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Self-reported smoking status and plasma cotinine concentrations among pregnant women in the Norwegian Mother and Child Cohort Study

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Abstract

Background—Underreporting of smoking in epidemiologic studies is common and may constitute a validity problem, leading to biased association measures. In this prospective study, we validated self-reported tobacco use against nicotine exposure assessed by plasma cotinine in the Norwegian Mother and Child Cohort Study (MoBa).

Methods—The study was based on a subsample of 2,997 women in MoBa who delivered during the period 2002–2003. Self-reported tobacco use (test variable) and plasma cotinine concentrations (gold standard) were assessed around gestational week 18.

Results—Daily smoking was reported by 9%, occasional smoking by 4% and non-smoking by 86% of the women. Sensitivity and specificity for self-reported smoking status were calculated by using a cotinine cut-off estimated from the current material (30 nmol/l). Plasma cotinine concentrations ≥ 30 nmol/l were found for 94% of self-reported daily smokers, 66% of occasional smokers and 2% of non-smokers. Adding the self-reported non-smokers with cotinine concentrations above cut-off increased the daily smoking prevalence from 9% to 11%. The sensitivity and specificity for self-reported daily smoking using 30 nmol/l as cut-off were 82% and 99%, respectively.

Conclusions—These findings suggest that self-reported tobacco use is a valid marker for tobacco exposure in the MoBa cohort.

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INTRODUCTION

Although the prevalence of maternal smoking during pregnancy has declined during the last 20 years,[1–3] smoking remains a strong environmental risk factor for adverse pregnancy outcomes and complications. In 2008, 16% of Norwegian pregnant women reported to smoke daily at the beginning of the pregnancy and 8% at the end of pregnancy.[3] Hence, many pregnant women are still exposed to tobacco smoke. This underscores the need for further epidemiologic research and public health prevention strategies.

There is, however, concern whether women report their true smoking status in epidemiological studies. By comparing self-reported smoking status with cotinine measurements, a study on pregnant women in the West of Scotland found a 25% underestimation of true smokers from self-reported smoking habits.[4] In a Swedish study, 6% of self-reported non-smokers were probably smokers and 3% had cotinine concentrations suggestive of passive smoking.[5] Such underreporting may constitute a serious validity problem, leading to biased association measures.[6]

In addition, missing data on self-reported smoking seems to be a common problem. A recent study from Norway found that 12% of pregnant women had not reported smoking habits to the population-based Medical Birth Registry of Norway.[2] In Sweden, smoking habits during pregnancy was missing for 9% and in Denmark 4% of babies had mothers with unregistered smoking habits.[7, 8]

Cotinine is the primary metabolite of nicotine and is a sensitive marker of tobacco smoking as well as use of snuff and nicotine replacements and is commonly used as a biomarker for environmental tobacco smoke exposure.[9, 10] In the present study we validated self-reported tobacco use in the Norwegian Mother and Child Cohort Study (MoBa) against maternal plasma cotinine. For this purpose, we also assessed a plasma cotinine cut-off to separate active smokers from passive smokers and non-smokers.

METHODS

Setting

MoBa is a prospective population-based pregnancy study established by the Norwegian Institute of Public Health.[11–13] Participants were recruited during the period 1999–2008, and 38.5% of the invited women consented to participate.[14] The cohort includes 108,639 children, 90,725 mothers and 71,574 fathers. Blood samples were obtained from both parents during pregnancy and from mothers and children (umbilical cord) at birth. Follow-up is conducted by questionnaires at regular intervals and linkage to national health registries, including the Medical Birth Registry of Norway. The current study is based on version 3 of the quality-assured data files released for research in April 2007.

Study population

For the purpose of this study, we used a sub-sample of 3,000 mothers with babies born during the period July 2002–December 2003. These women were drawn randomly among those who had donated a blood sample at the ultrasound screening and who where registered

in the Medical Birth Registry of Norway. In addition, they had returned a baseline questionnaire and a food frequency questionnaire during the second trimester.[15] We excluded 3 women who had no plasma cotinine results, leaving 2,997 women for analysis.

Informed consent was obtained from each participant and the study was approved by the Regional Committee for Medical Research Ethics.

