

Oral contraception, body mass index, and asthma: A cross-sectional Nordic-Baltic population survey

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Background: Emerging evidence suggests that sex steroid hormones may influence airways obstruction, and that metabolic status may modify potential effects.

Objective: This study investigated the association between use of oral contraceptive pills (OCPs) and asthma in a Nordic-Baltic population-based study, while taking into account possible interplay with body mass index (BMI).

Methods: Postal questionnaires were sent to subjects in Denmark, Estonia, Iceland, Norway, and Sweden from 1999 to 2001 (response rate in women, 77%). Pregnant women, women using hormone replacement therapy, and women >45 years were excluded. Analyses included 5791 women 25 to 44 years old, of whom 961 (17%) used OCP. Logistic regression analyses included adjustment for smoking, irregular menstruation, BMI, age, type of dwelling, and center.

Results: Oral contraceptive pills were associated with increased risk for asthma (odds ratio, 1.42; 95% CI, 1.09-1.86), asthma with hay fever (1.48; 1.08-2.03), wheeze with shortness of breath (1.27; 1.02-1.60), hay fever (1.25; 1.06-1.48), and ≥ 3 asthma symptoms (1.29; 1.05-1.58). The findings were consistent between centers. The associations were present only among normal weight women (BMI 20-25 kg/m², asthma: 1.45; 1.02-2.05) and overweight women (BMI >25 kg/m²: 1.91; 1.20-3.02), but not among lean women (BMI <20 kg/m²: 0.41; 0.12-1.40).

Interaction between BMI and OCP in association with asthma was significant ($P_{\text{interaction}} < .05$).

Conclusions: Women using oral contraceptive pills had more asthma. This was found only in normal weight and overweight women, indicating interplay between sex hormones and metabolic status in effect on the airways. The findings originate from a cross-sectional postal survey and should be interpreted with caution; it is recommended that asthma symptoms are included in clinical trials of oral contraception. (J Allergy Clin Immunol ■■■■;■■■:■■■-■■■.)

Key words: Asthma, oral contraceptives, body mass index, RHINE, ECRHS

Gestagens and estrogens combined in oral contraceptive pills (OCPs) have been in extensive use worldwide for the last 50 years. There has been great publicity around side effects of oral contraception, but there is hardly any knowledge about potential influences on respiratory health, an aspect that has not been included in clinical trials. The existing literature about OCP and respiratory disease is scarce and conflicting. No significant increase in asthma risk among women using OCP was found in the Copenhagen City Heart Study.¹ Hormonal contraceptives showed no influence on asthma severity in women with relatively mild asthma.² Salam et al³ showed that OCP was associated with more wheeze among subjects without asthma, and less wheeze among subjects with asthma. A modestly elevated asthma risk in past OCP users was observed in the Nurses Health Study.⁴ In the Tasmanian Asthma Survey, a 7% decrease in adult-onset asthma was indicated per year of OCP use.⁵

Increasing evidence suggests that sex steroid hormones play an important role in respiratory health. There are substantial sex differences in airway behavior and expression of airway diseases.⁶ In women, asthma and lung function vary according to hormonal status. In younger women early age of menarche was associated with more adult asthma,⁷ and women with irregular menstruation had lower lung function and more asthma⁸; among women in the menopausal transition, those with established menopause had lower lung function and more asthma.⁹ Respiratory health effects of exogenous sex hormones are controversial, but asthma appears to be more common among women taking hormone replacement therapy (HRT).^{1,10,11}

The association of asthma with body mass index (BMI) is well known.¹²⁻¹⁴ Shaheen et al¹³ and Camargo et al¹⁴ were among the first to emphasize the increase in asthma with increasing BMI among adults. Gunnbjörnsdóttir et al¹² showed increased asthma risk related to high BMI in the Respiratory Health in Northern Europe (RHINE) study. Castro-Rodriguez et al¹⁵ showed that

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Disclosure of potential conflict of interest: K. Franklin receives grant support from the Swedish Heart and Lung Foundation. L. Bjorge is a member of the Norwegian Cancer Society, the Amatheia Foundation in Hordaland, and the Norwegian Society for Obstetrics and Gynecology. The rest of the authors have declared that they have no conflict of interest.

