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The use of carbon monoxide screening to identify maternal smoking at the first antenatal visit

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ABSTRACT

Objectives: This prospective observational study evaluated breath carbon monoxide (BCO) testing in identifying maternal smokers.

Design: Prospective observational study conducted between January and September 2017.

Setting: A university obstetric hospital in an urban setting responsible for approximately 8500 deliveries per year.

Participants: After confirmation of an ongoing pregnancy, women were recruited at their convenience (n=250). A detailed questionnaire on smoking was completed and the BCO test was performed to measure recent exposure to CO sources. Women <18 years and those who did not understand English were excluded.

Primary and secondary outcome measures: The number of women who self-reported smoking and those that were positive on the BCO test. The characteristic differences between when who disclosed and did not disclose smoking status.

Results: A BCO cut-off point of ≥3ppm was calculated as the optimal level to identify ongoing smoking. Based on the history, 15% of the 250 women reported as current smokers. Using BCO levels ≥3ppm the rate of maternal smoking increased to 23%. When BCO levels ≥3ppm were combined with the detailed research questionnaire, the rate increased further to 25%. Non-disclosers were more likely to have spent longer in education than disclosers (P<0.01). Six disclosers had BCO levels <3ppm but five of these were light smokers and all six had not smoked during the previous four hours.

Conclusions: We found that 25% of women presenting for antenatal care continued to smoke in our population but only 60% of smokers report their smoking on routine questioning. BCO measurement is an inexpensive and practical test to improve identification of maternal

smoking. Improved identification means all smokers can be offered smoking cessation interventions in early pregnancy which may potentially prevent fetal growth restriction in the short-term and benefit both mother and baby in the long-term.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- Sensitivity and specificity analysis were carried out to determine the optimal cut off point to determine smoking as there are wide variations and no consensus in the literature, particularly in pregnancy populations.
- Our study collected details of daily exposure to environmental sources of CO as well as passive smoking exposure.
- Carbon monoxide analysis although the most practical and feasible screening tool to detect smoking in a large cohort, can only detect exposure from up to four hours previous.

BACKGROUND

Maternal smoking is arguably the most important modifiable risk factor for adverse pregnancy outcomes including perinatal death.[1] Passive smoking is also linked to adverse outcomes, in particular fetal growth restriction.[2,3] Smoking cessation either prepregnancy or in the first half of pregnancy can normalise fetal growth.[4]

Although smoking rates in non-pregnant adult women are falling in Ireland, over one in ten women report that they continue to smoke at their first antenatal visit.[5] Similar rates were found in other developed countries. However, younger women have consistently higher smoking rates, regardless of pregnancy status.[6,7] Many women may not disclose their smoking status when they present to the maternity services.[8] Non-disclosure of smoking leads to inaccurate smoking prevalence rates and missed opportunities to offer advice and support to quit.[9] This has led to the use of biochemical markers to identify people who fail to disclose their smoking behaviour.[10-12]

The most commonly used biomarkers of smoking include serum carboxy-hemoglobin or cotinine, a by-product of nicotine, from urine, saliva or urinary samples.[13] These methods, although valid, reliable and sensitive to recent smoking can be invasive, inconvenient and expensive as they require laboratory involvement for analysis. Thus, they may be only feasible in a research setting. A breath carbon monoxide (BCO) test is an alternative biomarker of cigarette exposure which is safe, cost-effective, quick and non-invasive.[14,15] Furthermore, the BCO test yields immediate results at the point of care.[13] BCO correlates well with serum and urine cotinine levels and has shown high sensitivity and specificity in distinguishing between smokers and non-smokers.[16] BCO is a practical option to help identify women who do not disclose their smoking in the antenatal outpatients.

A number of guidelines worldwide recommend the screening of carbon monoxide (CO) at the first antenatal visit.[17,18] The screening of all pregnant women with a BCO test has

two important purposes. Firstly, it can help identify women who continue to smoke in pregnancy and give staff the opportunity to advise and provide support to quit. Secondly, the BCO test can ensure that the woman and her baby are not inadvertently in contact with the poisonous gas.[17]

CO is not only a product of cigarette smoke exposure, it can also be produced by exhaust fumes or emitted from malfunctioning or poorly ventilated fossil or wood fuelled heating and cooking appliances.[19] It is a colourless, odourless, tasteless and poisoning gas that is potentially fatal at high levels. Exposure to CO is particularly dangerous during pregnancy because it replaces the oxygen available to the fetus, restricts growth and development, and increases the risk of fetal death, developmental disorders, and chronic cerebral lesions.[20]

The purpose of this prospective observational study was to evaluate the use of BCO screening to detect cigarette smoking in women presenting to a maternity hospital for antenatal care.

METHODS

This prospective observational cohort study was conducted between January and September 2017 in a large university maternity hospital responsible for approximately 8,500 deliveries per annum. At the first antenatal visit the woman's history was computerised by a trained midwife. Histories were taken in a standardised manner and included questions regarding a number of lifestyle issues such as self-reported smoking. On completion of the history, women were recruited by convenience sampling to the current study. Women were ineligible if they were under 18 years of age or did not understand English.

Eligible women were invited to participate in the study and informed that the BCO test would assess their exposure to CO sources such as tobacco smoke, exhaust fumes or poor

household ventilation etc. Women consented to provide a sample of expired air and to complete an additional research questionnaire. This questionnaire collected further sociodemographic information i.e. education level, potential environmental exposures to carbon monoxide such as passive smoke, and a repeated self-reported smoking status. Women were assured that all data were anonymous and would not affect their care in the hospital to encourage accurate reporting in the research questionnaire. Potential environmental exposures to CO were collected due to their potentially confounding nature in accurately identifying smokers.

Any individual in attendance with the woman at the first visit also offered participation in the study. The individual was also fully informed of the study procedures and written consent was obtained. The individuals followed the same study procedures as the pregnant woman. BCO was performed and completed an identical research questionnaire.

BCO levels were performed using the inexpensive, handheld Bedfont piCO+ Smokerlyzer® (Bedfont Scientific, Kent, United Kingdom). To perform the breath test, women were asked to exhale completely, inhale fully and breath-hold for 15 seconds. At the end of the breath hold, the women were asked to exhale slowly and fully into the Smokerlyzer device. Safety protocols were put in place to minimise the risk of missing potential cases of CO poisoning. [17] The Smokerlyzer measures BCO levels in parts per million (ppm). Breath holding allows the CO in the blood to form an equilibrium with the CO in the alveolar air. This is responsible for high level of correlation between breath CO levels and COHb concentration (Middleton et al. 2000, new reference1).

Based on previous work, we estimated that recruitment 233 women allowed for detection of a 10% rate of non-disclosure (power 99%, significance 5%). Due to large variations in the cut-off criteria used previously to distinguish between smokers and non-smokers a receiver-operating characteristic (ROC) plot was undertaken. The ROC assessed

the accuracy of the BCO test in predicting smoking and the BCO level (ppm) with the highest combined sensitivity and specificity value was used as the cut-off. Women who had a CO level greater than the cut-off point but reported she was a non-smoker were categorised as a non-discloser.

All results were analyzed by the SPSS statistical package (SPSS; Chicago, IL). Descriptive statistics were used to describe the characteristics of the study cohort. Normality of data were assessed using visual inspection of histograms, the data skewness and kurtosis and the Kolmogorov-Smirnov Test. Continuous data were reported as means and standard deviation if normally distributed and median and interquartile ranges (IQR) if data were non-normally distributed. Categorical data were reported as proportions. Chi-squared, analysis of variance (ANOVA) and Mann Whitney U were used to assess differences in proportions and means, respectively, between groups. Associations between CO levels and other variables were carried out using Spearman's correlations. Missing data are presented in the footnotes of tables.

RESULTS

The ROC results showed the BCO levels measured in parts per million (ppm) were predictors of maternal cigarette smoking (area under the curve (AUC) = 0.93, $p < 0.001$) (Supplementary Figure 1). The sensitivity and specificity curves crossed at a cut-off point of 3ppm (Supplementary Figure 2). The highest combined sensitivity and specificity of maternal smoking was also at the CO level 3ppm (Supplementary Table 1).

Two hundred and eighty-eight women were offered participation in the study of which 250 were recruited. Of the 38 women that did not take part, 20 declined due to time constraints and 18 accepted participation but left before completion of data collection.

Verified smoking was defined as having a CO level ≥ 3ppm and/or self-reported smoking either at the first antenatal visit or on the research questionnaire.

Table 1 shows the characteristics of the study group analysed by verified smoking status. Verified maternal smokers (n=61) were more likely to be younger (mean difference 3.4 years 95% Confidence Intervals (CI) 1.9-4.9, $p < 0.001$), unemployed (43% vs 22%, $p < 0.001$) and single (77% vs 39%, $p < 0.001$) than non-smokers (n=187). They also spent fewer years in continuous full time education (mean difference 1.9 years 95% CI 0.6-3.1, $p < 0.01$) and finished full time education at a younger age (mean difference 2.7 years 95% CI 1.2-4.2, $p < 0.001$) than non-smokers (n=181)

Of all environmental sources investigated, the number of self-reported cigarettes per day had the strongest association with BCO test levels (rho = 0.61, $p < 0.001$) followed by time since last cigarette (rho = -0.51, $p < 0.01$). Passive smoking was also associated with BCO levels (rho = 0.38, $p < 0.001$). However, when self-reported active smokers were removed from the analysis this association weakened (rho = 0.15, $p < 0.05$).

BCO tests were performed on 54 partners of the pregnant women (22%). The mean age of the partners was 33.1 years (6.5 years), 98.1% were male, 83.3% lived with their pregnant partner and median BCO level of the partners was 2.0ppm (interquartile range (IQR) 4.5ppm). Twenty-eight percent (n=15) of partners reported current smoking and five of these had a pregnant partner who also smoked. Of the 26 partners with positive BCO tests their median levels were 6.0 (IQR 8.0) similar to the median BCO of women with positive tests 7.0 (IQR 8.0). On examination of BCO levels 48% (n=26) had a CO ≥3ppm. The BCO levels in the partners were weakly associated with the BCO levels of the pregnant women (rho = 0.27, $p < 0.05$). However, median values of BCO levels in pregnant women were the same regardless of their partners CO levels being < or ≥ 3ppm.

Median BCO levels and rates of BCO < and ≥ 3ppm by both maternal characteristics and CO sources are shown in Tables 2 and 3. Of all known CO sources that were examined, self-reported maternal smoking in the current and previous pregnancy, cigarette quantity and timing of last cigarette were the only factors that were associated with an increased median BCO level.

Maternal characteristics of the disclosers and non-disclosers of smoking status were compared (Table 4). Non-disclosers were classified as women who did not report smoking at their first antenatal visit but had a CO level ≥3ppm and/or self-reported smoking in the research questionnaire. Non-disclosers had a lower median BCO level than disclosers (10.0 ppm (8.0) vs 4.0 ppm (3.0), $p < 0.01$). Non-disclosers were older than disclosers when they finished full time education (20.9 years (3.9) vs 17.9 years (2.1), $p < 0.05$) and spent more years in continuous full time education (16.5 years (3.6) vs 13.4 years (2.4), $p < 0.01$). They were also more likely to have planned their pregnancy (60% vs 37%, $p < 0.05$), less likely to have smoked in a previous pregnancy (20% vs 55%, $p < 0.01$) and spend less time around passive smoking daily (1.5 hours (1.6) vs 3.9 hours (3.5), $p < 0.05$).

Changes in self-reported smoking status from the first antenatal visit to self-reported smoking status collected in the research questionnaire is shown in Table 5. The largest difference was seen in women who reported 'never smoking' at the first antenatal visit to midwives with 17% changing their status to 'ex-smoker' on the research questionnaire. Six other women who reported they were never smokers to midwives at the first antenatal visit had a CO reading ≥3ppm. Of these, one woman changed her self-reporting on the research questionnaire to ex-smoking status and reported quitting two months previous. Two other women reported smoking cannabis which could be the reason for the CO ≥3ppm. At first visit 17 potential non-disclosers reported they were ex-smokers. Of these, six disclosed smoking

on the research questionnaire. Another five women reported they had only quit since the beginning of pregnancy and one was continuing to smoke cannabis.

Based on self-reported smoking status at the first antenatal visit, 15% (38/250) of women were maternal smokers. Based on self-reported smoking in the research questionnaire, the rate rose to 17% (42/250). When results from the BCO test levels ≥3ppm were used the rate increased to 23% (57/250). However, when BCO levels ≥3ppm were combined with self-reporting the rate of maternal smoking was 25% (63/250). Based on self-reported non-smoking, our study had a rate of non-disclosure of 12% (25/212).

Six women who reported smoking were not detected on CO screening. All six reported not having a cigarette in the previous four hours and five of the six women smoked ≤2 cigarettes daily.

DISCUSSION

We found that BCO testing in combination with self-reporting of smoking status in a research setting identified 10% more maternal smokers than self-reporting using routine questionnaires at the first antenatal visit. Two out of five women who continue to smoke in pregnancy were not being identified thus, maternity services were missing the opportunity to provide advice and support smoking cessation.

There is no consensus as to what constitutes the best cut-off point for determining smoking status. Some suggest a CO level as low as 2 parts per million (ppm), others as high as 10 ppm.[21-23] There are also variations due to different monitors used and the populations studied. The NICE guidelines recommend using a low cut-off point of 3ppm to avoid missing women due to light or infrequent smoking that may need help to quit smoking.[18]

Due to the conflicting appropriate cut-off points in the literature we undertook our own sensitivity and specificity analysis.[22] Similar to a large study in non-pregnant adults, we identified a cut-off point of 3ppm as the optimal to distinguish smokers from non-smokers in

terms of limiting both false positive and false negative results and maximise identification of smokers with a high degree of certainty.[22] Few studies have previously undertaken their own ROC making it difficult to interpret the sensitivity and specificity of their results.

We also collected data on other potential environmental sources of CO that may have contaminated results. Other studies do not take into account daily passive smoke exposure or sources such as motor vehicle use, fossil fuel exposure, gas/oil boiler servicing practices, ventilation etc. These factors did not affect median BCO levels in women in the present study, and did not increase rates of BCO levels ≥3ppm. One study in non-pregnant adults examined the effect of other sources of CO on BCO test levels and found that gender and motor vehicle use were associated with higher CO levels. However, the differences were minimal with <1ppm in the difference.[15]

A challenge of BCO testing is the half-life of CO. CO exposure in the previous 3 to 5 hours can be detected by a BCO test and it is, therefore, unable to detect active tobacco exposure from the previous day.[9] Cotinine samples from serum, urine and saliva, however, have a half-life of 20 hours and, therefore, are more robust measures of cigarette exposure.[24] Despite this, cotinine has the disadvantages of being invasive, requiring laboratory analysis and is more expensive as it is estimated to cost approximately $20 per sample compared to less than $1 per sample for BCO.[25]

Our study found a self-reported smoking rate of 15%, 4% higher than the rate reported in our previously study that analysed all deliveries in our hospital in 2015.[5] It is unlikely that the rate has risen, and this higher rate may be due to the convenience sampling.

Our study distinguishes characteristics between smokers and non-disclosers unlike most previous studies, which compare verified smokers to non-smokers.[12] Surprisingly, we found non-disclosers tend to have more similar characteristics to non-smokers than smokers. This may be influenced by the intensity of the 'anti-smoking environment' Not only has there

been increased media attention but national laws have prohibited unique branding on cigarette packages and replaced it with images depicting the negative affects smoking has on health and disease.[26] For example, women who are trying to quit are more likely to not disclose smoking status.[27,28] This may also be due to false positive results or 'white coat compliance'. For example, non-disclosers tended to be more educated, which suggests that they are aware of the risks of smoking and are conforming to the socially-desirable behavioural norms.[25] Another study comparing non-disclosers to smokers found the only difference between groups was ethnicity with no difference in educational years.[11]

We found that some women changed their smoking status, particularly from never smokers to ex-smokers, in the short period between the antenatal history taken by midwives and the researcher (CR). A meta-analysis found that non-pregnant populations self-report different smoking behaviours depending on the context.[25] However, these studies compared self-administered vs interviewer administered questionnaires.[25]

A number of different rates of non-disclosure have been reported in the literature, from as low as 5% to as high as 73% but it is difficult to compare these results to our study.[8,29] Firstly, the definition of 'non-disclosure' or 'miss-categorisation' is not standardised across studies. Different denominators are used. Some studies use the number of positive tests whereas others use total population, total self-reported non-smokers or self-reported quitters.[11,12,30,31] Secondly, studies to date have used conflicting cut-off points to verify smoking, for example, some use standard cut-of points, some use ROCs to find the optimal for their population and others use both which shows disparity in results.[11,28,30]

There are also large differences in sample sizes, from 74 to 7,405.[8,13] Furthermore, these samples vary in ethnicity, which is a contributing factor to non-disclosure rates.[11] Lastly, the samples in these studies are taken at different time points in pregnancy. Our study took BCO samples at the beginning of pregnancy. However, previous research found that

non-disclosure rates are increased from the beginning to later in pregnancy.[12,28] Sampling at the first visit is preferable because early identification and successful intervention in the first half of pregnancy may potentially normalise fetal growth.[31]

In conclusion, self-reporting of maternal smoking leads to inaccuracies in clinical practice disclosure which may result in missed opportunities to provide smoking cessation advice and support from the beginning of pregnancy. BCO screening can improve identification of smokers at the first antenatal visit. This screening complements routine history taking, but should not replace it as this test may produce a false negative in smokers who have not had a cigarette in the previous four hours. Screening in early pregnancy should use a low cut-off value because a once-off test resulting in a false positive test is preferable to a false negative test. BCO levels not only correlate with self-reporting numbers of cigarettes but also with timing of smoking. Finally, cotinine may need to also be used as an adjunct to CO screening in women with high CO levels who report that they are non-smokers to rule out a false positive test.