Blood sampling and cotinine analysis

The blood samples (non-fasting) were collected from the mothers at weeks 17–18 into ethylenediaminetetraacetic (EDTA) tubes, which were centrifuged within 30 minutes after collection, and placed in the refrigerators in the hospitals (4 °C). Samples were shipped by mail overnight to the biobank of MoBa. On the day of receipt, usually 1–2 days after blood donation, EDTA plasma were aliquoted onto polypropylene microtitre plates (300 μL per well, 96 well formats), sealed with heat-sealing foil sheets, and stored at minus 80 °C.

Plasma concentrations of cotinine were analysed by a published liquid chromatography tandem mass spectrometry method[16] at Bevital AS (www.bevital.no). The limit of detection of the method was 1 nmol/l (0.18 ng/ml). For women (n = 111) with plasma cotinine values below limit of detection, values were imputed by assigning each women a random plasma cotinine value between 0 and 1 nmol/l. The coefficients of variation were 2.3–2.9% (within-day) and 5.5–6.2% (between-day). Cotinine has a half life of about 9 hours among pregnant women.[17] A serum cotinine cut-off at 17 nmol/l (3 ng/ml) was previously recommended to distinguish smokers from non-smokers.[18]

Nicotine exposure

The information on nicotine exposure was extracted from the baseline questionnaire (www.fhi.no/moba) and included exposure to passive smoking at work or at home, mothers smoking habits ever, before pregnancy and during second trimester, as well as information regarding use of smokeless nicotine products. Notably, most women returned the baseline questionnaire around the timing of blood sampling. Women who did not return the questionnaire were sent a reminder 3–4 weeks after the ultrasound examination. Hence, the mean gestational age at self-reported smoking was 19.0 weeks (standard deviation (SD), 4.0), whereas the mean gestational age at blood collection for plasma cotinine measurement was 18.2 weeks (SD, 2.1). Accordingly, 15% of the women had a difference in gestational age between self-reporting and blood sampling of more than 4 weeks.

Covariates

Data on maternal age at delivery (< 25, 25–34, ≥ 35 years), marital status (married, cohabitation, single, other/missing) and parity (0, 1, 2, ≥ 3 previous deliveries) were obtained from the Medical Birth Registry of Norway, while data on smoking habits, prepregnancy body mass index (< 18.5, 18.5–24.9, 25.0–29.9 and ≥ 30 kg/m^2), and maternal education were obtained from the MoBa baseline questionnaire. Education was measured as highest level of completed education, and categorized as ≤ 12, 13–16 or ≥ 17 years.

Statistical analyses

Statistical analyses were carried out with SPSS (Statistical Package for the Social Sciences) version 15 and SAS (Statistical Analysis System) version 9.2 (SAS Institute, Inc., Cary, North Carolina). R version 2.8.1. (The R Foundation for Statistical Computing, www.r-project.org) software was used for graphical illustrations.

Plasma cotinine concentrations were log-transformed to achieve less skewed distribution of data, and were reported as geometric means, i.e., antilog of means of the logarithmic values.[19] Spearman's correlation coefficient with 95% CI was used to estimate the association between plasma cotinine and numbers of cigarettes smoked.

Active smokers were separated from passive and non-smokers by estimating the lowest point between two distinct distributions of log plasma cotinine. This was performed using non-parametric bootstrap method (the SURVEYSELECT procedure in SAS). Briefly, we re-sampled randomly 10,000 times from the total population, creating 10,000 alternative data sets. For each set, we located the lowest log plasma cotinine point between two peaks using kernel density estimation. Finally, from the 10,000 point estimates, we estimated the geometric mean, which was used as plasma cotinine cut-off between active smokers and passive/non-smokers. The corresponding 95% confidence interval (CI) was constructed by extracting the 2.5 percentile and 97.5 percentile of the 10,000 estimates. Based on the bootstrap procedure above, we simultaneously estimated the overall sensitivity and specificity for self-reported daily smoking. The uncertainty was addressed by extracting the 2.5^{th}, 25^{th}, 50^{th} 75^{th} and $97,5^{th}$ percentiles.

Using the cotinine cut-off found by the bootstrap method, we also estimated sensitivity and specificity of self-reported daily smoking according to background variables. The estimated plasma cotinine cut-off was considered the "gold standard" and self-report was considered the "test" in sensitivity and specificity calculations. Sensitivity is the percentage of women with plasma cotinine concentrations above cut-off that are correctly identified as daily smokers by self-report. Specificity is the percentage of women with plasma cotinine concentrations below cut-off that are correctly identified as non-smokers by self-report. The 95% CIs of sensitivity and specificity for self-reported daily smoking according to background variables were calculated by the Wilson procedure without a correction for continuity.[20]

RESULTS

Population characteristics

Of the 2,997 women, the mean maternal age at delivery was 29.8 years (SD, 4.6; range, 15–43), 44% of the participants were pregnant for the first time and 96% of the women were married or cohabitants (Table 1). 63% of the women had prepregnancy body mass index between 18.5 and 24.9 kg/m^2 and 42% of the mothers had education of 12 years or less.