Received for publication May 23, 2008; revised October 21, 2008; accepted for publication October 27, 2008.

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0091-6749/\$36.00

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doi:10.1016/j.jaci.2008.10.041

Abbreviations used

BMI: Body mass index
 ECRHS: European Community Respiratory Health Survey
 HRT: Hormone replacement therapy
 OCP: Oral contraceptive pill
 OR: Odds ratio
 RHINE: Respiratory Health in Northern Europe

overweight girls but not boys had an increased risk for developing asthma independent of physical activity.

Because sex hormones and body fat mass are closely interrelated, interplay between sex hormones and BMI in effects on asthma seems plausible. Interplay between HRT and BMI has been demonstrated by Gomez Real et al¹¹: HRT was associated with increased risk for asthma only among lean women. A similar interaction was demonstrated for associations of HRT and BMI with breast cancer.¹⁶ Interplay between menopause and BMI in effects on asthma and lung function was observed in the European Community Respiratory Health Survey (ECRHS).^{8,16} OCPs are known to exacerbate insulin resistance¹⁷; thus, an interaction of OCP with the underlying metabolic situation seems biologically plausible but has not been investigated.

In this study, we wanted to examine possible associations of OCP with asthma and allergy among women in fertile age in general population samples from Northern European countries with different prescription practices. In particular, we wanted to address possible interplay between OCP and BMI in associations with asthma.

METHODS**Design and subjects**

RHINE (www.rhine.nu) is a follow-up study of subjects from 7 Northern European centers who participated in ECRHS I stage I (www.ecrhs.org), a study that took place from 1990 to 1994. In ECRHS I stage I, men and women age 20 to 44 years were randomly selected from population registers within specific boundaries of each participating center. A postal questionnaire was sent to 3000 to 4300 subjects in each center. The population included in RHINE was responders from Reykjavik in Iceland; Bergen in Norway; Umeå, Uppsala, and Gothenburg in Sweden; Aarhus in Denmark; and Tartu in Estonia (n = 21,802; response rate, 83.7%). The eligible subjects (excluding 264 deaths) were sent a postal questionnaire from 1999 to 2001. In total 16,191 subjects answered the questionnaire, including 8588 women (response rate, 77%) born between 1945 and 1973. Written consent was obtained from all participants, and the local ethics committees approved the study.

This article presents a cross-sectional analysis of 5791 women age 25 to 45 years, excluding pregnant (n = 254) and menopausal women (n = 121, including 102 women using HRT).

Questionnaire

The first part of the questionnaire contained 12 questions repeated from ECRHS I stage I, covering respiratory symptoms, asthma medication, and hay fever. *Asthma* was defined as currently using asthma medication and/or having had asthma attacks during the last 12 months; *allergic asthma* was defined as having asthma and current hay fever. *Doctor's diagnosed asthma* was defined by the question, "Have you ever had asthma diagnosed by a doctor?" Three or more asthma symptoms were defined based on the following 8 symptoms: wheeze, wheeze with shortness of breath, wheeze without cold, waking with tightness in chest, waking with shortness of breath, waking with cough, asthma attacks, and current asthma medication.¹⁸ The second part of the

questionnaire covered various aspects including 7 questions related to hormonal status in women. Oral contraception was defined as answering yes to the question "Are you using the pill?" The women were also asked about current pregnancy, menopause, and current use of HRT.

Body mass index was based on self-reported weight and height, and calculated as weight in kilos per square of height in meters. Smoking history was assessed by 2 questions, "Are you a smoker?" and "Are you an ex-smoker?" defining never smokers, exsmokers, and current smokers. Type of dwelling (detached, semidetached, apartment, other) was used as a marker of social class. A socioeconomic index based on occupation was not considered optimal in women because housewives may belong to different social classes; however, because this measure of social class is commonly used, additional analyses with adjustment for socioeconomic index were performed and gave similar results as analyses adjusted for type of dwelling.