STATEMENT OF CONTRIBUTION

CR contributed to the conception and design of the study, performed the analysis of the data, interpreted data and wrote and edited this original article. RK,EOM and SS contributed to the writing and editing of this article. MT and BE contributed to the conception of the study, interpretation of data as well as contributing to the writing and editing of this article.

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DECLARATION OF INTERESTS

None of the authors have any conflicts of interest to declare.

PATIENT CONSENT

Written consent was obtained.

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DATA SHARING STATEMENT

Extra data is available by emailing ciara.reynolds@ucdconnect.ie

REFERENCES

1. Cnattingius S. The epidemiology of smoking during pregnancy: smoking prevalence, maternal characteristics, and pregnancy outcomes. Nicotine Tob Res 2004;6Suppl2:S125-40.
2. Rubin DH, Krasilnikoff PA, Leventhal JM, et al. Effect of passive smoking on birth-weight. Lancet 1986;2(8504):415-7.
3. Martinez FD, Wright AL, Taussig LM. The effect of paternal smoking on the birthweight of newborns whose mothers did not smoke. Group Health Medical Associates. Am J Public Health 1994;84(9):1489–91.
4. Lieberman E, Gremy I, Lang JM, et al. Low birthweight at term and the timing of fetal exposure to maternal smoking. *Am J Public Health* 1994;84: 1127–31.
5. Reynolds CME, Egan B, McKeating A, et al. Five year trends in maternal smoking behaviour reported at the first prenatal appointment. *Ir J Med Sci* 2017;186:971-9.
6. European Perinatal Health Report (2010) The health of pregnant women and babies in Europe in 2010.http://www.europeristat.com/images/European%20Perinatal%20Health%20Report_2010.pdf. Accessed 2 February 2016
7. Reitan T, Callinan S.Changes in Smoking Rates Among Pregnant Women and the General Female Population in Australia, Finland, Norway, and Sweden. Nicotine Tob Res 2017;19(3):282-9.
8. Webb DA, Boyd NR, Messina D, et al. The discrepancy between self-reported smoking status and urine cotinine levels among women enrolled in prenatal care at four publicly funded clinical sites. *J Public Health Manag Pract* 2003;9(4):322-5.

9. Russell T, Crawford M, Woodby L. Measurements for active cigarette smoke exposure in prevalence and cessation studies: why simply asking pregnant women isn't enough. *Nicotine Tob Res* 2004;6Suppl2:S141-51.

10. Shipton D, Tappin DM, Vadiveloo T, et al. Reliability of self-reported smoking status by pregnant women for estimating smoking prevalence: a retrospective, cross sectional study. *BMJ* 2009;29;339:b4347.

11. Dietz PM, Homa D, England LJ, et al. Estimates of nondisclosure of cigarette smoking among pregnant and nonpregnant women of reproductive age in the United States. *Am J Epidemiol* 2011;173:355-9.

12. Tong VT, Althabe F, Alemán A, et al. Accuracy of self-reported smoking cessation during pregnancy. *Acta Obstet Gynecol Scand* 2015;94:106-11.

13. Campbell E, Sanson-Fisher R, Walsh R. Smoking status in pregnant women assessment of self-report against carbon monoxide (CO). *Addict Behav* 2001;26:1-9.

14. Vogt TM, Selvin S, Widdowson G, et al. Expired air carbon monoxide and serum thiocyanate as objective measures of cigarette exposure. Am J Public Health 1977;67:545-9.

15. Cunnington AJ, Hormbrey P. Breath analysis to detect recent exposure to carbon monoxide. *Postgrad Med J* 2002;78:233-7.

16. Erb P, Raiff BR, Meredith SE, et al. The accuracy of a lower-cost breath carbon monoxide meter in distinguishing smokers from non-smokers. J Smok Cessat 2015;10:59-64.

17. HSC Public Health Agency. Carbon monoxide screening. Advice for health professionals. http://www.publichealth.hscni.net/publications/carbon-monoxide-screening-advice-health-professionals

18. The National Institute for Health and Care Excellence (NICE) Smoking: stopping in pregnancy and after childbirth. Public health guideline. https://www.nice.org.uk/guidance/ph26

19. Friedman P, Guo XM, Stiller RJ, et al. Carbon Monoxide Exposure During Pregnancy. *Obstet Gynecol Surv* 2015;70:705-12.

20. Raub JA, Mathieu-Nolf M, Hampson NB, Thom SR. Carbon monoxide poisoning-a public health perspective. *Toxicology* 2000;145:1-14.

21. Deveci SE, Deveci F, Açik Y, et al. The measurement of exhaled carbon monoxide in healthy smokers and non-smokers. *Respir Med* 2004;98:551-6.

22. Javors MA, Hatch JP, Lamb RJ. Cut-off levels for breath carbon monoxide as a marker for cigarette smoking. *Addiction* 2005;100:159-67.

23. Higgins ST, Heil SH, Badger GJ, et al. Biochemical verification of smoking status in pregnant and recently postpartum women. *Exp Clin Psychopharmacol* 2007;15:58-66.

24. Rebagliato M. Validation of self-reported smoking. *J Epidemiol Community Health* 2002;56:163–4.

25. Patrick DL, Cheadle A, Thompson DC. The validity of self-reported smoking: a review and meta-analysis. *Am J Public Health* 1994;84:1086–93.

26. Public Health (Standardised Packaging of Tobacco) Bill 2014. https://www.oireachtas.ie/viewdoc.asp?fn=/documents/bills28/bills/2014/5414/document1.htm

27. Sillett SW, Wilson MB, Malcolm RE, et al. Deception among smokers. *Br Med J* 1978;2:1185-86.

28. Ford RP, Tappin DM, Schluter PJ, et al. Smoking during pregnancy: how reliable are maternal self-reports in New Zealand? *J Epidemiol Community Health* 1997;51:246–51.

29. Pickett KE, Rathouz PJ, Kasza K, et al. Self-reported smoking, cotinine levels, and patterns of smoking in pregnancy. *Paediatr Perinat Epidemiol* 2005;19:368-76.

30. Boyd NR, Windsor RA, Perkins LL, et al. Quality of measurement of smoking status by self-report and saliva cotinine among pregnant women. *Matern Child Health J* 1998;2:77-83.

31. Lindqvist R, Lendahls L, Tollbom O, et al. Smoking during pregnancy: comparison of self-reports and cotinine levels in 496 women. *Acta Obstet Gynecol Scan* 2002;81:240-4.

32. Middleton ET, Morice AH. Breath carbon monoxide as an indication of smoking habit. *Chest* 2000;117:758-63.

Table 1. Characteristics of the study cohort based on self-reported and carbon monoxide confirmed smoking status at the first antenatal visit.

Characteristic	Total (n=250)	Non-smokers (n=187)	Verified smokers* (n=63)
Age (SD) (years)	31.0 (5.3)	31.8 (5.1)	28.4 (5.2)
BMI (SD) (kg/m^2)	26.4 (6.1)	26.3 (5.4)	27.0 (7.8)
Obese (%)	19.3	17.0	26.2
Nationality (%)			
Ireland	76.8	75.1	82.0
EU 14	4.8	3.7	8.2
EU 13	8.4	10.1	3.3
Other	10.0	11.1	6.6
Occupation (%)[a]			
Professional/managerial	25.8	32.1	6.7
Skilled manual/non-manual	29.9	32.1	23.3
Semi- manual/unskilled manual	16.8	13.6	26.7
Unemployed (%)	27.5	22.3	43.3
Married (%)	52.0	61.4	23.0
Nulliparas (%)	34.8	32.8	41.0
Planned pregnancy (%)	65.6	72.0	45.9
Daily passive smoke exposure (%)	28.0	15.9	65.6
Alcohol before pregnancy (%)	32.9	31.9	36.1
Alcohol during pregnancy (%)	2.8	2.6	3.3
Illicit drugs before pregnancy (%)			
Cannabis only	7.6	5.8	13.1
Other drugs	6.8	5.3	11.5
Illicit drugs during pregnancy (%)			
Cannabis only	2.4	1.1	6.6
Other drugs	1.2	0.0	4.9

*Women who self-report they are currently smoking and women who had a carbon monoxide level of ≥3ppm.
[a]Missing data n=6

Table 2. Median carbon monoxide levels and rates of carbon monoxide below and above cut off by maternal characteristic.

Factor	n	CO PPM (Median, IQR)	CO < 3 PPM (%)	CO ≥ 3 PPM (%)	p
Occupation					
Professional/managerial[a]	63	1.0 (1.0)	93.7	6.3	-
Skilled manual/non-manual	73	1.0 (1.0)	80.8	19.2	<0.001
Semi-manual/unskilled manual	41	2.0 (3.5)**	65.9	34.1	<0.01
Unemployed	67	2.0 (5.0)*	64.2	35.8	<0.001
Marital Status					
Married/civil partnership[a]	130	1.5 (1.0)	90.0	10.0	<0.001
Single	120	2.0 (4.0)***	63.3	36.7	<0.001
Age (years)					
<30[a]	96	2.0 (4.0)	65.6	34.4	<0.001
≥30	154	1.0 (1.0)*	84.4	15.6	<0.001
Pregnancy Intention					
Planned [a]	164	1.0 (1.0)	84.8	15.2	<0.001
Unplanned	86	2.0 (4.0)**	62.8	37.2	<0.001
Age completed education					
<18years	35	2.0 (6.0)	60.0	40.0	<0.05
≥18years	146	1.0 (1.0)	85.6	14.4	<0.001
Years of continuous education					
<14years	68	1.0 (1.0)	67.6	32.4	<0.001
>14years	114	1.0 (3.0)	88.6	11.4	<0.001

*0.05, **0.01, ***0.001. IQR= Interquartile range

P-values in final column indicate differences between CO ≤3ppm and CO ≥3ppm

Table 3. Median maternal carbon monoxide levels and rates of carbon monoxide below and above cut off by carbon monoxide sources

Factor	n	CO PPM (Median, IQR)	CO < 3 PPM (%)	CO ≥ 3 PPM (%)	p
Smoking status[a]					
Never smoked	105	1.0 (1.0)	93.3	6.7	<0.001
Ex-smoker	103	1.0 (1.0)	86.4	13.6	<0.001
Current smoker	42	10.0 (8.5)***	14.3	85.7	<0.001
Exposed to passive smoking					
No[a]	170	1.0 (1.0)	85.0	15.0	<0.001
Yes	38	1.0 (2.0)	52.4	47.6	NS
Numbers of cigarettes smoked per day					
0[a]	208	1.0 (1.0)	89.9	10.1	<0.001
1-5	24	5.5 (8.5)***	20.8	79.2	<0.001
6-10	18	11.0 (6.5)***	5.6	94.4	-
Time since last cigarette (hours)					
<1[a]	9	13.0 (11.0)	0.0	100.0	-
1-2	14	10.0 (8.0)	0.0	100.0	-
3-6	9	5.0 (8.5)	22.2	77.8	-
>6	7	2.0 (11.0)*	57.1	42.9	-
Smoked in previous pregnancy[a]					
No	191	1.0 (1.0)	84.3	15.7	<0.001
Yes	31	5.0 (10.0)***	25.8	74.2	<0.001
Uses a car or bus daily					
No	31	2.0 (4.0)	61.3	38.7	<0.05
Yes	219	1.0 (1.0)	79.5	20.5	<0.001
Asthma					
No	219	1.0 (1.0)	77.2	22.8	<0.001
Yes	27	2.0 (1.0)	77.8	22.2	<0.001
Lives beside main road					
No	104	1.0 (1.0)	83.7	16.3	<0.001
Yes	146	1.0 (2.0)	72.6	27.4	<0.001
Lives in a built up area					
No	72	1.0 (1.0)	84.7	15.3	<0.001
Yes	178	1.0 (2.0)	74.2	25.8	<0.001
Boiler serviced every year					
Yes	144	1.0 (1.0)	86.0	14.0	<0.001
No	50	1.0 (1.0)	77.1	22.9	<0.001
Uses fossil fuel fire					
No	118	1.0 (1.0)	78.0	22.0	<0.001
Yes	132	1.0 (1.0)	76.5	23.5	<0.001
Chimney cleaned every year					
Yes	53	1.0 (1.0)	81.8	18.2	<0.001
No	88	1.0 (1.0)	81.1	18.9	<0.001
Partners CO >3 ppm[b]					
<3ppm	32	1.0 (0.75)	90.6	9.4	-
≥3ppm	28	1.0 (2.75)	64.3	35.7	<0.05
Partner/spouse's smoking status[a]					
Non-smoker	40	1.0 (1.0)	87.5	12.5	<0.001
Current smoker	17	1.0 (4.0)	58.8	41.2	NS

*0.05, **0.01, ***0.001 IQR= Interquartile range

P-values in final column indicate differences between CO ≤3ppm and CO ≥3ppm

[a]Based on self-reported smoking status, [b]Missing data n=90

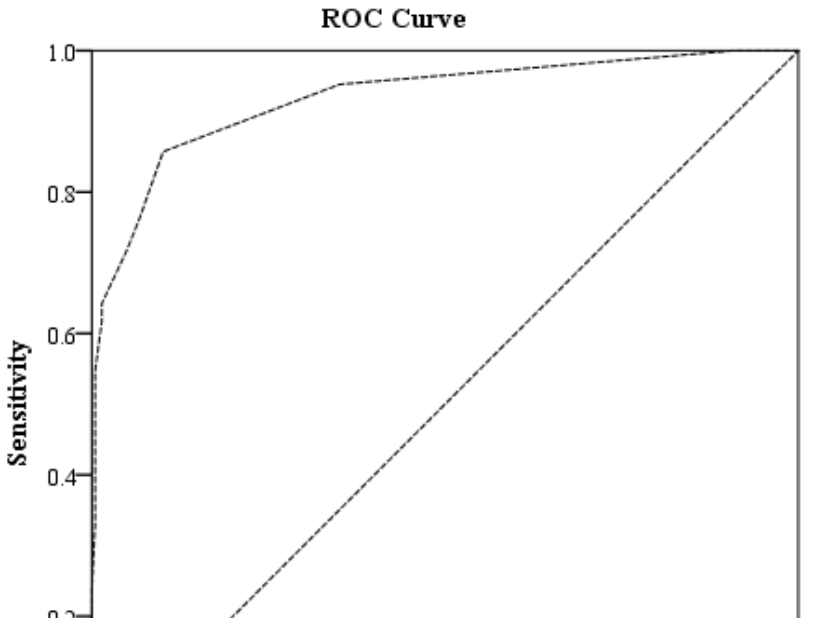
Table 4. Differences in maternal characteristics between disclosures and non-disclosures of smoking status.