Self-reported nicotine exposure

Of the 2,997 women, 263 (8.8%) reported daily smoking whereas 126 (4.2%) reported occasional smoking during pregnancy (Table 1). 1491 (50%) women reported ever smoking and 698 (23%) women reported daily smoking during the last 3 months before becoming pregnant. Daily smoking during pregnancy was more common among the youngest women, among women with higher parity, and among single women. Also women with low prepregnancy body mass index and low education smoked more than others. Similar profiles were observed for occasional smokers. Furthermore, passive smoking was reported by 472 women (16%). Of all women, 216 women (7.2%) reported passive smoking at work and 194 (6.5%) reported passive smoking at home, while 62 women (2.1%) reported passive smoking both at home and work. Of the 472 women reporting passive smoking, 111 reported being daily smokers, 38 reported occasional smoking, 321 reported being non-smokers and 2 had missing smoking status, i.e.3.7%, 1.6%, 11% and 0.1% of the total population, Overall, 27 women used smokeless nicotine products during pregnancy. Of these, 15 used chewing tobacco or snuff, 9 used nicotine chewing gum, 1 used nicotine adhesive patch and 2 used nicotine inhaler.

Cotinine concentrations and self-reported smoking status

Plasma cotinine concentration significantly increased with increasing cigarette consumption for both daily smokers and occasional smokers (Table 2). Overall, plasma cotinine was correlated (Spearman) with both number of cigarettes per day (r = 0.51; 95% CI: 0.42 – 0.60) and number of cigarettes per week (r = 0.48: 95% CI: 0.32 – 0.61).

Among women reporting both non-smoking and passive smoking, cotinine concentrations were low (geometric mean 1.9 nmol/l). Women using smokeless nicotine products had plasma cotinine concentrations around 100 nmol/l.

Cotinine cut-off and self-reported smoking

Plasma cotinine concentrations > 0 nmol/l were found for a total of 963 (32%) mothers. A density plot of these cotinine concentrations showed two distinct distributions (Figure 1A). Using kernel density estimation and bootstrap method, we estimated that the lowest point between the two distributions of log plasma cotinine concentrations corresponded to a geometric mean of 29.8 nmol/l, (95% CI: 20.0, 56.0) (Figure 1A and B and Table 3). In order to validate reported daily smoking, we excluded from the analyses occasional smokers and users of smokeless nicotine products (n=148) as well as women with missing smoking habits (n=22). The corresponding overall mean sensitivity and specificity for self-reported daily smoking was estimated to be 81.9% (95% CI: 77.3, 86.4) and 99.4% (95% CI 99.1, 99.7), respectively. The uncertainty in terms of percentile values appeared larger in estimates of sensitivity than specificity (Figure 1C and D and Table 3).

The plasma cotinine cut-off, 30 nmol/l, was further used to validate self-reported daily smoking according to background variables, such as maternal age, parity, marital status, prepregnancy body mass index and maternal education (Table 4). A total of 296 women had cotinine concentrations ≥ 30 nmol/l. Of these, 242 (82%) women reported daily smoking, and 54 (18%) reported non-smoking. Among the 54 women reporting non-smoking having

measured plasma cotinine ≥ 30 nmol/l, 45 reported ever smoking, 30 reported daily smoking during the last 3 months before pregnancy and 13 reported passive smoking. Adding the number of self-reported non-smokers having cotinine concentrations above cut-off to the self-reported daily smokers resulted in an increase in daily smoking prevalence from 8.8% (263/2997) to 11% (317/2997).

Cotinine and other nicotine exposures

Among the 121 occasional smokers (excluding women using smokeless nicotine products), 80 (66%) had cotinine concentrations ≥ 30 nmol/l. The sensitivity for combined self-reported occasional and daily smoking was 86% (95% CI: 82, 89) and the specificity 98% (95% CI: 97, 98).

Among the 27 women who used smokeless nicotine products during pregnancy, 16 reported non-smoking, 5 reported occasional smoking and 6 reported daily smoking. 21 (78%) had cotinine concentrations ≥ 30 nmol/l.