Statistical analysis

Logistic regression models were used to assess the effects of OCP on asthma and hay fever. Numbers at risk fluctuated slightly from outcome to outcome because of a varying number of missing for each variable. Adjustments were made for age (5-year categories), BMI (per unit, kg/m²), smoking habits (never smoker, exsmoker, and current smoker), study center, and type of dwelling. Analyses of OCP were stratified according to BMI categorized according to World Health Organization classification: lean, BMI <20 kg/m²; normal weight, BMI 20-25 kg/m²; and overweight, BMI >25 kg/m². The differences in associations of OCP with asthma between lean and normal/overweight women were analyzed by including interaction terms of BMI and OCP in the logistic regression models. Similarly, logistic regression models were used to assess effects of BMI as a continuous variable on asthma, and analyses were stratified by OCP use. Potential heterogeneity between centers was studied by meta-analyses according to derSimonian and Laird.¹⁹ Graphic descriptions using Generalized Additive Models²⁰ with binomial distribution and logistic link were made to visualize the prevalence of asthma and ≥3 asthma symptoms according to BMI and use of OCP. The analyses were performed by using the statistical software program Stata 10 (Stata Corp, College Station, Tex).

Ethical approval

The study was approved by local ethics committees in all the study centers.

RESULTS

Of 5791 women, 961 (17%) were using oral contraception. OCP was more widely used in Reykjavik (26%) and less used in Bergen and Tartu (11%; [Table I](#)).

General characteristics varied somewhat according to use of oral contraception. Women taking oral contraceptives were slightly younger, smoked slightly less, and reported less hypertension. They more often lived in apartments, possibly because of their younger age. Irregular menstruation was more often reported among women not taking oral contraception ([Table II](#)).

Women using oral contraception more often reported asthma, allergic asthma, asthma symptoms, and hay fever ([Table III](#)). OCP was significantly associated with asthma, allergic asthma, wheeze with shortness of breath, ≥3 asthma symptoms, and hay fever when adjusting for irregular menstruation, smoking habits, age, BMI, type of dwelling, and center ([Table III](#)). We have also shown how adjustment for hypertension altered the results. Analyses stratified by smoking habits showed very similar estimates for never smokers (odds ratio [OR]_{asthma}, 1.48; 95% CI, 1.02-2.16; OR_{asthma symptoms}, 1.37; 1.01-1.86) and for current smokers (OR_{asthma}, 1.53; 95% CI, 0.92-2.56; OR_{asthma symptoms}, 1.22; 0.86-1.72).

TABLE I. Characteristics of 5791 women age 25 to 45 years participating in the RHINE study

Center**	Study population (n)	Median age (y)	Median BMI (kg/m ²)	Current smokers (%)	OCP* n (%)	Asthma† (%)	≥3 Symptoms‡ (%)
Aarhus	923	37	22	33	165 (18)	5.6	14
Reykjavik	634	37	23	29	161 (26)	8.2	13
Bergen	887	37	23	37	101 (11)	7.4	16
Göteborg	781	36	23	29	141 (19)	6.6	14
Umeå	879	37	23	19	123 (14)	11	17
Uppsala	882	37	23	19	180 (21)	9.2	15
Tartu	805	33	22	28	90 (11)	1.6	14
Total	5791	36	23	28	961 (17)	7.1	15

*OCP as defined as answering yes to the question, "Are you on the pill?"

†Current asthma medication and/or asthma attacks last 12 months.

‡Symptoms included wheeze, wheeze with shortness of breath, wheeze without cold, waking with tightness in chest, waking with shortness of breath, waking with cough, asthma attacks, and current asthma medication.

**A *P* value for difference among centers was analyzed: for contraception *P* < .00, for asthma *P* < 0.00, and for 3 or more symptoms *P* < .229.