	Disclosers (n=38)	Non-disclosers (n=25)	p
BCO level (ppm) (median, IQR)	10.0 (8.0)	4.0 (3.0)	<0.01
Age (years) (mean, SD)	27.3 (5.0)	29.7 (5.2)	NS
BMI (kg/m^2) (mean, SD)	26.5 (8.4)	27.7 (7.1)	NS
Married (%)	15.8	32.0	NS
Nulliparas (%)	34.2	52.0	NS
Planned pregnancy (%)	36.8	60.0	<0.05
Age completed education (years) (mean, SD)[a]	17.9 (2.1)	20.9 (3.9)	<0.05
Continuous years of education (mean, SD)[a]	13.4 (2.4)	16.5 (3.6)	<0.01
Weekly alcohol before pregnancy (%)	57.9	72.0	NS
Alcohol binge before pregnancy (%)	23.7	52.0	<0.01
Drug use before pregnancy (%)	26.3	20.0	NS
Weekly alcohol in pregnancy (%)	2.6	4.0	-
Alcohol binge in pregnancy (%)	2.6	0.0	-
Drug use in pregnancy (%)	10.5	12.0	-
Smoked in previous pregnancy (%)	55.3	20.0	<0.01
Exposed to passive smoked daily (%)	73.7	56.0	NS
Exposure to passive smoke (hours) (mean, SD)	3.9 (3.5)	1.5 (1.6)	<0.05

P-values in final column indicate differences between disclosures and non-disclosures
SD = standard deviation, BCO = Breath carbon monoxide
[a]Missing data n=67

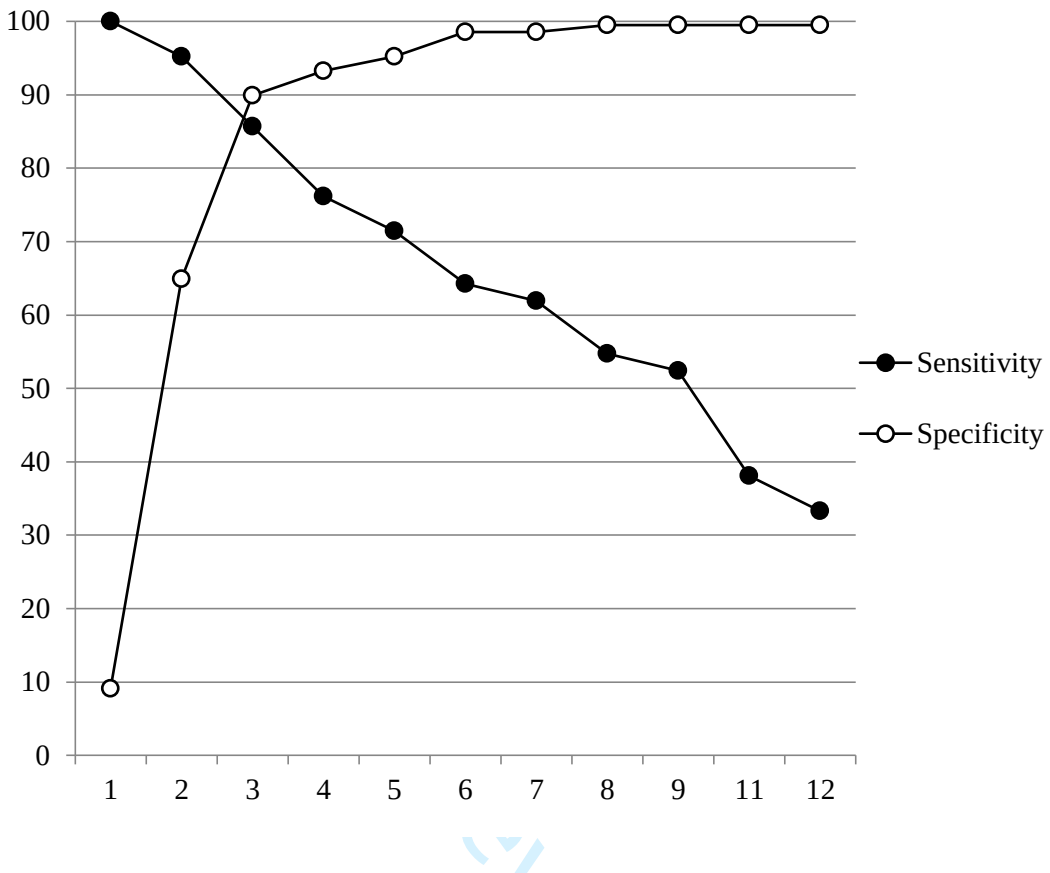
Table 5. Changes self-reported smoking status of the study cohort.

	Smoking status at first antenatal visit			
	Never smoked	Ex-smoker	Current smoker	Total
Smoking status research questionnaire	% (n)	% (n)	% (n)	% (n)
Never smoked	84% (96)	9% (9)	0% (0)	42% (105)
Ex-smoker	16% (19)	85% (82)	5% (2)	41% (103)
Current smoker	0% (0)	6% (6)	95% (36)	17% (42)
Total	100% (115)	100% (97)	100% (38)	100% (250)



Supplementary Figure 1

The percentage of false-positive results (100-specificity) plotted against the percentage of true-positive results (sensitivity) across the entire range of breath CO measures.



Supplementary Figure 2

Sensitivity and specificity were plotted at BCO cut-off levels from 1 to 12 ppm.
Sensitivity is the percentage of positive carbon monoxide breath tests at a specified cut-off.
Specificity is the percentage of negative carbon monoxide breath tests at a specified cut-off.

Supplementary Table 1. Sensitivity and specificity of the carbon monoxide analyser at various carbon monoxide breath test levels.

Carbon monoxide (ppm)	Sensitivity	Specificity	1-Specificity	Sensitivity + Specificity
1	1	0.09	0.91	1.09
2	0.95	0.65	0.35	1.60
3	**0.86**	**0.90**	**0.10**	**1.76**
4	0.76	0.93	0.07	1.69
5	0.71	0.95	0.05	1.67
6	0.64	0.99	0.01	1.63
7	0.62	0.99	0.01	1.60
8	0.55	1.00	0.00	1.54
9	0.52	1.00	0.00	1.52
11	0.38	1.00	0.00	1.38
12	0.33	1.00	0.00	1.33

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6-7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	7-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-9
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	Footnotes of tables
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	n/a
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	9-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

A prospective, observational study investigating the use of carbon monoxide screening to identify maternal smoking in a large university hospital in Ireland.

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ABSTRACT

Objectives: This study evaluated breath carbon monoxide (BCO) testing in identifying maternal smokers as well as the difference between disclosers and non-disclosers of smoking status. We also investigated if other extrinsic factors affected the women's' BCO levels in pregnancy.

Design: A prospective observational study.

Setting: A university obstetric hospital in an urban setting.

Participants: Women (n=250) and their partners (n=54) were recruited at their first antenatal visit. Women <18 years and those who did not understand English were excluded. A booking history, including collection of smoking status was collected by midwives. Following this women were recruited and completed a detailed research questionnaire on smoking and extrinsic/environmental BCO sources. A BCO test was performed on both the woman and her partner.

Primary and secondary outcome measures: The number of self-reported smokers and those that were positive on the BCO test. The characteristics of women who disclosed and did not disclose smoking status. The effect of extrinsic factors on the BCO test results.

Results: Based on the ROC a BCO cut-off point of ≥3ppm was the optimal level to identify ongoing smoking. At booking history, 15% women reported as current smokers. Based on BCO levels ≥3ppm combined with self-reported smoking in the research questionnaire, the rate increased to 25%. Non-disclosers had similar characteristics to non-smokers. No extrinsic factors affected maternal BCO levels.

Conclusions: Based on self-report and BCO levels a quarter of women presenting for antenatal care continued to smoke but only 60% reported their smoking to midwives. BCO measurement is an inexpensive, practical method of improving identification of maternal

smoking and it was not affected by extrinsic sources of BCO. Improved identification means smokers can be offered and supported to stop smoking in early pregnancy potentially improving the short and long term health of both mother and child.

Trial registration: n/a

Word count: 297/300

STRENGTHS AND LIMITATIONS OF THIS STUDY

- Sensitivity and specificity analysis were carried out to determine the optimal cut off point to determine smoking as there are wide variations and no consensus in the literature, particularly in pregnancy populations.
- Our study collected details of daily self-reported exposure to extrinsic sources of CO and directly measured exposure to passive smoking using BCO in a subset of partners.
- Carbon monoxide analysis although the most practical and feasible screening tool to detect smoking in a large cohort, can only detect exposure from up to four hours previous.

BACKGROUND

Maternal smoking is arguably the most important modifiable risk factor for adverse pregnancy outcomes including perinatal death.[1] Passive smoking is also linked to adverse outcomes, in particular fetal growth restriction.[2,3] Smoking cessation either pre-pregnancy or in the first half of pregnancy can normalise fetal growth.[4]

Although smoking rates in non-pregnant adult women are falling in Ireland, over one in ten women report that they continue to smoke at their first antenatal visit.[5] Similar to rates rates in maternal smoking have reported in other developed countries.[6,7] As many as three quarters of women may not disclose their smoking status when they present to the maternity services, however there are large discrepancies in the literature regarding rates of non-disclosure and none to date have been reported for Ireland.[8,9]

Non-disclosure of smoking leads to inaccurate smoking prevalence rates and missed opportunities to offer advice and support to quit.[10] This has led to the use of biochemical markers to identify people who fail to disclose their smoking behaviour.[11-13] The most commonly used biomarkers of smoking include serum carboxy-hemoglobin or cotinine, a by-product of nicotine, from urine, saliva or blood samples.[14] These methods, although valid, reliable and sensitive to cigarette smoke exposure of up to 20 hours, can be invasive, inconvenient and expensive as they require laboratory involvement for analysis. Cotinine samples can cost up to approximately $20 a sample and results can be affected by the use of nicotine replacement therapy.[15, 16] Thus, this method may be only feasible in a research setting.

A breath carbon monoxide (BCO) test is a more appropriate alternative biomarker of cigarette exposure for routine screening as it costs as little as $1 a sample.[15] Furthermore, the BCO test is safe, quick and non-invasive yields immediate results at the point of care.[17-19] A challenge of BCO testing is the half-life of CO. CO exposure in the previous 3 to 5 hours can

be detected by a BCO test and it is, therefore, unable to detect active tobacco exposure from the previous day.[10] Despite this, BCO correlates well with serum and urine cotinine levels and has shown high sensitivity and specificity in distinguishing between smokers and non-smokers.[19] Thus, BCO is a feasible option to help identify women who do not disclose their smoking in the antenatal outpatients.

Guidelines recommend the screening of carbon monoxide (CO) at the first antenatal visit, with the NICE guidelines in the UK recommend all women with a positive BCO test to be referred to an 'opt-out' stop smoking service (SSS).[20,21] The screening of all pregnant women with a BCO test has two important purposes. Firstly, it can help identify women who continue to smoke in pregnancy and give staff the opportunity to advise and provide support to quit. Secondly, the BCO test can ensure that the woman and her baby are not inadvertently in contact with the poisonous gas.[20] To date, no guidelines have been implemented in Ireland and just one out of all 19 units nationally conducted a BCO test in pregnancy.[22]

CO is a colourless, odourless, tasteless and poisoning gas that is potentially fatal at high levels. Exposure to CO is particularly dangerous during pregnancy because it replaces the oxygen available to the fetus, restricts growth and development, and increases the risk of fetal death, developmental disorders, and chronic cerebral lesions.[23] CO can also be produced by exhaust fumes or emitted from malfunctioning or poorly ventilated fossil or wood fuelled heating and cooking appliances, however there is a dearth of knowledge of the degree to which these extrinsic factors, as well as partners smoking habits and BCO levels can affect routine CO screening.[24, 25]

The purpose of this study was to evaluate the use of BCO screening in detecting cigarette smoking in women presenting to an Irish maternity hospital for antenatal care as well as characterise the difference between disclosers and non-disclosers of smoking status.

We also investigated if other extrinsic factors affected the women's' BCO levels in pregnancy.

METHODS

This prospective observational cohort study was conducted between January and September 2017 in a large university maternity hospital responsible for approximately 8,500 deliveries per annum. The study was approved by the Hospital Research Ethics Committee (17-2015).

There were three sources of data used in this study: maternal booking data collected by midwives and retrieved from the electronic medical record system 'K2', a carbon monoxide breath test conducted by the researcher (C.R.) and a fully supervised paper based research questionnaire (Figure 1.). At the first antenatal visit ('booking visit') the woman's history was computerised by a trained midwife onto K2. Histories were taken in a standardised manner and included questions regarding a number of lifestyle issues such as self-reported smoking prompted by the K2 system (Figure 1.).

The women's booking history and first antenatal dating scan are held on the same day at approximately 12 weeks gestation. Thus, on completion of the booking history, and before women presented for their first antenatal scan women were informed of the study by the researcher (C.R.) and advised to attend the research office after their dating scan should they wish to participate (Figure 1.).

On attendance at the research office women were screened for eligibility. Women were ineligible if they were under 18 years of age or did not understand English. Eligible women were then formally invited to participate in the study. Women were informed that the BCO test would assess their exposure to CO sources such as tobacco smoke, exhaust fumes or poor household ventilation etc.[18] Written consent was obtained to provide a sample of expired air and to complete an additional research questionnaire. This questionnaire collected

further sociodemographic and lifestyle information i.e. education level, potential environmental exposures to carbon monoxide such as passive smoke, and a repeated self-reported smoking status (Figure 1.). Assurance was given that all data were anonymous and would not affect care in the hospital in order to encourage accurate reporting in the research questionnaire. Other known environmental exposures to CO were collected due to their potentially confounding nature in accurately identifying smokers.[18]

Partners in attendance with the woman at the first visit were also offered participation in the study. The individual was also fully informed of the study procedures and written consent was obtained. The individuals followed the same study procedures as the pregnant woman. BCO was performed and an identical research questionnaire was completed.

BCO levels were performed using the inexpensive, handheld Bedfont piCO+ Smokerlyzer® (Bedfont Scientific, Kent, United Kingdom). To perform the breath test, women were asked to exhale completely, inhale fully and breath-hold for 15 seconds. At the end of the breath hold, the women were asked to exhale slowly and fully into the Smokerlyzer device. Safety protocols were put in place to minimise the risk of missing potential cases of CO poisoning.[20] The Smokerlyzer measures BCO levels in parts per million (ppm). Breath holding allows the CO in the blood to form equilibrium with the CO in the alveolar air. This technique is responsible for high level of correlation between breath CO levels and COHb concentration.[26]

We calculated that recruitment 233 women allowed for detection of a 10% rate of non-disclosure (power 99%, significance 5%).[13] Due to large variations in the cut-off criteria used previously to distinguish between smokers and non-smokers a receiver-operating characteristic (ROC) plot was undertaken.[13, 18, 25, 27, 28] The ROC assessed the accuracy of the BCO test in predicting smoking and the BCO level (ppm) with the highest combined

sensitivity and specificity value was used as the cut-off. Women who had a CO level greater than the cut-off point but reported as a non-smoker were categorised as non-disclosers.

All results were analyzed by the SPSS statistical package (SPSS; Chicago, IL). Descriptive statistics were used to describe the characteristics of the study cohort. Normality of data were assessed using visual inspection of histograms, the data skewness and kurtosis and the Kolmogorov-Smirnov Test. Continuous data were reported as means and standard deviations if normally distributed and median and interquartile ranges (IQR) if data were non-normally distributed. Categorical data were reported as proportions. Chi-squared, analysis of variance (ANOVA) and Mann Whitney U were used to assess differences between groups in proportions, means and medians respectively. Associations between CO levels and other variables were carried out using Spearman's correlations. Missing data are presented in the footnotes of tables.

Patient and Public Involvement

Previous research has shown just one out of the 19 maternity units in Ireland conduct the recommended carbon monoxide screening to identify maternal smokers.[22] Furthermore, there is dearth of information on the disclosure rate of maternal smoking in an Irish population. This was the stimulus for our research question.

The patients were not directly involved in the study design however the studies questionnaire was piloted on ten patients who gave feedback on the questions included. Patients were also not involved in the recruitment process; however, the Hospital Research Ethics Committee includes members of the public involved in reviewing the methods, patient information leaflets, questionnaires and consent form.

The results of our study were not disseminated to the study population. Results will be presented locally to educate staff on our findings with the aim of implementing BCO

screening to identify maternal smokers and provide them with smoking cessation information and support.

RESULTS

The ROC results showed the BCO levels measured in parts per million (ppm) were predictors of maternal cigarette smoking (area under the curve (AUC) = 0.93, $p < 0.001$) (Supplementary Figure 1). The sensitivity and specificity curves crossed at a cut-off point of 3ppm (Supplementary Figure 2). The highest combined sensitivity and specificity of maternal smoking was also at the CO level 3ppm (Supplementary Table 1).

Two hundred and eighty-eight women were offered participation in the study of which 250 were recruited. Of the 38 women that did not take part, 20 declined due to time constraints and 18 left immediately after their scan without reason for non-participation. Verified smoking was defined as having a CO level ≥3ppm and/or self-reported smoking either at the first antenatal visit or on the research questionnaire.

Table 1 shows the characteristics of the study group analysed by verified smoking status. Verified maternal smokers (n=61) were more likely to be younger (mean difference 3.4 years 95% Confidence Intervals (CI) 1.9-4.9, $p < 0.001$), unemployed (43% vs 22%, $p < 0.001$) and single (77% vs 39%, $p < 0.001$) compared to non-smokers (n=187). They also spent fewer years in continuous full time education (mean difference 1.9 years 95% CI 0.6-3.1, $p < 0.01$) and finished full time education at a younger age (mean difference 2.7 years 95% CI 1.2-4.2, $p < 0.001$) than non-smokers (n=181).