Self-reported smoking habits during pregnancy were unknown for only 22 (0.7%) women; cotinine concentrations were < 1 (n = 13), < 5 (n = 6), 76.1 (n = 1), 475 (n = 1) and 597 (n = 1) nmol/l.

DISCUSSION

Principal findings

This prospective study validated self-reported smoking status against plasma cotinine concentration among 2,997 pregnant women in MoBa. Our study suggested a plasma cotinine concentration of 30 nmol/l (5.3 ng/ml) as the best cut-off for separating active smokers from passive and non-smokers. By using this cut-off further in the calculation of sensitivity and specificity, we found that self-reported smoking status had a sensitivity of 82% and a specificity of 99%.

Strengths and weaknesses

The study population comprised a subsample of 2,997 pregnancies in MoBa, allowing for precise estimates overall as well as in subgroups. Furthermore, we had detailed self-reported data on daily and occasional smoking and for passive smoking. Data on self-reported smoking was missing for only 0.7%. We also had the opportunity to examine smokeless nicotine exposure, such as snuff, nicotine chewing gum, nicotine adhesive patch and nicotine inhaler.

One limitation of this study is the time difference for some women between returning the baseline questionnaire and the blood sampling. About 85% of the women returned the questionnaires within 4 weeks from the blood sampling, while the remaining 15% had a longer period between donating blood sample and completing the questionnaire. Since smoking behaviour may change around the time of the ultrasound screening, such difference could lead to misclassification of smokers and non-smokers. Furthermore, women with a large time span between smoking and blood sampling could appear as non-smokers based on

cotinine analysis. Such misclassification would be more common among occasional smokers with a variable time span since the last cigarette.

The participants were informed that the blood samples from themselves and their children would be used for research purposes, but not that blood samples would reveal nicotine exposure. Neither were the attending nurses aware of the purpose of the blood samples. It is therefore unlikely that knowledge of specific blood test(s) could have caused changes in smoking behaviour prior to blood sampling, or have affected self-reported smoking status.

Cotinine cut-off levels in pregnant women

In the present population, we observed a bimodal distribution of log plasma cotinine concentrations (Figure 1A), suggesting a separation of active smokers from passive and non-smokers.[21, 22] By identifying the lowest point between the two distributions, we suggest cut-off of 30 nmol/l (5.3 ng/ml) (95% CI: 20, 56) for plasma cotinine.

Earlier studies of non-pregnant subjects have indicated serum cotinine of 80–85 nmol/l as a cut-off for identifying active smokers.[22–24] Other studies on pregnant women have used cut-off between 57 and 99 nmol/l (10–18 ng/ml).[4, 5, 25–29] However, a study based on a representative sample of the US population recommend 17 nmol/l (3 ng/ml) as the overall cut-off.[18] All these results are outside our estimated confidence limits. Thus, a general cotinine cut-off in pregnant smokers has yet to be established.

Selection bias

A recent study compared women participating in MoBa to all women giving birth in Norway, using data from the Medical Birth Registry of Norway in the period 2000–2006.[13] The cigarette consumption at the end of pregnancy was significantly lower in MoBa than in the total population (6.9 versus 7.4 cigarettes). There were also fewer women with unknown smoking habits in MoBa than in the total population. Because MoBa is a selected sample, smokers in MoBa may also have a lower nicotine intake than in the general population. This may further have resulted in a lower plasma cotinine cut-off than that seen in other pregnancy-related studies.

Validation and under-reporting of smoking status

Precise and valid monitoring of smoking status in pregnancy has significant public health implication, and is essential in epidemiological research. A recent study showed higher nondisclosure rates of tobacco smoking among pregnant women compared to non-pregnant women.[30] The stigma associated with smoking during pregnancy might reduce the overall reliance of self reported smoking in health studies. In our study the lowest sensitivity for self-reported smoking habits were found among women with the highest education.