The association of OCP with asthma showed no significant heterogeneity between centers ($P_{\text{heterogeneity}} = .5$; Fig 1, A), nor did the association of OCP with 3 or more asthma symptoms ($P_{\text{heterogeneity}} = .23$; Fig 1, B).

When analyses were stratified according to BMI (Table IV), OCP was not significantly associated with asthma or asthma symptoms among lean women. Among normal weight women, those using oral contraception had significantly higher risk for asthma and asthma symptoms. In overweight women, OCP was associated with significantly higher asthma risk and with an indicated, but nonsignificant, increase in asthma symptoms (Table IV). The interactions of BMI with OCP were significant ($P < .05$) with regard to associations with asthma and borderline significant ($P = .091$) with regard to asthma symptoms (Table IV). The prevalence of asthma increased with increasing BMI in women using or not using OCP (Fig 2, A), but the increase in asthma with increasing BMI was stronger ($P_{\text{interaction}} = .064$) in OCP users (OR, 1.07; 95% CI, 1.03-1.12; $P < .001$) than in women not using OCP (OR, 1.03; 95% CI, 1.003-1.05; $P = .030$) after adjusting for irregular menstruation, smoking habits, age, BMI, type of dwelling, and center. Similar trends were observed for the prevalence of asthma symptoms according to BMI and use of oral contraception (Fig 2, B).

DISCUSSION

In this cross-sectional postal survey of Northern European populations, women using oral contraception had increased risk for asthma, allergic asthma, asthma symptoms, and hay fever. These associations did not differ between centers with different prevalence of oral contraception and different prescription practices. Associations were similar for allergic and nonallergic asthma, but were stronger for symptoms more specific for asthma compared with those less specific, like wheeze. Adjusted analyses showed slightly larger differences than unadjusted analyses, reflecting negative confounding by smoking—women using OCP less often smoked than women not taking the pill. The population attributable risk of oral contraceptives for asthma was calculated to be 5.3% (95% CI, 0.6-9.7). Unadjusted analyses suggested that 2% to 3% of women using OCP might have asthma as a side effect to this medication. Although oral contraceptive use implies a possible risk of modest importance on a population level, the magnitude is substantial when considering that this may

TABLE II. Characteristics of women taking oral contraceptives

	No OCP (n = 4728)	OCP (n = 961)	<i>P</i> value
Age, median (y)	37	34	>.001
BMI, median (kg/m ²)	22.9	22.5	.07
Smoking status			.018
Current smokers (%)	28	25	
Exsmokers (%)	24	23	
Never smokers (%)	46	50	
Dwelling			>.001
Detached house	41	35	
Semidetached house	14	15	
Apartment	42	48	
Other	2	2	
Irregular menstruation (%)	15	9.2	>.001
Hypertension (%)	4.3	2.9	.049
Heart disease (%)	2.1	1.7	.34
Diabetes mellitus (%)	1.3	1.0	.60

possibly reveal an unrecognized side effect to a commonly used drug. The current study does not have a study design that allows causal inference, but these findings strongly suggest that clinical trials of oral contraception should investigate asthma as a potential side effect.

The literature on oral contraception and airway disease is limited and inconsistent, and the studies are not easily comparable because of differences in design and analyses. The modestly increased risk for asthma associated with OCP in our study is supported by an analysis of the Nurses Health Study⁴ reporting modestly increased asthma risk in past OCP users, by the report of Salam et al³ showing more wheeze in women without asthma when using OCP, and by case reports describing exacerbation of premenstrual asthma caused by oral contraceptives.²¹ Our findings are conflicting with an apparent protective role of OCP for asthma, as suggested by an analysis of the Tasmanian Asthma Survey.²² These findings were borderline significant, women of this cohort were younger than our study population, and BMI was not considered. Our study cannot disentangle the conflicting findings in the scarce literature but suggests that BMI should be accounted for in future studies. However, when also considering other literature showing that sex hormones play a role in airways physiology, our results warrants proper investigation by including asthma in future clinical trials of oral contraception. Our study