Median BCO levels and rates of BCO < 3 and ≥ 3ppm by maternal characteristics and CO sources are shown in Tables 2 and 3. Of all known CO sources that were examined, self-reported maternal smoking in the current and previous pregnancy, cigarette quantity and

timing of last cigarette were the only factors that were associated with an increased median BCO level.

Supplementary table 2 shows that on further examination, using correlation analysis, the number of self-reported cigarettes per day had the strongest association with BCO test levels (rho = 0.61, $p < 0.001$) followed by time since last cigarette (rho = -0.51, $p < 0.01$). Hours exposed to passive smoking was also associated with BCO levels (rho = 0.31, $p < 0.01$). However, when self-reported active smokers were removed from this analysis this association disappeared (rho = -0.06, NS).

BCO tests were performed on 54 partners of the pregnant women (22%). The mean age of the partners was 33.1 years (6.5 years), 98.1% were male, 83.3% lived with their pregnant partner and the median BCO level of the partners was 2.0ppm (interquartile range (IQR) 4.5ppm). Twenty-eight percent (n=15) of partners reported current smoking and five of these had a pregnant partner who also smoked. Of the 26 partners with positive BCO tests their median levels were 6.0 (IQR 8.0) similar to the median BCO of women with positive tests 7.0 (IQR 8.0). On examination of BCO levels 48% (n=26) had a CO ≥3ppm. The BCO levels in the partners were weakly associated with the BCO levels of the pregnant women (rho = 0.34, $p < 0.05$) but when active maternal smokers were removed from analysis the relationship disappeared. However, median values of BCO levels in pregnant women were the same regardless of their partners CO levels being < or ≥ 3ppm.

Maternal characteristics of the disclosers and non-disclosers of smoking status were compared (Table 4). Non-disclosers were classified as women who did not report smoking at their first antenatal visit but had a CO level ≥3ppm and/or self-reported smoking in the research questionnaire. Non-disclosers had a lower median BCO level than disclosers (10.0 ppm (IQR 8.0) vs 4.0 ppm (IQR 3.0), $p <0.01$). Non-disclosers were older than disclosers when they finished full time education (20.9 years (IQR 3.9) vs 17.9 years (IQR 2.1), p <

0.05) and spent more years in continuous full time education (16.5 years (IQR 3.6) vs 13.4 years (IQR 2.4), $p < 0.01$). They were also more likely to have planned their pregnancy (60% vs 37%, $p < 0.05$), less likely to have smoked in a previous pregnancy (20% vs 55%, $p < 0.01$) and spend less time around passive smoking daily (1.5 hours (IQR 1.6) vs 3.9 hours (IQR 3.5), $p < 0.05$).

Changes in self-reported smoking status from the first antenatal visit to self-reported smoking status collected in the research questionnaire are shown in Supplementary Table 3. The largest difference was seen in women who reported 'never smoking' at the first antenatal visit to midwives with 17% changing their status to 'ex-smoker' on the research questionnaire. Six other women who reported they were never smokers to midwives at the first antenatal visit had a CO reading ≥3ppm. Of these, one woman changed her self-reporting on the research questionnaire to ex-smoking status and reported quitting two months previous. Two other women reported smoking cannabis which could be the reason for the CO ≥3ppm. At first visit 17 potential non-disclosers reported they were ex-smokers. Of these, six disclosed smoking on the research questionnaire. Another five women reported they had only quit since the beginning of pregnancy and one was continuing to smoke cannabis.

Based on self-reported smoking status at the first antenatal visit, 15% (38/250) of women were maternal smokers. Based on self-reported smoking in the research questionnaire, the rate rose to 17% (42/250). When results from the BCO test levels ≥3ppm were used the rate increased to 23% (57/250). However, when BCO levels ≥3ppm were combined with self-reporting the rate of maternal smoking was 25% (63/250). Based on self-reported non-smoking, our study had a rate of non-disclosure of 12% (25/212). Overall, 39.6% (25/63) of all maternal smokers did not report as smokers to midwives when booking at their first antenatal visit.

Six women who reported smoking were not detected on CO screening. All six reported not having a cigarette in the previous four hours and five of the six women smoked ≤2 cigarettes daily.

DISCUSSION

We found that BCO testing in combination with self-reporting of smoking status in a research setting identified 10% more maternal smokers than self-reporting using routine practice at the first antenatal visit. Two out of five women who continued to smoke in pregnancy were not identified thus, maternity services were missing the opportunity to provide advice and smoking cessation support.

There is no consensus as to what constitutes the best cut-off point for determining smoking status. Some suggest a CO level as low as 2 parts per million (ppm), others as high as 10 ppm.[14, 28-32] Due to the conflicting appropriate cut-off points in the literature we undertook a sensitivity and specificity analysis.[30] Similar to a large American longitudinal study, we identified a cut-off point of 3ppm as the optimal to distinguish smokers from non-smokers in terms of limiting both false positive and false negative results and maximise identification of smokers with a high degree of certainty.[30] Few studies have previously undertaken their own ROC making it difficult to interpret the sensitivity and specificity of their results.

There is a dearth of knowledge on what factors other than active smoking can effect BCO levels and stop smoking services (SSS) staff often find difficult to explain high results in non-smokers.[25] Our study collected data on other potential extrinsic sources of CO that may have contaminated results. Other studies do not take into account daily passive smoke exposure, partners BCO levels or sources such as motor vehicle use, fossil fuel exposure, gas/oil boiler servicing practices, ventilation etc. These factors did not affect median BCO levels in women in the present study, and did not increase rates of BCO levels ≥3ppm. Fifty

four partners took part in this study and we found a weak positive relationship between partner BCO levels and maternal BCO, however when active smokers were excluded, no relationship existed. One other study, in non-pregnant adults, examined the effect of other sources of CO on BCO test levels and found that gender and motor vehicle use were associated with higher CO levels. However, the differences were minimal with less than 1ppm in the difference.[18]

A limitation of our study is that we did not collect cotinine samples for verification of smoking status; however, our aim was not to compare screening methods, but to report the levels of non-disclosures in Ireland using current guidelines.[21] Furthermore, our lower cut-off point provided high sensitivity values and has been supported by previous research that also identified this value as optimal when identification of smoking abstinence with a high degree of certainty is of high importance.[30]

Our study found a self-reported smoking rate of 15%, 4% higher than the rate reported in our previously study that analysed all deliveries in our hospital in 2015.[5] It is unlikely that the rate has risen, and this higher rate may be due to the convenience sampling employed.

Our study distinguishes characteristics between smokers and non-disclosers unlike previous studies, which compare verified smokers to non-smokers.[13] We found non-disclosers had more similar characteristics to non-smokers than smokers. This could be due to a number of reasons. Firstly, we used a lower cut-off point compared to other studies in pregnant populations.[25,28,32] One other study that carried out an ROC curve found its highest specificity and sensitivity at the cut-off point >4ppm, however, this cut-off had a lower sensitivity value (0.79) than our study (0.86).[28] Our studies lower cut-off point may therefore be too sensitive and include non-smoking women in the non-disclosure group (false

positives). If our cut-off was raised to that of other studies, however, our sensitivity would be reduced and fewer smokers would be identified correctly.

Prior to implementation of the NICE guideline in the UK healthcare staff were worried that that BCO testing would unjustly accuse women who don't smoke of smoking and that it would affect their relationships with the women.[25] However, following implementation they found it had little effect on their relationships with women and the SSS staff found that it provided them a unique opportunity to address second-hand smoke, smoke free homes and the effects of smoking around children with non-smokers who may be regularly exposed to passive smoke.[25]

For healthcare professionals who continue to have concerns over false positives being wrongly accused of smoking and referred to SSS an alternative pathway could be implemented whereby cotinine is sampled and tested only in self-reported non-smokers who have a high BCO level in order to keep the expense on maternity services as low as possible.

A further concern is that women who may smoke but did not report doing so at their first appointment may not wish to receive cessation advice. However, guidelines recommend an opt-out referral system whereby women who are identified as smokers in early pregnancy and those who do not specifically object are referred to smoking cessation services.[21] Thus this non-mandatory referral system is centred on the patient's best interests and it does not overrule personal choice.

A number of different rates of non-disclosure have been reported in the literature, from as low as 5% to as high as 73% but it is difficult to compare these results to our study.[8,9] Firstly, the definition of 'non-disclosure' or 'miss-categorisation' is not standardised across studies. Different denominators are used. Some studies use the number of positive tests whereas others use total population, total self-reported non-smokers or self-reported quitters.[12,13,33,34] Secondly, studies to date have used conflicting cut-off points to verify

smoking, for example, some use standard cut-of points, some use ROCs to find the optimal for their population and others use both which shows disparity in results.[12,33,35]

Additionally, the samples in these studies are taken at different time points in pregnancy. Our study took BCO samples at the beginning of pregnancy. However, previous research found that non-disclosure rates are increased from the beginning to later in pregnancy.[13, 35] Sampling at the first visit is preferable because early identification and successful intervention in the first half of pregnancy may potentially normalise fetal growth.[4]

A UK study that with recruitment methods but a higher BCO cut-off point of >4ppm reported that 22.9% of all smokers did not disclose smoking at booking, much lower than our 39.6%.[32] However this higher cut-off point was previously criticised for missing both self-reported smokers and smokers verified by cotinine.[28, 36]

In conclusion, self-reporting of maternal smoking leads to inaccuracies in clinical practice disclosure which may result in missed opportunities to provide smoking cessation advice and support from the beginning of pregnancy. BCO screening can improve identification of smokers at the first antenatal visit. This screening complements routine history taking, but should not replace it as this test may produce a false negative in smokers who have not had a cigarette in the previous four hours. Screening in early pregnancy should use a low cut-off value because a once-off test resulting in a false positive test is preferable to a false negative test. BCO levels not only correlate with self-reporting numbers of cigarettes but also with timing of smoking and do not appear to be effected by extrinsic carbon monoxide sources. Finally, cotinine may need to also be used as an adjunct to CO screening in women with high CO levels who report that they are non-smokers to rule out a false positive test.

STATEMENT OF CONTRIBUTION

CR contributed to the conception and design of the study, performed the analysis of the data, interpreted data and wrote and edited this original article. RK, EOM and SS contributed to the writing and editing of this article. MT and BE contributed to the conception of the study, interpretation of data as well as contributing to the writing and editing of this article.

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DECLARATION OF INTERESTS

None of the authors have any conflicts of interest to declare.

PATIENT CONSENT

Written consent was obtained.

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DATA SHARING STATEMENT

Additional unpublished data is available. For further details contact ciara.reynolds@ucdconnect.ie.

REFERENCES

1. Cnattingius S. The epidemiology of smoking during pregnancy: smoking prevalence, maternal characteristics, and pregnancy outcomes. Nicotine Tob Res 2004;6Suppl2:S125-40.
2. Rubin DH, Krasilnikoff PA, Leventhal JM, et al. Effect of passive smoking on birth-weight. Lancet 1986;2(8504):415-7.
3. Martinez FD, Wright AL, Taussig LM. The effect of paternal smoking on the birthweight of newborns whose mothers did not smoke. Group Health Medical Associates. Am J Public Health 1994;84(9):1489–91.
4. Lieberman E, Gremy I, Lang JM, et al. Low birthweight at term and the timing of fetal exposure to maternal smoking. *Am J Public Health* 1994;84: 1127–31.
5. Reynolds CME, Egan B, McKeating A, et al. Five year trends in maternal smoking behaviour reported at the first prenatal appointment. *Ir J Med Sci* 2017;186:971-9.
6. European Perinatal Health Report (2010) The health of pregnant women and babies in Europe in 2010.http://www.europeristat.com/images/European%20Perinatal%20Health%20Report_2010.pdf. Accessed 2 February 2016
7. Reitan T, Callinan S.Changes in Smoking Rates Among Pregnant Women and the General Female Population in Australia, Finland, Norway, and Sweden. Nicotine Tob Res 2017;19(3):282-9.
8. Webb DA, Boyd NR, Messina D, et al. The discrepancy between self-reported smoking status and urine cotinine levels among women enrolled in prenatal care at four publicly funded clinical sites. *J Public Health Manag Pract* 2003;9(4):322-5.
9. Pickett KE, Rathouz PJ, Kasza K, et al. Self-reported smoking, cotinine levels, and patterns of smoking in pregnancy. *Paediatr Perinat Epidemiol* 2005;19:368-76.

10. Russell T, Crawford M, Woodby L. Measurements for active cigarette smoke exposure in prevalence and cessation studies: why simply asking pregnant women isn't enough. *Nicotine Tob Res* 2004;6Suppl2:S141-51.

11. Shipton D, Tappin DM, Vadiveloo T, et al. Reliability of self-reported smoking status by pregnant women for estimating smoking prevalence: a retrospective, cross sectional study. *BMJ* 2009;29;339:b4347.

12. Dietz PM, Homa D, England LJ, et al. Estimates of nondisclosure of cigarette smoking among pregnant and nonpregnant women of reproductive age in the United States. *Am J Epidemiol* 2011;173:355-9.

13. Tong VT, Althabe F, Alemán A, et al. Accuracy of self-reported smoking cessation during pregnancy. *Acta Obstet Gynecol Scand* 2015;94:106-11.

14. Campbell E, Sanson-Fisher R, Walsh R. Smoking status in pregnant women assessment of self-report against carbon monoxide (CO). *Addict Behav* 2001;26:1-9.

15. Patrick DL, Cheadle A, Thompson DC. The validity of self-reported smoking: a review and meta-analysis. *Am J Public Health* 1994;84:1086–93.

16. Benowitz NL, Hukkanen J, Jacob P. Nicotine chemistry, metabolism, kinetics and biomarkers. *Handb Exp Pharmacol* 2009;192:29–60.

17. Vogt TM, Selvin S, Widdowson G, et al. Expired air carbon monoxide and serum thiocyanate as objective measures of cigarette exposure. Am J Public Health 1977;67:545-9.

18. Cunnington AJ, Hormbrey P. Breath analysis to detect recent exposure to carbon monoxide. *Postgrad Med J* 2002;78:233-7.

19. Erb P, Raiff BR, Meredith SE, et al. The accuracy of a lower-cost breath carbon monoxide meter in distinguishing smokers from non-smokers. J Smok Cessat 2015;10:59-64.

20. HSC Public Health Agency. Carbon monoxide screening. Advice for health professionals. http://www.publichealth.hscni.net/publications/carbon-monoxide-screening-advice-health-professionals

21. The National Institute for Health and Care Excellence (NICE) Smoking: stopping in pregnancy and after childbirth. Public health guideline. https://www.nice.org.uk/guidance/ph26

22. Reynolds CM, Egan B, Cawley S, Kennedy R, Sheehan SR, Turner MJ. A National Audit of Smoking Cessation Services in Irish Maternity Units. *IMJ* 2017;110(6):580.

23. Raub JA, Mathieu-Nolf M, Hampson NB, Thom SR. Carbon monoxide poisoning-a public health perspective. *Toxicology* 2000;145:1-14.

24. Friedman P, Guo XM, Stiller RJ, et al. Carbon Monoxide Exposure During Pregnancy. *Obstet Gynecol Surv* 2015;70:705-12.

25. Campbell KA, Bowker KA, Naughton F, Sloan M, Cooper S, Coleman T. Antenatal clinic and stop smoking services staff views on "opt-out" referrals for smoking cessation in pregnancy: A framework analysis. *Int J Environ Res Public Health* 2016;13:1004.

26. Middleton ET, Morice AH. Breath carbon monoxide as an indication of smoking habit. *Chest* 2000;117:758-63.

27. West R, Hajek P, Stead L, Stapleton J. Outcome criteria in smoking cessation trials: proposal for a common standard. *Addiction* 2005;100:299-303.

28. Bauld L, Hackshaw L, Ferguson J, Coleman T, Taylor G, Salway R. Implementation of routine biochemical validation and an 'opt out'referral pathway for smoking cessation in pregnancy. *Addiction* 2012;107:53-60.

29. Deveci SE, Deveci F, Açik Y, et al. The measurement of exhaled carbon monoxide in healthy smokers and non-smokers. *Respir Med* 2004;98:551-6.

30. Javors MA, Hatch JP, Lamb RJ. Cut-off levels for breath carbon monoxide as a marker for cigarette smoking. *Addiction* 2005;100:159-67.

31. Higgins ST, Heil SH, Badger GJ, et al. Biochemical verification of smoking status in pregnant and recently postpartum women. *Exp Clin Psychopharmacol* 2007;15:58-66.

32. Campbell KA, Cooper S, Fahy SJ, Bowker K, Leonardi-Bee J, McEwen A, Whitemore R, Coleman T. 'Opt-out'referrals after identifying pregnant smokers using exhaled air carbon monoxide: impact on engagement with smoking cessation support. *Tob control* 2017;26:300-6.