There is uncertainty about the added value of cotinine measurement to assess smoking status.[25] We found about 94% of daily smokers who did not use smokeless nicotine products had cotinine concentrations ≥ 30 nmol/l. About 98% of non-smokers who did not use smokeless nicotine products had cotinine concentrations below cut-off. A study measuring cotinine in cord serum found cotinine concentrations above cut-off (80 nmol/l (14 ng/ml))

among 88% of women reporting daily smoking and cotinine concentrations below cut-off among 96% of women reporting non-smoking.[29] However, studies have found that 23–26% of pregnant smokers did not report that they smoked when comparing self-report with cotinine concentrations.[4, 6, 30]

A study showed an overestimation of the odds ratio for small for gestational age as well as the smoking related reduction in birth weight, when comparing results before and after reclassification of smokers based on cotinine measurement around gestational week 28. However, it did not alter the directions of the associations.[6] Other studies of pregnant women comparing self-reported smoking status with cotinine values have found self-report to be a poor indicator of smoking status with sensitivity of 47.4% and 89.5% and specificity of 94.9% and 65.3%.[31, 32]

Occasional smokers

A Norwegian study measuring umbilical cord serum cotinine at delivery as fetal exposure to tobacco products, indicated a considerable interindividual variation in fetal nicotine exposure among newborns of occasional smoking mothers, with 46% having cotinine values above the chosen cut-off.[29] In our study 66% of the occasional smokers had cotinine concentrations above cut-off. This might be explained by variable time span since the last cigarette in occasional smokers.

Conclusion

In conclusion, we showed self-reported smoking status in pregnancy in a sub-study of a large cohort study to have a sensitivity of 82% and a specificity of 99% at plasma cotinine cut-off 30 nmol/l. Our results indicate that self-reported smoking is a valid marker for tobacco exposure in the MoBa cohort.

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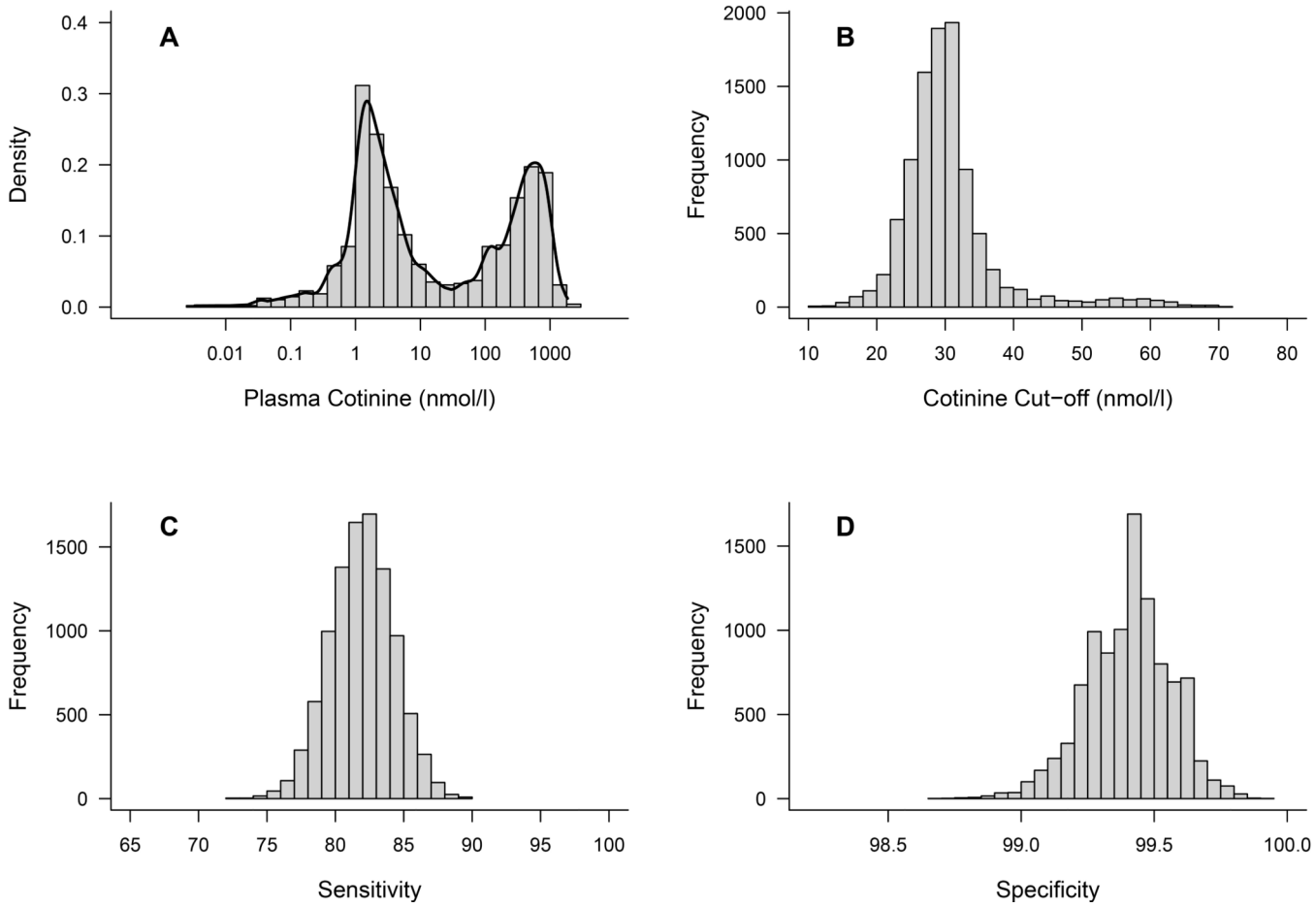