TABLE III. Asthma and hay fever according to use of OCP among 5791 women

	No OCP (%) (n = 4728)	OCP (%) (n = 961)	Crude OR (95% CI)	Adjusted OR (95% CI)*	P value (adjusted)
Asthma†	6.8	9.0	1.36 (1.06-1.75)	1.45 (1.11-1.90)	.01
Allergic asthma‡	4.4	6.2	1.46 (1.09-1.97)	1.55 (1.12-2.12)	.01
Nonallergic asthma	2.6	3.9	1.52 (1.04-2.23)	1.74 (1.17-2.60)	.01
Wheeze	21	20	0.96 (0.81-1.15)	1.10 (0.91-1.32)	.32
Wheeze with shortness of breath	11	13	1.15 (0.93-1.43)	1.28 (1.02-1.61)	.035
Wheeze when not having a cold	12	13	1.07 (0.87-1.33)	1.22 (0.97-1.53)	.01
Three or more symptoms§	15	17	1.13 (0.94-1.37)	1.30 (1.06-1.60)	.01
Hay fever	24	29	1.30 (1.11-1.51)	1.25 (1.06-1.48)	.01

*From logistic regression models with adjustment for irregular menstruation, smoking habits, BMI, age, center, hypertension, and type of dwelling.

†Asthma medication and/or asthma attacks in the last 12 months.

‡Asthma and hay fever.

§Symptoms included wheeze, wheeze with shortness of breath, wheeze without cold, waking with tightness in chest, waking with shortness of breath, waking with cough, asthma attacks, and current asthma medication.

||Hay fever or nasal allergies.

showed interplay between OCP and BMI in associations with asthma; oral contraceptives were associated with increased risk for asthma only among normal weight and overweight women. Further, although asthma increased with increasing BMI in all women, this increase was stronger among women taking the pill.

Interplay between oral contraceptives and BMI in effects on asthma, as observed in this study, is a novel finding. However, interplay between other measures of hormonal status in women and BMI have been described previously in studies of obstructive airway disease^{9-11,23} and in studies of breast cancer,¹⁶ and such interplay is considered biologically plausible.²⁴ The particular pattern of interaction between BMI and OCP in associations with asthma was different from the pattern observed for HRT; this is not unexpected because HRT and OCP are different medications used for different purposes in different groups of women.

Strengths of the current study include the large number of participants, the population-based design and the multicentric structure of the study. When investigating hormonal factors in women, a large study population is needed to obtain sufficient numbers in the exposure group and a suitable reference group. The women were randomly selected from the population, and the findings may be applicable to a general population rather than to selected groups usually enrolled in pharmaceutical trials. Because findings were not heterogeneous across centers, this supports an interpretation in terms of biological mechanisms rather than confounding by sociocultural factors that are likely to differ between centers.

The major limitations of this study are the use of a cross-sectional postal survey with self-reported asthma, OCP, and BMI. The cross-sectional design is an important limitation in the interpretation of the time sequence of exposure and outcome. Although it seems unlikely that asthma could be a determinant for OCP use, common underlying physiological features might possibly in a few cases lead to both asthma and OCP use. However, OCP influencing the airways is the most likely explanation for the association of OCP with asthma. Women-specific factors appear to be reported with reasonable certainty, as demonstrated for age of menarche²⁵ and menstrual status.²⁶ Prevalence of OCP as reported in the current study agrees with data from the Norwegian statistical bureau²⁷ and with corresponding figures from Sweden and Denmark. We did not have information on type of oral contraceptives, and it is likely that some OCP users were taking progesterone-only pills (3% to 5% on the Norwegian market). The high-dose progesterone pill was introduced in