33. Boyd NR, Windsor RA, Perkins LL, et al. Quality of measurement of smoking status by self-report and saliva cotinine among pregnant women. *Matern Child Health J* 1998;2:77-83.

34. Lindqvist R, Lendahls L, Tollbom O, et al. Smoking during pregnancy: comparison of self-reports and cotinine levels in 496 women. *Acta Obstet Gynecol Scan* 2002;81:240-4.

35. Ford RP, Tappin DM, Schluter PJ, et al. Smoking during pregnancy: how reliable are maternal self-reports in New Zealand? *J Epidemiol Community Health* 1997;51:246–51.

36. Jatlow P, Toll BA, Leary V, Krishnan-Sarin S, O'Malley SS. Comparison of expired carbon monoxide and plasma cotinine as markers of cigarette abstinence. *Drug Alcohol Depend* 2008;98:203-9.

Table 1. Characteristics of the study cohort based on self-reported and carbon monoxide confirmed smoking status at the first antenatal visit.

Characteristic	Total (n=250)	Non-smokers (n=187)	Verified smokers* (n=63)	p-value
Age (SD) (years)	31.0 (5.3)	31.8 (5.1)	28.4 (5.2)	<0.001
BMI (SD) (kg/m^2)	26.4 (6.1)	26.3 (5.4)	27.0 (7.8)	0.481
Obese (%)	19.3	17.0	26.2	0.078
Nationality (%)				
Ireland	76.8	75.1	82.0	0.106
EU 14	4.8	3.7	8.2	0.089
EU 13	8.4	10.1	3.3	-
Other	10.0	11.1	6.6	-
Occupation (%)[a]				
Professional/managerial	25.8	32.1	6.7	-
Skilled manual/non-manual	29.9	32.1	23.3	0.079
Semi- manual/unskilled manual	16.8	13.6	26.7	<0.001
Unemployed (%)	27.5	22.3	43.3	<0.001
Married (%)	52.0	61.4	23.0	<0.001
Years of continuous education (years)	16.0 (3.5)	16.4 (3.5)	14.5 (3.2)	<0.01
Age completed education (years)	21.2 (4.2)	21.8 (4.2)	19.0 (3.1)	<0.001
Nulliparas (%)	34.8	32.8	41.0	0.106
Planned pregnancy (%)	65.6	72.0	45.9	<0.001
Daily passive smoke exposure (%)	28.0	15.9	65.6	<0.001
Alcohol before pregnancy (%)	32.9	68.3	63.5	0.259
Alcohol during pregnancy (%)	2.8	2.6	3.3	-
Illicit drugs before pregnancy (%)				
Cannabis only	7.6	5.8	13.1	0.038
Other drugs	6.8	5.3	11.5	0.058
Illicit drugs during pregnancy (%)				
Cannabis only	2.4	1.1	6.6	-
Other drugs	1.2	0.0	4.9	-

*Women who self-report they are currently smoking and women who had a carbon monoxide level of ≥3ppm.

p-values indicate significance between non-smokers and verified smokers

[a]Missing data n=6

-The number of values for this variable was too small to statistically analyse

Table 2. Median carbon monoxide levels and rates of carbon monoxide below and above cut off by maternal characteristic.

Factor	n	CO PPM (Median, IQR)	CO < 3 PPM (%)	CO ≥ 3 PPM (%)	p
Occupation					
Professional/managerial[a]	63	1.0 (1.0)	93.7	6.3	-
Skilled manual/non-manual	73	1.0 (1.0)	80.8	19.2	<0.001
Semi-manual/unskilled manual	41	2.0 (3.5)**	65.9	34.1	<0.01
Unemployed	67	2.0 (5.0)*	64.2	35.8	<0.001
Marital Status					
Married/civil partnership[a]	130	1.5 (1.0)	90.0	10.0	<0.001
Single	120	2.0 (4.0)***	63.3	36.7	<0.001
Age (years)					
<30[a]	96	2.0 (4.0)	65.6	34.4	<0.001
≥30	154	1.0 (1.0)*	84.4	15.6	<0.001
Pregnancy Intention					
Planned [a]	164	1.0 (1.0)	84.8	15.2	<0.001
Unplanned	86	2.0 (4.0)**	62.8	37.2	<0.001
Age completed education					
<18years	35	2.0 (6.0)	60.0	40.0	<0.05
≥18years	146	1.0 (1.0)	85.6	14.4	<0.001
Years of continuous education					
<14years	68	1.0 (1.0)	67.6	32.4	<0.001
>14years	114	1.0 (3.0)	88.6	11.4	<0.001

*0.05, **0.01, ***0.001. IQR= Interquartile range

P-values in final column indicate differences between CO ≤3ppm and CO ≥3ppm

Table 3. Median maternal carbon monoxide levels and rates of carbon monoxide below and above cut off by carbon monoxide sources

Factor	n	CO PPM (Median, IQR)	CO < 3 PPM (%)	CO ≥ 3 PPM (%)	p
Smoking status[a]					
Never smoked	105	1.0 (1.0)	93.3	6.7	<0.001
Ex-smoker	103	1.0 (1.0)	86.4	13.6	<0.001
Current smoker	42	10.0 (8.5)***	14.3	85.7	<0.001
Exposed to passive smoking					
No[a]	170	1.0 (1.0)	85.0	15.0	<0.001
Yes	38	1.0 (2.0)	52.4	47.6	NS
Numbers of cigarettes smoked per day					
0[a]	208	1.0 (1.0)	89.9	10.1	<0.001
1-5	24	5.5 (8.5)***	20.8	79.2	<0.001
6-10	18	11.0 (6.5)***	5.6	94.4	-
Time since last cigarette (hours)					
<1[a]	9	13.0 (11.0)	0.0	100.0	-
1-2	14	10.0 (8.0)	0.0	100.0	-
3-6	9	5.0 (8.5)	22.2	77.8	-
>6	7	2.0 (11.0)*	57.1	42.9	-
Smoked in previous pregnancy[a]					
No	191	1.0 (1.0)	84.3	15.7	<0.001
Yes	31	5.0 (10.0)***	25.8	74.2	<0.001
Uses a car or bus daily					
No	31	2.0 (4.0)	61.3	38.7	<0.05
Yes	219	1.0 (1.0)	79.5	20.5	<0.001
Lives beside main road					
No	104	1.0 (1.0)	83.7	16.3	<0.001
Yes	146	1.0 (2.0)	72.6	27.4	<0.001
Lives in a built up area					
No	72	1.0 (1.0)	84.7	15.3	<0.001
Yes	178	1.0 (2.0)	74.2	25.8	<0.001
Boiler serviced every year					
Yes	144	1.0 (1.0)	86.0	14.0	<0.001
No	50	1.0 (1.0)	77.1	22.9	<0.001
Uses fossil fuel fire					
No	118	1.0 (1.0)	78.0	22.0	<0.001
Yes	132	1.0 (1.0)	76.5	23.5	<0.001
Chimney cleaned every year					
Yes	53	1.0 (1.0)	81.8	18.2	<0.001
No	88	1.0 (1.0)	81.1	18.9	<0.001
Partners CO >3 ppm[b]					
<3ppm	28	1.0 (0.00)	90.6	9.4	-
≥3ppm	26	1.0 (2.50)	64.3	35.7	<0.05
Partner/spouse's smoking status[a]					
Non-smoker	36	1.0 (1.0)	87.5	12.5	<0.001
Current smoker	15	1.0 (4.0)	58.8	41.2	NS

*0.05, **0.01, ***0.001 IQR= Interquartile range

P-values in final column indicate differences between CO ≤3ppm and CO ≥3ppm

[a]Based on self-reported smoking status, [b]Missing data n=90

Table 4. Differences in maternal characteristics between disclosures and non-disclosures of smoking status.

	Disclosers (n=38)	Non-disclosers (n=25)	p
BCO level (ppm) (median, IQR)	10.0 (8.0)	4.0 (3.0)	<0.01
Age (years) (mean, SD)	27.3 (5.0)	29.7 (5.2)	NS
BMI (kg/m^2) (mean, SD)	26.5 (8.4)	27.7 (7.1)	NS
Married (%)	15.8	32.0	NS
Nulliparas (%)	34.2	52.0	NS
Planned pregnancy (%)	36.8	60.0	<0.05
Age completed education (years) (mean, SD)[a]	17.9 (2.1)	20.9 (3.9)	<0.05
Continuous years of education (mean, SD)[a]	13.4 (2.4)	16.5 (3.6)	<0.01
Weekly alcohol before pregnancy (%)	57.9	72.0	NS
Alcohol binge before pregnancy (%)	23.7	52.0	<0.01
Drug use before pregnancy (%)	26.3	20.0	NS
Weekly alcohol in pregnancy (%)	2.6	4.0	-
Alcohol binge in pregnancy (%)	2.6	0.0	-
Drug use in pregnancy (%)	10.5	12.0	-
Smoked in previous pregnancy (%)	55.3	20.0	<0.01
Exposed to passive smoked daily (%)	73.7	56.0	NS
Exposure to passive smoke (hours) (mean, SD)	3.9 (3.5)	1.5 (1.6)	<0.05

P-values in final column indicate differences between disclosures and non-disclosures
SD = standard deviation, BCO = Breath carbon monoxide
[a]Missing data n=67
-The number of values for this variable was too small to statistically analyse

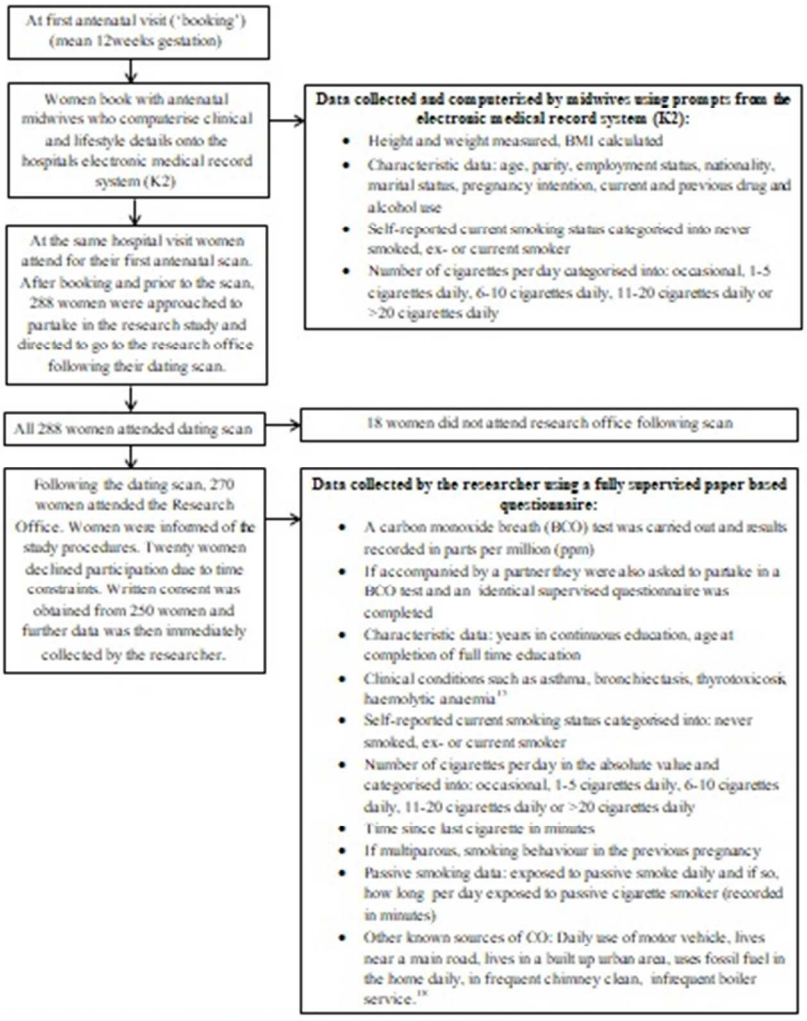
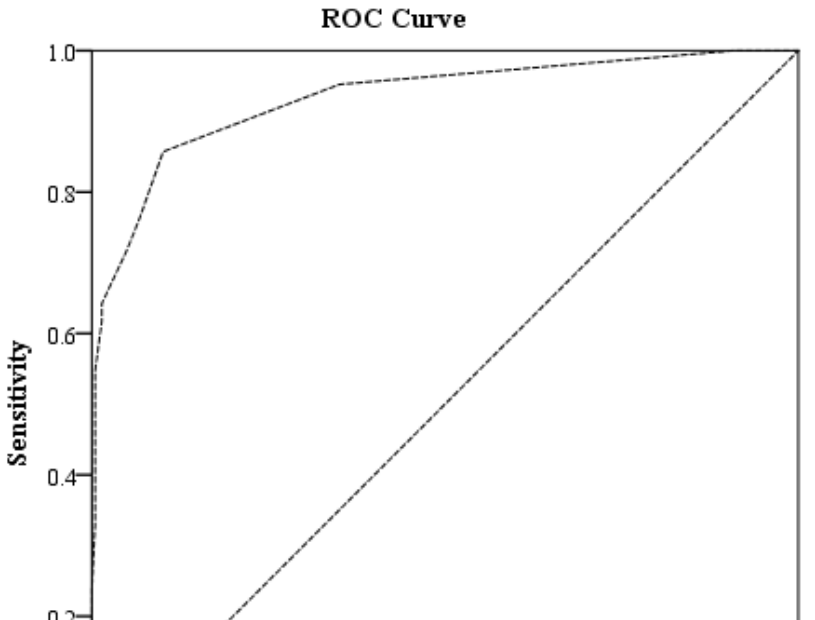


Figure 1. Flow diagram of participant recruitment and data collection.

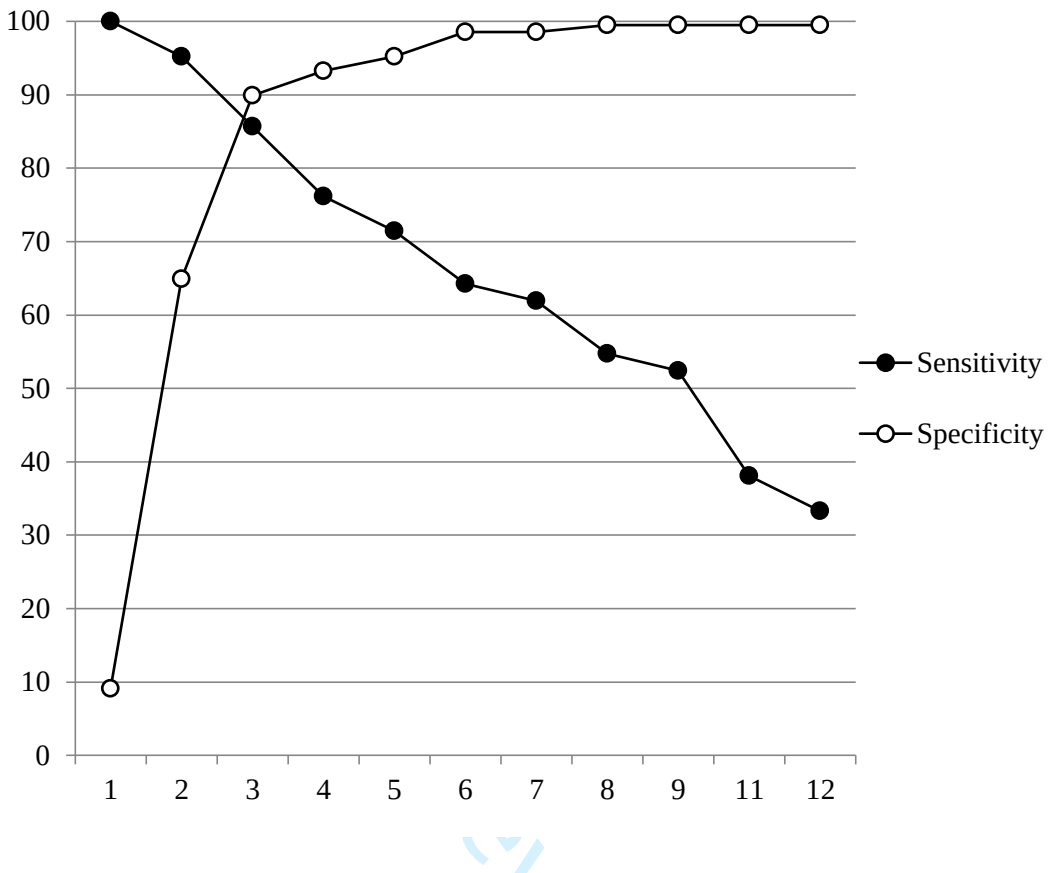
Flow diagram of participant recruitment and data collection

35x45mm (300 x 300 DPI)



Supplementary Figure 1

The percentage of false-positive results (100-specificity) plotted against the percentage of true-positive results (sensitivity) across the entire range of breath CO measures.