Figure 1.

Distributions of log plasma cotinine, plasma cotinine cut-offs, and sensitivity and specificity for self-reported daily smokers based on 10,000 resamples from The Norwegian Mother and Child Cohort Study, 2002–2003. (A) A density plot of log plasma cotinine concentrations obtained by using kernel density estimation. (B) The distribution of the cut-offs from the 10,000 resamplings. (C, D) The distributions of the sensitivities and specificities estimated for each cut-off from the 10,000 resamplings.

Table 1

Maternal Tobacco Exposure During Pregnancy According to Maternal Characteristics Among 2,997 Women in The Norwegian Mother and Child Cohort Study, 2002–2003[a]

Characteristics	Total	Non-smoking (*n* = 2,586)	Occasional smoking (*n* = 126)	Daily smoking (*n* = 263)	Missing (*n* = 22)	Passive smoking (*n* = 472)	Smokeless nicotine products (*n* = 27)
	N (%)	*%*	*%*	*%*	*%*	*%*	*%*
All women	2,997 (100)	86	4.2	8.8	0.7	16	0.9
Maternal age (year)							
< 25	379 (13)	76	8.7	14	0.8	33	-
25–34	2,152 (72)	89	3.4	7.3	0.7	14	1.1
≥ 35	456 (15)	84	4.2	11	1.1	12	0.9
Parity							
0	1,303 (44)	87	4.5	8.0	0.6	20	1.2
1	1,116 (37)	87	3.8	8.6	0.7	12	0.6
2	435 (15)	84	5.1	10	1.1	12	0.9
≥3	133 (4)	84	2.3	13	0.8	16	0.8
Marital status							
Single	80 (3)	61	13	24	2.5	43	2.5
Cohabitation	1,342 (45)	83	5.1	12	0.6	20	1.3
Married	1,539 (51)	91	2.9	5.3	0.8	11	0.5
Prepregnancy body mass index (kg/m^2)							
< 18.5	81 (3)	75	8.6	16	-	17	2.5
18.5–24.9	1,876 (63)	88	3.9	7.9	0.6	14	0.8
25–29.9	609 (20)	87	4.6	8.0	0.7	17	0.8
≥ 30.0	315 (11)	85	3.5	11	0.6	21	0.6
Maternal education (year)							
≤ 12	1,254 (42)	77	6.1	16	1.0	26	0.9
13–16	1,166 (39)	92	3.3	3.9	0.6	9.4	1.1
≥ 17	500 (17)	95	1.8	3.2	0.2	4.8	0.6

[a]Information on passive smoking, maternal age, parity, marital status, prepregnancy body mass index and maternal education was missing for 20, 10, 10, 36, 116 and 77 women, respectively

Table 2

Plasma Cotinine Concentrations According to Tobacco Exposures During Pregnancy Among 2,997 Women in The Norwegian Mother and Child Cohort Study, 2002–2003

Tobacco exposure	Total number of subjects	Plasma cotinine (nmol/l)	
		Geometric mean[a]	95% confidence interval
Daily smokers, cigarettes per day			
All[b]	263	346	295–406
1–4	69	135	92.1–199
5–9	103	430	344–538
10–14	64	520	413–656
≥15	22	645	505–824
Occasional smokers, cigarettes per week			
All[c]	126	49.7	32.7–75.8
1–4	44	16.7	8.2–33.8
5–9	27	78.4	40.5–152
10–14	24	99.2	39.8–247
≥15	19	244	116–511
Passive smokers			
All	472	8.3	6.5–10.5
At work	216	3.1	2.4–4.1
At home	194	18.1	12.1–26.9
Both at home and at work	62	23.3	11.3–48.2
Daily smoking only	152	329	263–410
Both daily and passive smoking	111	371	294–468
Occasional smoking only	88	52.6	31.3–88.3
Both occasional and passive smoking	38	43.7	20.7–92.3
Passive smoking only	321	1.8	1.6–2.1
Smokeless nicotine products	27	96.9	35.8–262

[a] Geometric mean; i.e. antilog of mean of logarithmic values.