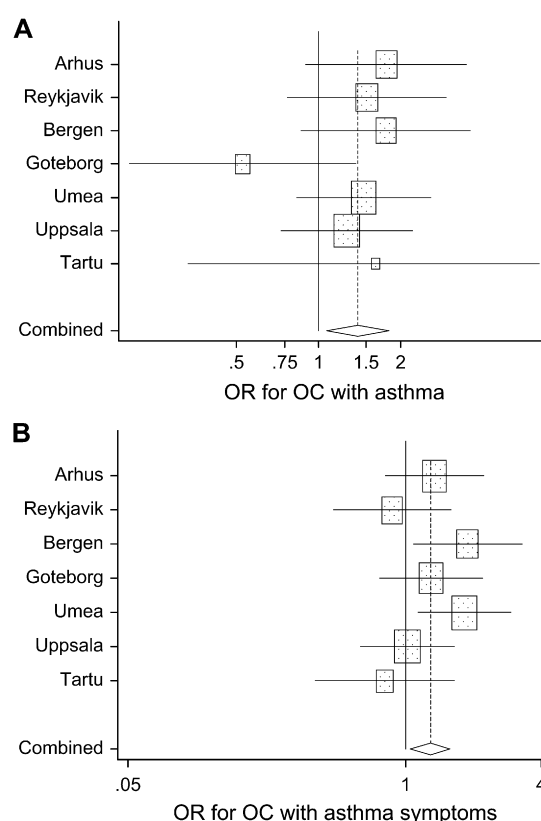


FIG 1. Meta-analysis of the association of oral contraceptive (OC) pills with asthma (A) and ≥ 3 asthma symptoms (B) by center. The size of the squares is proportional with the study sample from each center. The horizontal lines show the 95% CIs. The diamond shows the combined OR with 95% CI.

Northern Europe after the RHINE data were collected. Misclassification of OCP is not likely to be systematic with regard to asthma in a similar way across centers, and have most likely attenuated true effects. Self-reported asthma appears to be a reasonably good measure of asthma compared with a doctor's diagnosis of asthma,²² but misclassification is always present to some extent. BMI is one of the criteria defining metabolic syndrome according to the World Health Organization²⁸ and was the only indicator of metabolic syndrome registered in RHINE. BMI calculated from self-reported weight and height appears to be fairly reliable,²⁹

TABLE IV. Asthma in 5791 women according to use of OCP, stratified by BMI

	No OCP (%) (n = 4728)	OCP (%) (n = 961)	OR (95% CI)*	P value
BMI <20 kg/m² (n = 804)				
Asthma†	5.5	3.0	0.41 (0.12-1.40)	.2
Three or more symptoms§	13	12	0.81 (0.43-1.53)	.5
Allergic asthma	3.5	2.3	0.63 (0.18-2.23)	.5
Wheeze with shortness of breath	9.5	9.1	0.88 (0.43-1.78)	.7
Hay fever	22	27	1.25 (0.79-1.79)	.3
20 kg/m² < BMI <25 kg/m² (n = 3306)				
Asthma†	6.4	8.5	1.45 (1.02-2.05)	.04
Three or more symptoms§	13	16	1.45 (1.11-1.89)¶	.006
Allergic asthma	4.0	6.6	1.73 (1.15-2.59)	.008
Wheeze with shortness of breath	10	12	1.24 (0.92-1.68)	.15
Hay fever	24	29	1.24 (1.003-1.53)	.047
BMI >25 kg/m² (n = 1595)				
Asthma†	8.1	14	1.91 (1.20-3.02)	.006
Three or more symptoms§	19	21	1.28 (0.88-1.87)	.2
Allergic asthma	5.4	8.0	1.50 (0.85-2.65)	.16
Wheeze with shortness of breath	14	18	1.52 (1.02-2.28)	.041
Hay fever	25	30	1.23 (0.88-1.72)	.2

*From logistic regression models with adjustment for smoking habits, BMI (within tertile), age, center, and type of dwelling (as a proxy for social class).

†Asthma medication and/or asthma attacks last 12 months.

§Symptoms included wheeze, wheeze with shortness of breath, wheeze without cold, waking with tightness in chest, waking with shortness of breath, waking with cough, asthma attacks, and current asthma medication.

||Interaction in effect of OCP on asthma between lean and normal/overweight women; $P_{\text{interaction}} = .049/.041$.