Supplementary Figure 2

Sensitivity and specificity were plotted at BCO cut-off levels from 1 to 12 ppm.
Sensitivity is the percentage of positive carbon monoxide breath tests at a specified cut-off.
Specificity is the percentage of negative carbon monoxide breath tests at a specified cut-off.

Supplementary Table 1. Sensitivity and specificity of the carbon monoxide analyser at various carbon monoxide breath test levels.

Carbon monoxide (ppm)	Sensitivity	Specificity	1-Specificity	Sensitivity + Specificity
1	1	0.09	0.91	1.09
2	0.95	0.65	0.35	1.60
3	**0.86**	**0.90**	**0.10**	**1.76**
4	0.76	0.93	0.07	1.69
5	0.71	0.95	0.05	1.67
6	0.64	0.99	0.01	1.63
7	0.62	0.99	0.01	1.60
8	0.55	1.00	0.00	1.54
9	0.52	1.00	0.00	1.52
11	0.38	1.00	0.00	1.38
12	0.33	1.00	0.00	1.33

Supplementary Table 2. Correlations between maternal carbon monoxide levels (ppm) and factors associated with carbon monoxide exposure.

	n	Correlation co-efficient (rho)	p-value
Self-reported number of cigarettes per day	250	0.61	<0.001
Time since last cigarette (hours)[a]	39	-0.51	<0.01
Partners BCO	54	0.34	<0.05
Partners BCO[b]	45	0.19	NS
Passive smoking exposure (hours)	70	0.31	<0.01
Passive smoke exposure only (hours)[b]	38	-0.06	NS

[a] missing data n=3

[b] excluded active maternal smokers from analysis

Supplementary Table 3. Changes self-reported smoking status of the study cohort.

	Smoking status at first antenatal visit			
Smoking status research questionnaire	Never smoked % (n)	Ex-smoker % (n)	Current smoker % (n)	Total % (n)
Never smoked	84% (96)	9% (9)	0% (0)	42% (105)
Ex-smoker	16% (19)	85% (82)	5% (2)	41% (103)
Current smoker	0% (0)	6% (6)	95% (36)	17% (42)
Total	100% (115)	100% (97)	100% (38)	100% (250)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6-7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	7-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-9
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	Footnotes of tables
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	n/a
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	9-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

A prospective, observational study investigating the use of carbon monoxide screening to identify maternal smoking in a large university hospital in Ireland.

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ABSTRACT

Objectives: This study evaluated breath carbon monoxide (BCO) testing in identifying maternal smokers as well as the difference between disclosers and non-disclosers of smoking status. We also investigated if other extrinsic factors affected the women's' BCO levels in pregnancy.

Design: A prospective observational study.

Setting: A university obstetric hospital in an urban setting in Ireland.

Participants: Women (n=250) and their partners (n=54) were recruited at their first antenatal visit. Women <18 years and those who did not understand English were excluded. A booking history, including collection of smoking status was collected by midwives. Following this women were recruited and completed a detailed research questionnaire on smoking and extrinsic/environmental BCO sources. A BCO test was performed on both the woman and her partner.

Primary and secondary outcome measures: The number of self-reported smokers and those that were positive on the BCO test. The characteristics of women who disclosed and did not disclose smoking status. The effect of extrinsic factors on the BCO test results.

Results: Based on the ROC a BCO cut-off point of ≥3ppm was the optimal level to identify ongoing smoking. At booking history, 15% of women reported as current smokers. Based on BCO levels ≥3ppm combined with self-reported smoking in the research questionnaire, the rate increased to 25%. Non-disclosers had similar characteristics to non-smokers. No extrinsic factors affected maternal BCO levels.

Conclusions: Based on self-report and BCO levels a quarter of women presenting for antenatal care continued to smoke but only 60% reported their smoking to midwives. BCO measurement is an inexpensive, practical method of improving identification of maternal

smoking and it was not affected by extrinsic sources of BCO. Improved identification means more smokers can be supported to stop smoking in early pregnancy potentially improving the short and long term health of both mother and child.

Trial registration: n/a

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- Sensitivity and specificity analysis were carried out to determine the optimal cut off point to determine smoking as there are wide variations and no consensus in the literature, particularly in pregnant populations.
- Our study collected details of daily self-reported exposure to extrinsic sources of CO and directly measured exposure to passive smoking using BCO in a subset of partners.
- Carbon monoxide analysis, although the most practical and feasible screening tool to detect smoking in a large cohort, can only detect exposure from the previous four hours.

BACKGROUND

Maternal smoking is arguably the most important modifiable risk factor for adverse pregnancy outcomes including perinatal death.[1] Passive smoking is also linked to adverse outcomes, in particular fetal growth restriction.[2,3] Smoking cessation either pre-pregnancy or in the first half of pregnancy can normalise fetal growth.[4]

Although smoking rates in non-pregnant adult women are falling in Ireland, over one in ten women report that they continue to smoke at their first antenatal visit.[5] Similar rates have been reported in other developed countries.[6,7] As many as three quarters of women may not disclose their smoking status when they present to maternity services, however there are large discrepancies in the literature regarding rates of non-disclosure and none to date have been reported for Ireland.[8,9]

Non-disclosure of smoking leads to inaccurate smoking prevalence rates and missed opportunities to offer advice and support to quit.[10] This has led to the use of biochemical markers to identify people who fail to disclose their smoking behaviour.[11-13] The most commonly used biomarkers include serum carboxy-hemoglobin or cotinine, a by-product of nicotine, from urine, saliva or blood samples.[14] These methods, although valid, reliable and sensitive to cigarette smoke exposure of up to 20 hours, can be invasive, inconvenient and expensive as they require laboratory involvement for analysis. Cotinine samples can cost up to approximately $20 a sample and results can be affected by the use of nicotine replacement therapy.[15, 16] Thus, this method may be only feasible in a research setting.

A breath carbon monoxide (BCO) test is a more appropriate alternative biomarker of cigarette exposure for routine screening as it costs as little as $1 per sample.[15] Furthermore, the BCO test is safe, quick, non-invasive and yields immediate results at the point of care.[17-19] A challenge of BCO testing is the half-life of carbon monoxide (CO). CO exposure in the previous 3 to 5 hours can be detected by a BCO test and it is, therefore, unable to detect

active tobacco exposure from the previous day.[10] Despite this, BCO correlates well with serum and urine cotinine levels and has shown high sensitivity and specificity in distinguishing between smokers and non-smokers.[19] Thus, BCO is a feasible option to help identify women who do not disclose their smoking in the antenatal outpatients.

Guidelines recommend the screening of CO at the first antenatal visit, with the NICE guidelines in the UK recommending that all women with a positive BCO test are referred to an 'opt-out' stop smoking service (SSS).[20,21] The screening of all pregnant women with a BCO test has two important purposes. Firstly, it can help identify women who continue to smoke in pregnancy and give staff the opportunity to advise and provide support to quit. Secondly, the BCO test can ensure that the woman and her baby are not inadvertently in contact with the poisonous gas.[20] To date, no guidelines have been implemented in Ireland and just one out of all 19 units nationally conduct a BCO test in pregnancy.[22]

CO is a colourless, odourless, tasteless and poisonous gas that is potentially fatal at high levels. Exposure to CO is particularly dangerous during pregnancy because it replaces the oxygen available to the fetus, restricts growth and development, and increases the risk of fetal death, developmental disorders, and chronic cerebral lesions.[23] CO is emitted from cigarette smoke, exhaust fumes and from malfunctioning or poorly ventilated fossil/ wood fuelled heating and cooking appliances.[20, 23] However, there is a dearth of knowledge of the degree to which these extrinsic factors, as well as partners smoking habits can affect routine CO screening.[24, 25]

The purpose of this study was to evaluate the use of BCO screening to detect cigarette smoking in women presenting to an Irish maternity hospital for antenatal care as well as characterise the difference between disclosers and non-disclosers of smoking status. We also investigated if other extrinsic factors affected the women's' BCO levels in pregnancy.

METHODS

This prospective observational cohort study was conducted between January and September 2017 in a large Irish university maternity hospital responsible for approximately 8,500 deliveries per annum. The study was approved by the Hospital Research Ethics Committee (17-2015).

There were three sources of data used in this study: maternal booking data collected and computerised by midwives and retrieved by the researcher from the electronic medical record system 'K2', a carbon monoxide breath test conducted by the researcher (C.R.) and a fully supervised paper based research questionnaire (Figure 1.). At the first antenatal visit ('booking visit') the woman's history was computerised by a trained midwife onto K2. Histories were taken in a standardised manner and included questions regarding a number of lifestyle factors such as self-reported smoking prompted by the K2 system (Figure 1.).

The women's booking history and first antenatal dating scan are held on the same day at approximately 12 weeks gestation. Thus, on completion of the booking history, and before women presented for their first antenatal scan women were informed of the study by the researcher (C.R.) and advised to attend the research office after their dating scan should they wish to participate (Figure 1.).

On attendance at the research office women were screened for eligibility. Women were ineligible if they were under 18 years of age or did not understand English. Eligible women were then formally invited to participate in the study. Women were informed that the BCO test would assess their exposure to CO sources such as tobacco smoke, exhaust fumes, poor household ventilation etc.[18] Written consent was obtained to provide a sample of expired air and to complete an additional research questionnaire. The questionnaire collected further sociodemographic and lifestyle information i.e. education level, potential environmental exposures to carbon monoxide such as passive smoke, and a repeated self-reported smoking

status (Figure 1.). Assurance was given that all data were anonymous and would not affect care in the hospital in order to encourage accurate reporting in the research questionnaire. Other known environmental exposures to CO were collected due to their potentially confounding nature in accurately identifying smokers.[18]

Partners in attendance with the woman at the first visit were also offered participation in the study. The partner was fully informed of the study procedures and written consent was obtained. The individuals followed the same study procedures as the pregnant woman. BCO was performed and the research questionnaire was completed.

BCO levels were performed using the inexpensive, handheld Bedfont piCO+ Smokerlyzer® (Bedfont Scientific, Kent, United Kingdom). To perform the breath test women were asked to exhale completely, inhale fully and breath-hold for 15 seconds. At the end of the breath hold, the women were asked to exhale slowly and fully into the Smokerlyzer device. Safety protocols were put in place to minimise the risk of missing potential cases of CO poisoning.[20] The Smokerlyzer measures BCO levels in parts per million (ppm). Breath holding allows the CO in the blood to form equilibrium with the CO in the alveolar air. This technique is responsible for high level of correlation between breath CO levels and COHb concentration.[26]

We calculated that recruitment of 233 women allowed for detection of a 10% rate of non-disclosure (power 99%, significance 5%). Due to large variations in the cut-off criteria used previously to distinguish between smokers and non-smokers a receiver-operating characteristic (ROC) plot was undertaken.[13, 14, 25, 27, 28] The ROC assessed the accuracy of the BCO test in predicting smoking and the BCO level (ppm) with the highest combined sensitivity and specificity value was used as the cut-off. Women who had a CO level greater than the cut-off point but reported as a non-smoker were categorised as non-disclosers.

All results were analyzed by the SPSS statistical package version 24 (SPSS; Chicago, IL). Descriptive statistics were used to describe the characteristics of the study cohort. Normality of data were assessed using visual inspection of histograms, the data skewness and kurtosis and the Kolmogorov-Smirnov Test. Continuous data were reported as means and standard deviations if normally distributed and median and interquartile ranges (IQR) if data were non-normally distributed. Categorical data were reported as proportions. Chi-squared, analysis of variance (ANOVA) and Mann Whitney U were used to assess differences between groups in terms of proportions, means and medians respectively. Associations between CO levels and other variables were carried out using Spearman's correlations. Missing data are presented in the footnotes of tables.

Patient and Public Involvement

Previous research has shown that just one out of the 19 maternity units in Ireland conduct the recommended CO screening to identify maternal smokers.[22] Furthermore, there is dearth of information on the disclosure rate of maternal smoking in an Irish population. This was the stimulus for our research question.

The patients were not directly involved in the study design however the study questionnaire was piloted on ten patients who provided feedback on the questions included. Patients were also not involved in the recruitment process; however, the Hospital Research Ethics Committee includes members of the public involved in reviewing the methods, patient information leaflets, questionnaires and consent form.

The results of our study were not disseminated to the study population. Results will be presented locally to educate staff on our findings with the aim of implementing BCO screening to identify maternal smokers in our hospital.

RESULTS

The ROC results showed the BCO levels measured in parts per million (ppm) were predictors of maternal cigarette smoking (area under the curve (AUC) = 0.93, $p < 0.001$) (Supplementary Figure 1). The sensitivity and specificity curves crossed at a cut-off point of 3ppm (Supplementary Figure 2). The highest combined sensitivity and specificity of maternal smoking was also at the CO level 3ppm (Supplementary Table 1).

Two hundred and eighty-eight women were offered participation in the study of which 250 were recruited. Of the 38 women that did not take part, 20 declined due to time constraints and 18 left immediately after their scan without reason for non-participation. Verified smoking was defined as having a CO level ≥3ppm and/or self-reported smoking either at the first antenatal visit or on the research questionnaire.

Table 1 shows the characteristics of the study group analysed by verified smoking status. Verified maternal smokers (n=63) were more likely to be younger (mean difference 3.4 years 95% Confidence Intervals (CI) 1.9-4.9, $p < 0.001$), unemployed (43% vs 22%, $p < 0.001$) and single (77% vs 39%, $p < 0.001$) compared to non-smokers (n=187). They also spent fewer years in continuous full time education (mean difference 1.9 years 95% CI 0.6-3.1, $p < 0.01$) and finished full time education at a younger age (mean difference 2.8 years 95% CI 1.2-4.2, $p < 0.001$) than non-smokers.

Median BCO levels and rates of BCO < 3 and ≥ 3ppm by maternal characteristics and CO sources are shown in Tables 2 and 3. Of all known CO sources that were examined, self-reported maternal smoking in the current and previous pregnancy and cigarette quantity were the only factors that were associated with an increased median BCO level above 3ppm.

Supplementary table 2 shows that on further examination, using correlation analysis, the number of self-reported cigarettes per day had the strongest association with BCO test levels (rho = 0.61, $p < 0.001$) followed by time since last cigarette (rho = -0.51, $p < 0.01$).

Hours exposed to passive smoking was also associated with BCO levels (rho = 0.31, $p < 0.01$). However, when self-reported active smokers were removed from this analysis this association disappeared (rho = -0.06, NS).

BCO tests were performed on 54 partners of the pregnant women (22%). The mean age of the partners was 33.1 years (6.5 years), 98.1% were male, 83.3% lived with their pregnant partner and the median BCO level of the partners was 2.0ppm (interquartile range (IQR) 4.5ppm). Twenty-eight percent (n=15) of partners reported current smoking and five of these had a pregnant partner who also smoked. Of the 26 partners with positive BCO tests their median levels were 6.0 (IQR 8.0), similar to the median BCO of women with positive tests 7.0 (IQR 8.0). On examination of BCO levels 48% (n=26) had a CO ≥3ppm. The BCO levels of partners were weakly associated with the BCO levels of the pregnant women (rho = 0.34, $p < 0.05$) but when active maternal smokers were removed from analysis the relationship disappeared. Median BCO levels in pregnant women were the same regardless of their partners CO levels being < or ≥ 3ppm.

Maternal characteristics of the disclosers and non-disclosers of smoking status were compared (Table 4). Non-disclosers were classified as women who did not report smoking at their first antenatal visit but had a CO level ≥3ppm and/or self-reported smoking in the research questionnaire. Non-disclosers had a lower median BCO level than disclosers (10.0 ppm (IQR 8.0) vs 4.0 ppm (IQR 3.0), $p <0.01$). Non-disclosers were older than disclosers when they finished full time education (20.9 years (IQR 3.9) vs 17.9 years (IQR 2.1), $p < 0.05$) and spent more years in continuous full time education (16.5 years (IQR 3.6) vs 13.4 years (IQR 2.4), $p < 0.01$). They were also more likely to have planned their pregnancy (60% vs 37%, $p < 0.05$), less likely to have smoked in a previous pregnancy (20% vs 55%, $p < 0.01$) and spend less time around passive smoking daily (1.5 hours (IQR 1.6) vs 3.9 hours (IQR 3.5), $p < 0.05$).

Changes in self-reported smoking status from the first antenatal visit to self-reported smoking status collected in the research questionnaire are shown in Supplementary Table 3. The largest difference was seen in women who reported 'never smoking' at the first antenatal visit to midwives with 16% changing their status to 'ex-smoker' on the research questionnaire. Six other women who reported they were never smokers to midwives at the first antenatal visit had a CO reading ≥3ppm. Of these, one woman changed her self-reporting on the research questionnaire to ex-smoking status and reported quitting two months previous. Two other women reported smoking cannabis which could be the reason for the CO ≥3ppm. At first visit 17 potential non-disclosers reported they were ex-smokers. Of these, six disclosed smoking on the research questionnaire. Another five women reported they had only quit since the beginning of pregnancy and one was continuing to smoke cannabis.