[b] Includes 5 women who reported daily smoking but provided no information on the number of cigarettes smoked per day.

[c] Includes 12 women who reported occasional smoking but provided no information on cigarette dose.

Table 3

Summary Statistics of Cut-off Between Active Smokers and Non-smokers /Passive Smokers Among 2,997 Women in The Norwegian Mother and Child Cohort Study, 2002–2003[a]

		Percentile				
	Mean	**2.5th**	**25th**	**50th**	**75th**	**97.5th**
Cut-off (cotinine units: nmol/l)[b]	29.8	20.0	26.5	29.6	32.2	56.0
Sensitivity (%)[c]	81.9	77.3	80.4	82.0	83.5	86.4
Specificity (%)[c]	99.4	99.1	99.3	99.4	99.6	99.7

[a] Estimates found by 10,000 re-samplings of the observed data (non-parametric bootstrap method).

[b] Antilog of logarithmic values.

[c] Sensitivity and specificity for self-reported daily smoking: information on smoking habits during pregnancy was missing for 22 women and excluded for 27 women using other kinds of nicotine products.

Table 4

Sensitivity and Specificity For Self-reported Daily Smoking According To the Geometric Mean Plasma Cotinine Cut-off at 30 nmol/l Among 2,997 Women in The Norwegian Mother and Child Cohort Study, 2002–2003[a]

	Non-smokers		Daily smokers					
Characteristics	**< 30 nmol/l**	**≥ 30 nmol/l**	**< 30 nmol/l**	**≥ 30 nmol/l**	**Sensitivity**		**Specificity**	
	N	*N (%)*	*N*	*N (%)*	*%*	*95% CI*[b]	*%*	*95% CI*[b]
All women	2,516	54 (2.1)	15	242 (94)	82	77–86	99.4	99.0–99.6
Maternal age (year)								
< 25	283	6 (2.1)	5	49 (91)	89	78–95	98	96–99
25–34	1,856	37 (2.0)	9	144 (94)	80	73–85	99.5	99.1–99.7
≥ 35	369	11 (2.9)	1	47 (98)	81	69–89	99.7	98.5–100
Parity								
0	1,100	22 (2.0)	9	93 (91)	81	73–87	99.2	98.5–99.6
1	940	25 (2.6)	5	90 (95)	78	70–85	99.5	98.8–99.8
2	362	2 (0.5)	1	40 (98)	95	84–98.7	99.7	98.5–100
≥ 3	106	5 (4.5)	0	17 (100)	77	57–90	100	97–100
Marital status								
Single	47	2 (4.1)	2	15 (88)	88	66–97	96	86–99
Cohabitation	1,064	33 (3.0)	12	144 (92)	81	75–86	98.9	98.1–99.4
Married	1,378	19 (1.4)	1	77 (99)	80	71–87	99.9	99.6–100
Prepregnancy body mass index (kg/m^2)								
< 18.5	57	2 (3.4)	0	13 (100)	87	62–96	100	94–100
18.5–24.9	1,600	33 (2.0)	9	137 (94)	81	74–86	99.4	98.9–99.7
25–29.9	514	11 (2.1)	4	43 (92)	80	67–88	99.2	98.0–99.7
≥ 30.0	263	5 (1.9)	0	33 (100)	87	73–94	100	98.6–100
Maternal education (year)								
≤ 12	932	31 (3.2)	11	181 (94)	85	80–90	98.8	98–99
13–16	1,050	17 (1.6)	2	43 (96)	72	59–82	99.8	99.3–99.9
≥ 17	466	6 (1.3)	2	13 (87)	68	46–85	99.6	98.5–99.9

Abbreviations: CI, confidence interval

[a] Information on smoking habits during pregnancy was missing for 22 women and excluded for 27 women using other kinds of nicotine products.

[b] CIs of sensitivity and specificity were calculated by the Wilson procedure without a correction for continuity