¶Interaction in effect of OCP on 3 or more symptoms between lean and normal women; $P_{\text{interaction}} = .091$.

but poor definition of metabolic situation is more likely to have attenuated associations than to have produced spurious results. Overall, it seems likely that misclassification may have attenuated true associations; however, it is difficult to estimate the effect of misclassification in complex analyses with errors in several variables.

Doctor's bias is a potential problem in the interpretation of the results. This was investigated by analyzing, first, only the 411 women with doctor's diagnosed asthma, to see whether asthma was less severe among OCP-using subjects with asthma compared with subjects with asthma not using OCP. This was not found; the number of asthma symptoms leading to a diagnosis of asthma was similar in women taking OCP (3.7) and women not taking OCP (3.6). Second, we analyzed 858 women with ≥ 3 asthma symptoms to see whether having a diagnosis of asthma among symptomatic women was influenced by seeing a doctor to get OCP. No difference was found; about one third of women with symptoms had a diagnosis of asthma in both groups (36% in women using OCP and 33% in women not using OCP). Thus, while doctor's bias cannot be completely disregarded, these analyses did not indicate a doctor's bias.

Previous analysis has shown that women with irregular menstruations not using OCP had more asthma.³⁰ Because OCP can be a treatment option for irregular menstruations, the current analyses of OCP and asthma were adjusted for menstrual irregularity. However, the issue is complex because use of OCP may influence the classification of menstrual status. Because adjustment for irregular menstruation did not alter the effect estimates, residual confounding by irregular menstruation seems unlikely. Residual confounding by smoking was not found, because results were similar when analyzing never smokers separately.

Oral contraceptives consist of ethinylestradiol and different gestagens. The direct effect of these substances on the airways has not been investigated. However, it seems plausible that OCP might influence the airways through various mechanisms.

Estrogens have well known proinflammatory effects.³¹ Kirsch et al³² showed that estrogens stimulated endothelial nitric oxide synthase in human bronchiolar epithelial cells, with nitric oxide an important mediator of physiologic processes in the airways. Levels of exhaled nitric oxide are reported to be at a maximum midcycle when estrogen levels are highest.^{32,33} Ethinylestradiol is a very potent estrogen, which might have direct inflammatory effects on the airways; we might also speculate whether such effects could increase with higher BMI to explain the observed interplay between OCP and BMI.

Progesterone appears to have a respiration-driving influence—that is, in pregnancy.³⁴ Patients with asthma receiving OCP had attenuated cyclical change in airway reactivity and reduced diurnal peak expiratory flow rate variability, which was associated with suppression of the normal luteal phase rise in sex hormones.³⁵ Beneficial effects of treatment with large doses of progesterone were seen in women with severe premenstrual asthma.³⁶ Leynaert et al³⁷ showed that women with asthma had a longer period with low progesterone levels than women without asthma. OCP inhibits the natural surge in progesterone in the luteal phase, and replaces it with 20-fold lower daily amounts of progesterone. One could speculate whether progesterone deficit might contribute to increased asthma risk; a stronger effect in women who need a higher respiratory drive because of higher BMI could possibly contribute to the observed interplay with BMI.

Altered sex hormone cyclicity is another characteristic of OCP use. Asthma varies during the menstrual cycle, possibly worsening premenstrually³⁸ or preovulatorily.³⁹ Possibly, altered cyclicity by itself could influence airways physiology. Further, although OCP generally stabilizes the hormones levels, the pill-free weeks may imply large shifts in hormonal levels, which might influence the airways.