Based on self-reported smoking status at the first antenatal visit, 15% (38/250) of women were maternal smokers. Based on self-reported smoking in the research questionnaire, the rate rose to 17% (42/250). When results from the BCO test levels ≥3ppm were used the rate increased to 23% (57/250). However, when BCO levels ≥3ppm were combined with self-reporting the rate of maternal smoking was 25% (63/250). Based on self-reported non-smoking, our study had a rate of non-disclosure of 12% (25/212). Overall, 39.6% (25/63) of all maternal smokers did not report as smokers to midwives when booking at their first antenatal visit.

Six women who reported smoking were not detected on CO screening. All six reported not having a cigarette in the previous four hours and five of the six women smoked ≤2 cigarettes daily.

DISCUSSION

We found that BCO testing in combination with self-reporting of smoking status in a research setting identified 10% more maternal smokers than self-reporting using routine

practice at the first antenatal visit. Two out of five women who continued to smoke in pregnancy were not identified thus, maternity services were missing the opportunity to provide advice and smoking cessation support.

There is no consensus as to what constitutes the best cut-off point for determining smoking status. Some suggest a CO level as low as 2 parts per million (ppm), others as high as 10 ppm.[14, 28-32] Due to the conflicting appropriate cut-off points in the literature we undertook a sensitivity and specificity analysis.[30] Similar to a large American longitudinal study, we identified a cut-off point of 3ppm as the optimal to distinguish smokers from non-smokers in terms of limiting both false positive and false negative results and maximising identification of smokers with a high degree of certainty.[30] Few studies have previously undertaken their own ROC making it difficult to interpret the sensitivity and specificity of results.

There is a dearth of knowledge on what factors other than active smoking can effect BCO levels and stop smoking services (SSS) staff often find difficult to explain high results in non-smokers.[25] Our study collected data on other potential extrinsic sources of CO that may have contaminated results. Other studies do not take into account daily passive smoke exposure, partners BCO levels or sources such as motor vehicle use, fossil fuel exposure, gas/oil boiler servicing practices, ventilation etc. These factors did not affect median BCO levels in women in the present study, and did not increase rates of BCO levels ≥3ppm. Fifty four partners took part in this study. We found a weak positive relationship between partner BCO levels and maternal BCO, however when active smokers were excluded, no relationship existed. One other study, in non-pregnant adults, examined the effect of other sources of CO on BCO test levels and found that gender and motor vehicle use were associated with higher CO levels. However, the differences were minimal (<1ppm).[18]

A limitation of our study is that we did not collect cotinine samples for verification of smoking status; however, our aim was not to compare screening methods, but to report the levels of non-disclosures in Ireland using current guidelines.[21] Furthermore, our lower cut-off point provided high sensitivity values and has been supported by previous research that also identified this value as optimal when identification of smoking abstinence with a high degree of certainty is of high importance.[30]

Our study found a self-reported smoking rate of 15%, 4% higher than the rate reported in our previous study that analysed all deliveries in our hospital in 2015.[5] It is unlikely that the rate has risen, and this higher rate may be due to the convenience sampling employed.

Our study distinguishes characteristics between smokers and non-disclosers unlike previous studies that compared verified smokers to non-smokers.[13] We found non-disclosers had more similar characteristics to non-smokers than smokers. This could be due to a number of reasons. Firstly, we used a lower cut-off point compared to other studies in pregnant populations.[25, 28, 32] Another study that carried out an ROC curve found its highest specificity and sensitivity at the cut-off point >4ppm, however, this cut-off had a lower sensitivity value (0.79) than our study (0.86).[28] Our studies lower cut-off point may therefore be too sensitive and include non-smoking women in the non-disclosure group (false positives). If our cut-off was raised to that of other studies, however, our sensitivity would be reduced and fewer smokers would be identified correctly.

Prior to implementation of the NICE guideline in the UK healthcare staff were worried that that BCO testing would unjustly accuse women who don't smoke of doing so and that it would affect their relationships with the women.[25] However, following implementation they found it had little effect on their relationships with women and the SSS staff found that it provided them with a unique opportunity to address second-hand smoke,

smoke free homes and the effects of smoking around children with non-smokers who may be regularly exposed to passive smoke.[25]

For healthcare professionals who continue to have concerns over false positives being wrongly accused of smoking and referred to SSS an alternative pathway could be implemented whereby cotinine is sampled and tested only in self-reported non-smokers who have a high BCO level in order to keep the expense on maternity services as low as possible.

A further concern is that women who may smoke but did not report doing so at their first appointment may not wish to receive cessation advice. However, guidelines recommend an opt-out referral system whereby women who are identified as smokers in early pregnancy and those who do not specifically object are referred to smoking cessation services.[21] Thus this non-mandatory referral system is centred on the patient's best interests and it does not overrule personal choice.

A number of different rates of non-disclosure have been reported in the literature, from as low as 5% to as high as 73% but it is difficult to compare these results to our study.[8,9] Firstly, the definition of 'non-disclosure' or 'miss-categorisation' is not standardised across studies. Different denominators are used. Some studies use the number of positive tests whereas others use total population, total self-reported non-smokers or self-reported quitters.[12,13,33,34] Secondly, studies to date have used conflicting cut-off points to verify smoking, for example, some use standard cut-off points, some use ROCs to find the optimal for their population and others use both which demonstrate disparity in results.[12,33,35]

Additionally, the samples in previous studies were taken at different time points in pregnancy. Our study took BCO samples at the beginning of pregnancy. However, previous research found that non-disclosure rates are increased from the beginning to later in pregnancy.[13, 35] Sampling at the first visit is preferable because early identification and

successful intervention in the first half of pregnancy has the potential to normalise fetal growth.[4]

A UK study with similar recruitment methods but a higher BCO cut-off point of >4ppm reported that 22.9% of all smokers did not disclose smoking at booking, much lower than our 39.6%.[32] However, this higher cut-off point was previously criticised for missing both self-reported smokers and smokers verified by cotinine.[28, 36]

In conclusion, self-reporting of maternal smoking leads to missed opportunities to provide smoking cessation advice and support from the beginning of pregnancy. BCO screening can improve identification of smokers at the first antenatal visit. This screening complements routine history taking, but should not replace it as this test may produce a false negative in smokers who have not had a cigarette in the previous four hours. Screening in early pregnancy should use a low cut-off value because a once-off test resulting in a false positive result, in this case, is preferable to a false negative result. BCO levels not only correlate with self-reported quantity of cigarettes per day but also with timing of smoking and do not appear to be effected by extrinsic carbon monoxide sources. Finally, cotinine may need to be used as an adjunct to CO screening in women with high CO levels who report that they are non-smokers to rule out a false positive test.

STATEMENT OF CONTRIBUTION

CR contributed to the conception and design of the study, performed the analysis of the data, interpreted data and wrote and edited this original article. RK, EOM and SS contributed to the writing and editing of this article. MT and BE contributed to the conception of the study, interpretation of data as well as contributing to the writing and editing of this article.

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DECLARATION OF INTERESTS

None of the authors have any conflicts of interest to declare.

PATIENT CONSENT

Written consent was obtained.

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DATA SHARING STATEMENT

Additional unpublished data is available. For further details contact ciara.reynolds@ucdconnect.ie.

REFERENCES

1. Cnattingius S. The epidemiology of smoking during pregnancy: smoking prevalence, maternal characteristics, and pregnancy outcomes. Nicotine Tob Res 2004;6Suppl2:S125-40.
2. Rubin DH, Krasilnikoff PA, Leventhal JM, et al. Effect of passive smoking on birth-weight. Lancet 1986;2(8504):415-7.
3. Martinez FD, Wright AL, Taussig LM. The effect of paternal smoking on the birthweight of newborns whose mothers did not smoke. Group Health Medical Associates. Am J Public Health 1994;84(9):1489–91.
4. Lieberman E, Gremy I, Lang JM, et al. Low birthweight at term and the timing of fetal exposure to maternal smoking. *Am J Public Health* 1994;84: 1127–31.
5. Reynolds CME, Egan B, McKeating A, et al. Five year trends in maternal smoking behaviour reported at the first prenatal appointment. *Ir J Med Sci* 2017;186:971-9.
6. European Perinatal Health Report (2010) The health of pregnant women and babies in Europe in 2010.http://www.europeristat.com/images/European%20Perinatal%20Health%20Report_2010.pdf. Accessed 2 February 2016
7. Reitan T, Callinan S.Changes in Smoking Rates Among Pregnant Women and the General Female Population in Australia, Finland, Norway, and Sweden. Nicotine Tob Res 2017;19(3):282-9.
8. Webb DA, Boyd NR, Messina D, et al. The discrepancy between self-reported smoking status and urine cotinine levels among women enrolled in prenatal care at four publicly funded clinical sites. *J Public Health Manag Pract* 2003;9(4):322-5.
9. Pickett KE, Rathouz PJ, Kasza K, et al. Self-reported smoking, cotinine levels, and patterns of smoking in pregnancy. *Paediatr Perinat Epidemiol* 2005;19:368-76.

10. Russell T, Crawford M, Woodby L. Measurements for active cigarette smoke exposure in prevalence and cessation studies: why simply asking pregnant women isn't enough. *Nicotine Tob Res* 2004;6Suppl2:S141-51.

11. Shipton D, Tappin DM, Vadiveloo T, et al. Reliability of self-reported smoking status by pregnant women for estimating smoking prevalence: a retrospective, cross sectional study. *BMJ* 2009;29;339:b4347.

12. Dietz PM, Homa D, England LJ, et al. Estimates of nondisclosure of cigarette smoking among pregnant and nonpregnant women of reproductive age in the United States. *Am J Epidemiol* 2011;173:355-9.

13. Tong VT, Althabe F, Alemán A, et al. Accuracy of self-reported smoking cessation during pregnancy. *Acta Obstet Gynecol Scand* 2015;94:106-11.

14. Campbell E, Sanson-Fisher R, Walsh R. Smoking status in pregnant women assessment of self-report against carbon monoxide (CO). *Addict Behav* 2001;26:1-9.

15. Patrick DL, Cheadle A, Thompson DC. The validity of self-reported smoking: a review and meta-analysis. *Am J Public Health* 1994;84:1086–93.

16. Benowitz NL, Hukkanen J, Jacob P. Nicotine chemistry, metabolism, kinetics and biomarkers. *Handb Exp Pharmacol* 2009;192:29–60.

17. Vogt TM, Selvin S, Widdowson G, et al. Expired air carbon monoxide and serum thiocyanate as objective measures of cigarette exposure. Am J Public Health 1977;67:545-9.

18. Cunnington AJ, Hormbrey P. Breath analysis to detect recent exposure to carbon monoxide. *Postgrad Med J* 2002;78:233-7.

19. Erb P, Raiff BR, Meredith SE, et al. The accuracy of a lower-cost breath carbon monoxide meter in distinguishing smokers from non-smokers. J Smok Cessat 2015;10:59-64.

20. HSC Public Health Agency. Carbon monoxide screening. Advice for health professionals. http://www.publichealth.hscni.net/publications/carbon-monoxide-screening-advice-health-professionals

21. The National Institute for Health and Care Excellence (NICE) Smoking: stopping in pregnancy and after childbirth. Public health guideline. https://www.nice.org.uk/guidance/ph26

22. Reynolds CM, Egan B, Cawley S, Kennedy R, Sheehan SR, Turner MJ. A National Audit of Smoking Cessation Services in Irish Maternity Units. *IMJ* 2017;110(6):580.

23. Raub JA, Mathieu-Nolf M, Hampson NB, Thom SR. Carbon monoxide poisoning-a public health perspective. *Toxicology* 2000;145:1-14.

24. Friedman P, Guo XM, Stiller RJ, et al. Carbon Monoxide Exposure During Pregnancy. *Obstet Gynecol Surv* 2015;70:705-12.

25. Campbell KA, Bowker KA, Naughton F, Sloan M, Cooper S, Coleman T. Antenatal clinic and stop smoking services staff views on "opt-out" referrals for smoking cessation in pregnancy: A framework analysis. *Int J Environ Res Public Health* 2016;13:1004.

26. Middleton ET, Morice AH. Breath carbon monoxide as an indication of smoking habit. *Chest* 2000;117:758-63.

27. West R, Hajek P, Stead L, Stapleton J. Outcome criteria in smoking cessation trials: proposal for a common standard. *Addiction* 2005;100:299-303.

28. Bauld L, Hackshaw L, Ferguson J, Coleman T, Taylor G, Salway R. Implementation of routine biochemical validation and an 'opt out'referral pathway for smoking cessation in pregnancy. *Addiction* 2012;107:53-60.

29. Deveci SE, Deveci F, Açik Y, et al. The measurement of exhaled carbon monoxide in healthy smokers and non-smokers. *Respir Med* 2004;98:551-6.

30. Javors MA, Hatch JP, Lamb RJ. Cut-off levels for breath carbon monoxide as a marker for cigarette smoking. *Addiction* 2005;100:159-67.

31. Higgins ST, Heil SH, Badger GJ, et al. Biochemical verification of smoking status in pregnant and recently postpartum women. *Exp Clin Psychopharmacol* 2007;15:58-66.

32. Campbell KA, Cooper S, Fahy SJ, Bowker K, Leonardi-Bee J, McEwen A, Whitemore R, Coleman T. 'Opt-out'referrals after identifying pregnant smokers using exhaled air carbon monoxide: impact on engagement with smoking cessation support. *Tob control* 2017;26:300-6.

33. Boyd NR, Windsor RA, Perkins LL, et al. Quality of measurement of smoking status by self-report and saliva cotinine among pregnant women. *Matern Child Health J* 1998;2:77-83.

34. Lindqvist R, Lendahls L, Tollbom O, et al. Smoking during pregnancy: comparison of self-reports and cotinine levels in 496 women. *Acta Obstet Gynecol Scan* 2002;81:240-4.

35. Ford RP, Tappin DM, Schluter PJ, et al. Smoking during pregnancy: how reliable are maternal self-reports in New Zealand? *J Epidemiol Community Health* 1997;51:246–51.

36. Jatlow P, Toll BA, Leary V, Krishnan-Sarin S, O'Malley SS. Comparison of expired carbon monoxide and plasma cotinine as markers of cigarette abstinence. *Drug Alcohol Depend* 2008;98:203-9.

Table 1. Characteristics of the study cohort based on self-reported and carbon monoxide confirmed smoking status at the first antenatal visit.

Characteristic	Total (n=250)	Non-smokers (n=187)	Verified smokers* (n=63)	p-value
Age (SD) (years)	31.0 (5.3)	31.8 (5.1)	28.4 (5.2)	<0.001
BMI (SD) (kg/m^2)	26.4 (6.1)	26.3 (5.4)	27.0 (7.8)	0.481
Obese (%)	19.3	17.0	26.2	0.078
Nationality (%)				
Ireland	76.8	75.1	82.0	0.106
EU 14	4.8	3.7	8.2	0.089
EU 13	8.4	10.1	3.3	-
Other	10.0	11.1	6.6	-
Occupation (%)[a]				
Professional/managerial	25.8	32.1	6.7	-
Skilled manual/non-manual	29.9	32.1	23.3	0.079
Semi- manual/unskilled manual	16.8	13.6	26.7	<0.001
Unemployed (%)	27.5	22.3	43.3	<0.001
Married (%)	52.0	61.4	23.0	<0.001
Years of continuous education[b] (years)	16.0 (3.5)	16.4 (3.5)	14.5 (3.2)	<0.01
Age completed education[b] (years)	21.2 (4.2)	21.8 (4.2)	19.0 (3.1)	<0.001
Nulliparas (%)	34.8	32.8	41.0	0.106
Planned pregnancy (%)	65.6	72.0	45.9	<0.001
Daily passive smoke exposure (%)	28.0	15.9	65.6	<0.001
Alcohol before pregnancy (%)	32.9	68.3	63.5	0.259
Alcohol during pregnancy (%)	2.8	2.6	3.3	-
Illicit drugs before pregnancy (%)				
Cannabis only	7.6	5.8	13.1	0.038
Other drugs	6.8	5.3	11.5	0.058
Illicit drugs during pregnancy (%)				
Cannabis only	2.4	1.1	6.6	-
Other drugs	1.2	0.0	4.9	-

*Women who self-report they are currently smoking and women who had a carbon monoxide level of ≥3ppm.

p-values indicate significance between non-smokers and verified smokers

[a]Missing data n=6, [b]Missing data n=67

-The number of values for this variable was too small to statistically analyse

Table 2. Median carbon monoxide levels and rates of carbon monoxide below and above cut off by maternal characteristic.

