: 594–8
2 Windsor RA, Li CQ, Lowe JB, Perkins LL, Ershoff D, Glynn T. The dissemination of smoking cessation methods for pregnant women: achieving the year 2000 objectives. *Am J Public Health* 1993; **83**: 173–8
3 Fisher F. Smoking in pregnancy. *Br J Hosp Doc* 1993; **50**: 13–5
4 Klebanoff MA, Levine RJ, Morris CD, Hauth JC, Sibai BM, Curet LB, *et al.* Accuracy of self-reported cigarette smoking among pregnant women in the 1990s. *Paediatr Perinat Epidemiol* 2001; **15**: 140–3
5 Haddow JE, Knight GJ, Palomaki GE. Measuring serum cotinine to aid in smoking cessation during pregnancy and to enhance assessment of smoking-related morbidity. In: Poswillo D, Alberman E, eds. *Effects of Smoking on the Fetus, Neonate, and Child.* Oxford: Oxford University Press, 1992: 207–22
6 Kendrick JS, Zahniser C, Miller N, Salas N, Stine J, Gargiullo PM, *et al.* Integrating smoking cessation into routine public prenatal care: the smoking cessation in pregnancy project. *Am J Public Health* 1995; **85**: 217–22
7 Ellard GA, Johnstone FD, Prescott RJ, Ji-Xian W, Jian-Hua M. Smoking during pregnancy: the dose dependence of birthweight deficits. *Br J Obstet Gynaecol* 1996; **103**: 806–13
8 Mathai M, Skinner A, Lawton K, Weindling AM. Maternal smoking, urinary cotinine levels and birth-weight. *Aust N Z J Obstet Gynaecol* 1990; **30**: 33–6
9 Mathews F, Smith R, Yudkin P, Neil A. Are cotinine assays of value in predicting adverse pregnancy outcome? *Ann Clin Biochem* 1999; **36**: 468–76
10 Lerman C, Orleans CT, Engstrom PF. Biological markers in smoking cessation treatment. *Semin Oncol* 1993; **20**: 359–67
11 DiClemente CC. The role of feedback in the process of health behavior change. *Am J Health Behav* 2001; **25**: 217–27
12 McClure JB. Are biomarkers useful treatment aids for promoting health behavior change? *Am J Prev Med* 2002; **22**: 200–7
13 Cope G, Nayyar P, Holder R, Gibbons J, Bunce R. A simple near-patient test for nicotine and its metabolites in urine to assess smoking habit. *Clin Chim Acta* 1996; **256**: 135–49
14 Brosky G. Why do pregnant women smoke and can we help them quit? *Can Med Assoc J* 1995; **152**: 163–6
15 Haddow JE, Knight GJ, Kloza EM, Palomaki GE, Wald NJ. Cotinine-assisted intervention in pregnancy to reduce smoking and low birthweight delivery. *Br J Obstet Gynaecol* 1991; **98**: 859–65
16 Macleod Clark J, Maclaine K. The effects of smoking in pregnancy: a review of approaches to behavioural change. *Midwifery* 1992; **8**: 19–30
17 Moore L, Campbell R, Whelan A, Mills N, Lupton P, Misselbrook E, Frohlich J. Self help smoking cessation in pregnancy: cluster randomised controlled trial. *BMJ* 2002; **325**: 1383–6
18 Cope GF, Nayyar P, Holder R. Measurement of nicotine intake in pregnant women: associations to changes in blood cell count. *Nicotine Tobacco Res* 2001; **3**: 119–22

Accepted for publication 1 May 2003