Studies show that oral contraception may exacerbate insulin resistance.^{17,40} Increasing insulin resistance is associated with

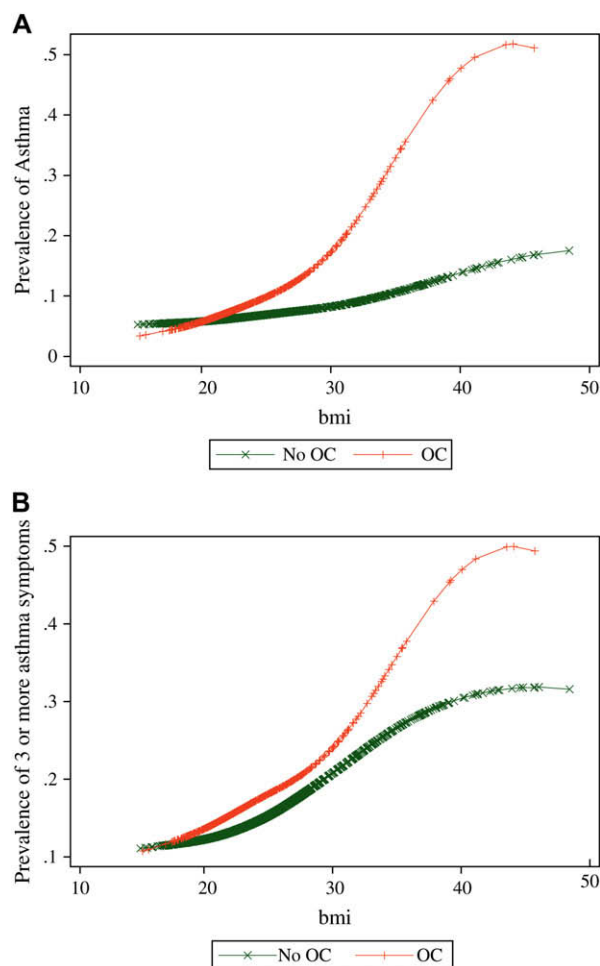


FIG 2. Generalized additive model curves showing prevalence (proportion) of asthma (**A**) and ≥ 3 asthma symptoms (**B**) according to BMI with or without oral contraceptives (OC).

lower lung function.^{41,42} An association of irregular menstruation, which is a manifestation of insulin resistance, with asthma and lung function^{8,30} supports the idea that insulin resistance may be of importance for respiratory health. Oral contraception might influence airway inflammation by contributing to increased insulin resistance⁴¹⁻⁴⁴; a larger impact of the negative metabolic properties of OCP with increasing BMI might contribute to the observed interplay between OCP and BMI.

In conclusion, women taking oral contraceptives had more asthma and allergy. However, this association was modified by BMI and was only present among normal weight and overweight women, not among lean women. These findings add to the literature suggesting that sex steroid hormones may be of importance for respiratory health, and that sex hormones may interact with metabolic status in effect on the airways. The study further suggests that asthma may be a side effect to oral contraception in 2% to 3% of OCP users. However, this cross-sectional postal survey was not designed to investigate side effects of drugs, and the results should be interpreted with great caution. Women are not advised to stop taking OCPs; women who believe they have asthma related to using the pill should discuss antiasthmatic treatment with their doctors, and

alternatively other forms of contraception. Even if future clinical trials should confirm effects of oral contraceptive pills on airways obstruction, the individual health risks related to unwanted pregnancies are much larger than a slightly elevated asthma risk. However, on the basis of the current findings and previous evidence suggesting a role for sex hormones in airways physiology, it is strongly recommended that asthma is investigated among potential side effects in clinical trials of oral contraceptives.

The following scientists in the Rhine study group are acknowledged for helpful contributions: T. Blöndal, U. S. Björnsdóttir, G. Boman, B. Forsberg, D. Gislason, A. Gulsvik, M. Gunnbjörnsdóttir, E. Juel Jensen, M.-C. Ledin, L. Lillienberg, B. Lundbäck, B. N. Lærum, E. Norrman, A.-C. Olin, E. Rydén, U. Spetz-Nyström, K. Stenudd Cashelunge, J. Talvik, A. Tunsäter, and G. Wieslander. E. Plana, a scientist in the Centre de Recerca en Epidemiologia Ambiental-Institut Municipal d'Investigació Mèdica, Barcelona, Spain, is acknowledged for helpful contributions.

Clinical implications: Clinicians should be aware of a possible increased asthma risk in women using oral contraception, and asthma symptoms should be included in future clinical trials of oral contraception.

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