Factor	n	CO PPM (Median, IQR)	CO < 3 PPM (%)	CO ≥ 3 PPM (%)	p
Occupation					
Professional/managerial[a]	63	1.0 (1.0)	93.7	6.3	-
Skilled manual/non-manual	73	1.0 (1.0)	80.8	19.2	<0.001
Semi-manual/unskilled manual	41	2.0 (3.5)**	65.9	34.1	<0.01
Unemployed	67	2.0 (5.0)*	64.2	35.8	<0.001
Marital Status					
Married/civil partnership[a]	130	1.5 (1.0)	90.0	10.0	<0.001
Single	120	2.0 (4.0)***	63.3	36.7	<0.001
Age (years)					
<30[a]	96	2.0 (4.0)	65.6	34.4	<0.001
≥30	154	1.0 (1.0)*	84.4	15.6	<0.001
Pregnancy Intention					
Planned [a]	164	1.0 (1.0)	84.8	15.2	<0.001
Unplanned	86	2.0 (4.0)**	62.8	37.2	<0.001
Age completed education					
<18years	35	2.0 (6.0)	60.0	40.0	<0.05
≥18years	146	1.0 (1.0)	85.6	14.4	<0.001
Years of continuous education					
<14years	68	1.0 (1.0)	67.6	32.4	<0.001
>14years	114	1.0 (3.0)	88.6	11.4	<0.001

*0.05, **0.01, ***0.001. IQR= Interquartile range

P-values in final column indicate differences between CO ≤3ppm and CO ≥3ppm

Table 3. Median maternal carbon monoxide levels and rates of carbon monoxide below and above cut off by carbon monoxide sources

Factor	n	CO PPM (Median, IQR)	CO < 3 PPM (%)	CO ≥ 3 PPM (%)	p
Smoking status[a]					
Never smoked	105	1.0 (1.0)	93.3	6.7	<0.001
Ex-smoker	103	1.0 (1.0)	86.4	13.6	<0.001
Current smoker	42	10.0 (8.5)***	14.3	85.7	<0.001
Exposed to passive smoking					
No[a]	170	1.0 (1.0)	85.0	15.0	<0.001
Yes	38	1.0 (2.0)	52.4	47.6	NS
Numbers of cigarettes smoked per day					
0[a]	208	1.0 (1.0)	89.9	10.1	<0.001
1-5	24	5.5 (8.5)***	20.8	79.2	<0.001
6-10	18	11.0 (6.5)***	5.6	94.4	-
Time since last cigarette (hours)					
<1[a]	9	13.0 (11.0)	0.0	100.0	-
1-2	14	10.0 (8.0)	0.0	100.0	-
3-6	9	5.0 (8.5)	22.2	77.8	-
>6	7	2.0 (11.0)*	57.1	42.9	-
Smoked in previous pregnancy[a]					
No	191	1.0 (1.0)	84.3	15.7	<0.001
Yes	31	5.0 (10.0)***	25.8	74.2	<0.001
Uses a car or bus daily					
No	31	2.0 (4.0)	61.3	38.7	<0.05
Yes	219	1.0 (1.0)	79.5	20.5	<0.001
Lives beside main road					
No	104	1.0 (1.0)	83.7	16.3	<0.001
Yes	146	1.0 (2.0)	72.6	27.4	<0.001
Lives in a built up area					
No	72	1.0 (1.0)	84.7	15.3	<0.001
Yes	178	1.0 (2.0)	74.2	25.8	<0.001
Boiler serviced every year					
Yes	144	1.0 (1.0)	86.0	14.0	<0.001
No	50	1.0 (1.0)	77.1	22.9	<0.001
Uses fossil fuel fire					
No	118	1.0 (1.0)	78.0	22.0	<0.001
Yes	132	1.0 (1.0)	76.5	23.5	<0.001
Chimney cleaned every year					
Yes	53	1.0 (1.0)	81.8	18.2	<0.001
No	88	1.0 (1.0)	81.1	18.9	<0.001
Partners CO >3 ppm					
<3ppm	28	1.0 (0.00)	90.6	9.4	-
≥3ppm	26	1.0 (2.50)	64.3	35.7	<0.05
Partner/spouse's smoking status[a]					
Non-smoker	36	1.0 (1.0)	87.5	12.5	<0.001
Current smoker	15	1.0 (4.0)	58.8	41.2	NS

*0.05, **0.01, ***0.001 IQR= Interquartile range

P-values in final column indicate differences between CO ≤3ppm and CO ≥3ppm

[a]Based on self-reported smoking status

Table 4. Differences in maternal characteristics between disclosures and non-disclosures of smoking status.

	Disclosers (n=38)	Non-disclosers (n=25)	p
BCO level (ppm) (median, IQR)	10.0 (8.0)	4.0 (3.0)	<0.01
Age (years) (mean, SD)	27.3 (5.0)	29.7 (5.2)	NS
BMI (kg/m^2) (mean, SD)	26.5 (8.4)	27.7 (7.1)	NS
Married (%)	15.8	32.0	NS
Nulliparas (%)	34.2	52.0	NS
Planned pregnancy (%)	36.8	60.0	<0.05
Age completed education (years) (mean, SD)[a]	17.9 (2.1)	20.9 (3.9)	<0.05
Continuous years of education (mean, SD)[a]	13.4 (2.4)	16.5 (3.6)	<0.01
Weekly alcohol before pregnancy (%)	57.9	72.0	NS
Alcohol binge before pregnancy (%)	23.7	52.0	<0.01
Drug use before pregnancy (%)	26.3	20.0	NS
Weekly alcohol in pregnancy (%)	2.6	4.0	-
Alcohol binge in pregnancy (%)	2.6	0.0	-
Drug use in pregnancy (%)	10.5	12.0	-
Smoked in previous pregnancy (%)	55.3	20.0	<0.01
Exposed to passive smoked daily (%)	73.7	56.0	NS
Exposure to passive smoke (hours) (mean, SD)	3.9 (3.5)	1.5 (1.6)	<0.05

P-values in final column indicate differences between disclosures and non-disclosures
SD = standard deviation, BCO = Breath carbon monoxide
[a]Missing data n=67
-The number of values for this variable was too small to statistically analyse

Figure 1 legend

Figure 1 shows a flow diagram of the studies data collection and recruitment processes.

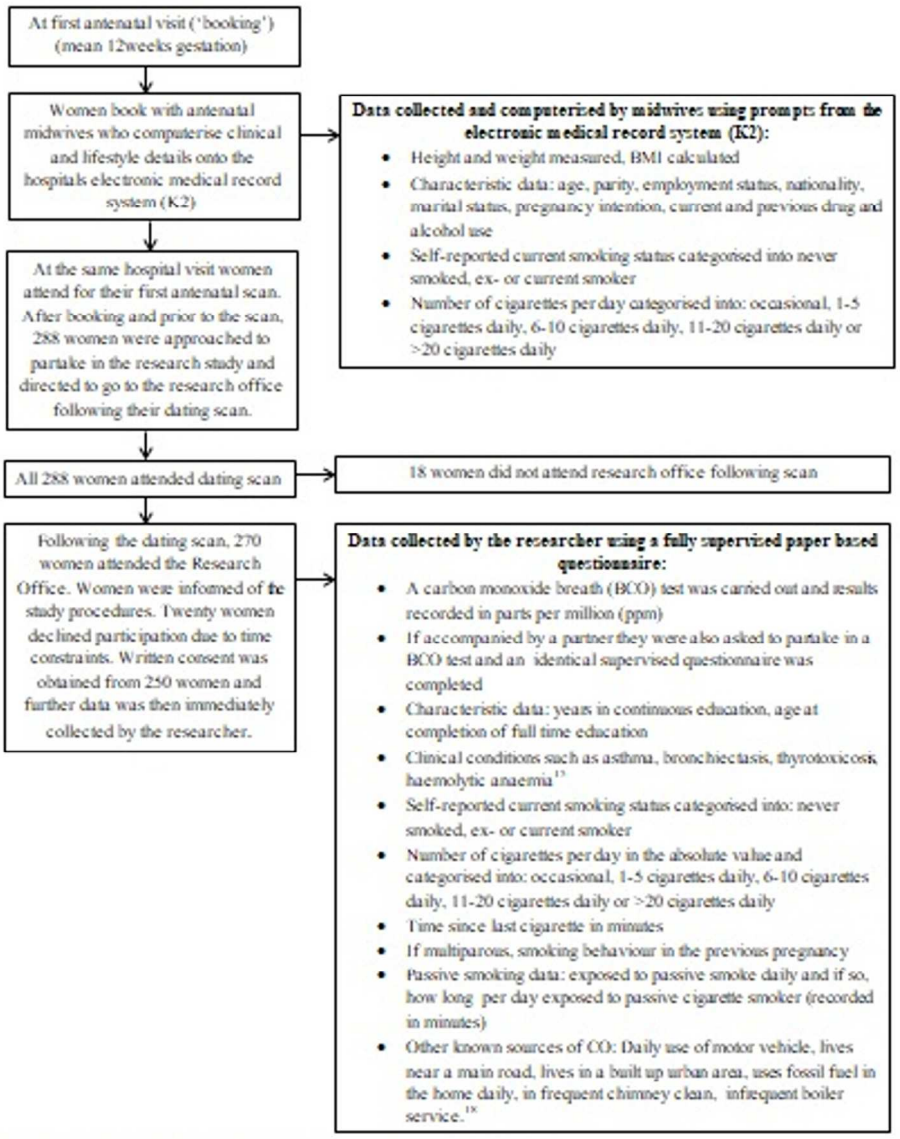

Figure 1. Flow diagram of participant recruitment and data collection

Figure 1 shows a flow diagram of the studies data collection and recruitment processes.

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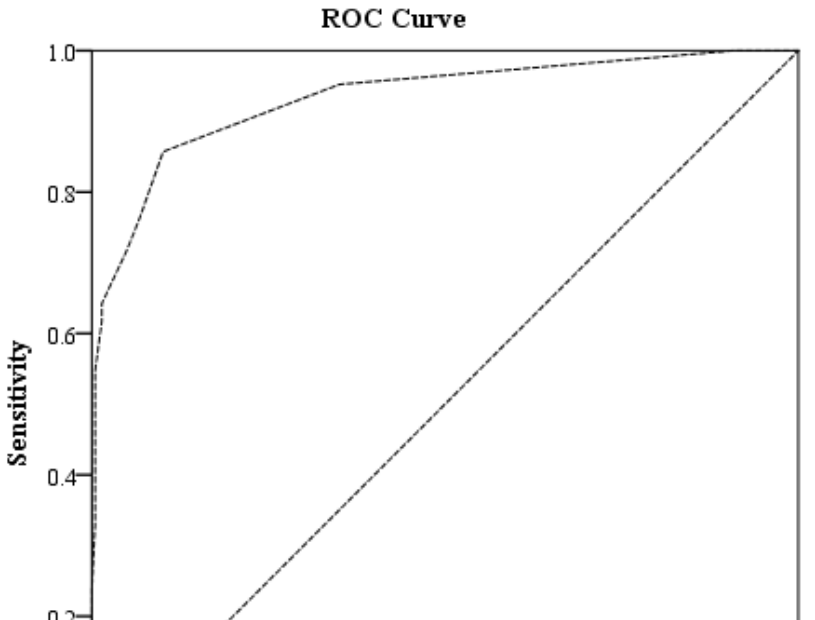
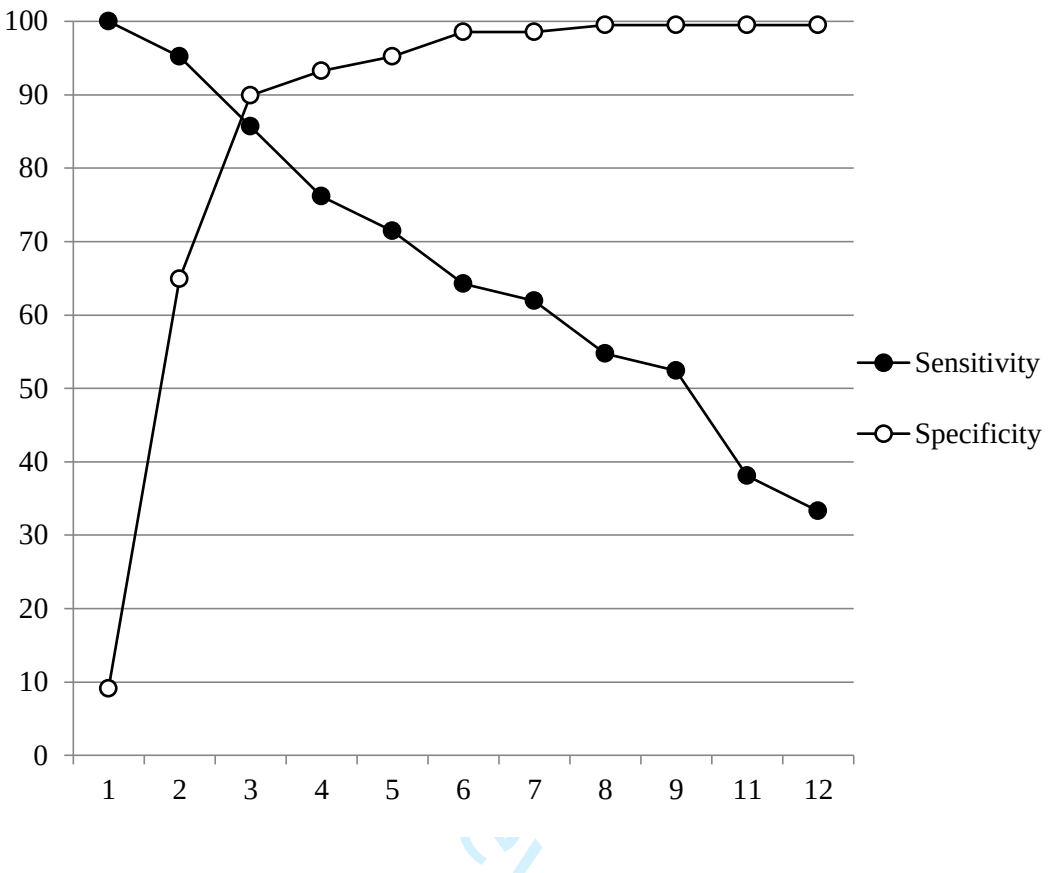


Supplementary Figure 1

The percentage of false-positive results (100-specificity) plotted against the percentage of true-positive results (sensitivity) across the entire range of breath CO measures.



Supplementary Figure 2

Sensitivity and specificity were plotted at BCO cut-off levels from 1 to 12 ppm.
Sensitivity is the percentage of positive carbon monoxide breath tests at a specified cut-off.
Specificity is the percentage of negative carbon monoxide breath tests at a specified cut-off.

Supplementary Table 1. Sensitivity and specificity of the carbon monoxide analyser at various carbon monoxide breath test levels.

Carbon monoxide (ppm)	Sensitivity	Specificity	1-Specificity	Sensitivity + Specificity
1	1	0.09	0.91	1.09
2	0.95	0.65	0.35	1.60
3	**0.86**	**0.90**	**0.10**	**1.76**
4	0.76	0.93	0.07	1.69
5	0.71	0.95	0.05	1.67
6	0.64	0.99	0.01	1.63
7	0.62	0.99	0.01	1.60
8	0.55	1.00	0.00	1.54
9	0.52	1.00	0.00	1.52
11	0.38	1.00	0.00	1.38
12	0.33	1.00	0.00	1.33

Supplementary Table 2. Correlations between maternal carbon monoxide levels (ppm) and factors associated with carbon monoxide exposure.

	n	Correlation co-efficient (rho)	p-value
Self-reported number of cigarettes per day	250	0.61	<0.001
Time since last cigarette (hours)[a]	39	-0.51	<0.01
Partners BCO	54	0.34	<0.05
Partners BCO[b]	45	0.19	NS
Passive smoking exposure (hours)	70	0.31	<0.01
Passive smoke exposure only (hours)[b]	38	-0.06	NS

[a] missing data n=3

[b] excluded active maternal smokers from analysis

Supplementary Table 3. Changes self-reported smoking status of the study cohort.

	Smoking status at first antenatal visit			
Smoking status research questionnaire	Never smoked % (n)	Ex-smoker % (n)	Current smoker % (n)	Total % (n)
Never smoked	84% (96)	9% (9)	0% (0)	42% (105)
Ex-smoker	16% (19)	85% (82)	5% (2)	41% (103)
Current smoker	0% (0)	6% (6)	95% (36)	17% (42)
Total	100% (115)	100% (97)	100% (38)	100% (250)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6-7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	7-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-9
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	Footnotes of tables
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	n/a
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	9-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.