

1 **Use of hormonal contraceptives and occurrence of pregnancy-related pelvic pain: a**
2 **prospective cohort study in Norway**

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1 **Abstract**

2 **Background**

3 Pregnancy-related pelvic pain is a common condition, and use of hormonal contraceptives
4 before pregnancy has been proposed as a risk factor. We used data from a sub-sample of women
5 participating in the “Norwegian Women and Cancer study” (NOWAC) to assess the association
6 between hormonal contraceptive use and pelvic pain in pregnancy.

7 **Methods**

8 From a sub-group of 2078 parous women participating in the NOWAC study, information was
9 collected from a self-instructive four-page questionnaire containing questions about lifestyle and
10 medical conditions. We calculated odds ratios (OR) and 95% confidence intervals (CI), using
11 unconditional logistic regression.

12 **Results**

13 In this study, the prevalence of pelvic pain in women was 26.5% during the first pregnancy and
14 increased with parity. Use of hormonal contraceptives before a woman’s first pregnancy was
15 associated with an increased risk of pelvic pain in her first full-term pregnancy (OR=1.6; 95%
16 confidence interval 1.2-2.2). There was no association between use of hormonal contraceptives
17 and pelvic pain in the second or third pregnancy. Occurrence of pelvic pain in a previous
18 pregnancy was the only factor associated with pelvic pain in subsequent pregnancies (OR=51.1;
19 95% CI 32.9-79.5 in the second pregnancy and OR=28.3; 95% CI 15.4-53.1 in the third
20 pregnancy).

21 **Conclusion**

22 Use of hormonal contraceptives was associated with an increased risk of pelvic pain in a
23 woman’s first full-term pregnancy. The most important determinant of pelvic pain in the second
24 or third pregnancy was the history of pelvic pain in the preceding pregnancy.

25

1 **Background**

2 The first documented description of pelvic pain in pregnancy was published by Snelling in the
3 American Journal of Medicine in 1870 [1]. However, it is believed that Hippocrates recognized
4 the disease among pregnant women in Ancient Greece as far back as 400 BC. Pelvic pain in
5 pregnancy is one of the many terms used to describe a collection of typical symptoms [2-5].
6 Other terms used in scientific literature are: low back pain [6-8], back pain [3,9-11], backache
7 [12] and symphyseal pain [10]. In Norway this condition is termed “bekkenløsning”. This word
8 incorporates pregnancy-related low back pain and pelvic pain. The symptoms vary in strength
9 from discomfort to complete immobilization. Several studies have indicated that pelvic pain in
10 pregnancy is a widespread, and possibly increasing, health problem among women in
11 industrialized countries [7,9,13-15]. The prevalence of pelvic pain in pregnancy varies between
12 25-50% in different studies [7-9,12]. Several risk factors for this condition have been
13 hypothesized, such as age, parity, education, back pain before pregnancy, type of employment,
14 body size, smoking habits, and use of hormonal contraceptives [2].
15 We present here results from a study of pelvic pain in pregnancy in relation to hormonal
16 contraceptive use before the first pregnancy and between pregnancies.

17 **Methods**

18 **Study population**

19 The “Norwegian Women and Cancer study” (NOWAC) was implemented between 1991 and
20 1997. A total of 179,388 women from 30-70 years of age were invited to participate, and
21 102,443 agreed [16]. All women were sampled randomly from the national population register
22 of Norway. This register records the addresses of all persons alive and residing in the country,
23 and the dates of death or migration to and from Norway since 1960. In this register, each person
24 is identified by a unique 11-digit national registration number. The first six digits encode
25 information on the date of birth, and the last five digits use an algorithm to ensure a unique
26 number, and include information on gender [17]. Health survey questionnaires were mailed to

1 women in batches for convenience. In 1991-2, as part of NOWAC, a four-page questionnaire
2 was mailed to a batch of 4,000 women born between 1943 and 1957 (35-49 years of age).
3 Women who did not return the questionnaire in a few weeks were mailed a reminder with an
4 identical letter of introduction and questionnaire. The questionnaires were returned to the
5 Institute of Community Medicine in Tromsø, Norway.
6 The questionnaire assessed lifestyle characteristics, reproductive history, including number and
7 duration of each pregnancy, prevalent diseases, and other different medical conditions, including
8 pelvic pain during each pregnancy. We asked about the occurrence of pregnancy-related pelvic
9 pain (Did you suffer from pelvic pain in any of your pregnancies?) and the grade or severity of
10 the symptoms during each of the first three full-term pregnancies (severe disability, problems
11 with walking, painful walking, problems in doing housework, normal physical function level).
12 We used the severity question to classify pelvic pain in the first three pregnancies. Hormonal
13 contraceptives were introduced on the Norwegian market in 1967. Questions about hormonal
14 contraceptive use were summary measures (as ever having used, total estimated overall duration
15 of use, and use before first pregnancy) with detailed questions for each period of use, such as
16 age when use began, brand used, age when use was interrupted, and duration of use. A folder
17 with photos of almost all the 36 hormonal contraceptive brands that have ever been on the
18 Norwegian market was enclosed with the questionnaire to help women to recall use of these
19 drugs.

20 **Data analysis**

21 From the 4,000 women randomly selected for this sub-study we excluded 52 women who had
22 emigrated, were dead at the time the questionnaire was sent, or had a severe mental handicap.
23 Altogether 2,400 women agreed to participate in the study and returned a completed
24 questionnaire, giving a crude response rate of 60.0 % or a corrected response rate of 60.8%. Of
25 these, 2,188 women reported at least one pregnancy lasting six months or more.

1 We further excluded 35 women due to a lack of information on the use of hormonal
2 contraceptives and 75 women who did not answer the question about pelvic pain. Thus, 2,078
3 women were included in the final analysis presented here.

4 We registered twin pregnancies as one pregnancy. We classified hormonal contraceptives in two
5 ways. Firstly, all hormonal contraceptives – regardless of the mode of administration (oral or
6 injectable), and hormonal content (combined estrogen-progestin contraceptives, and
7 medroxyprogesterone acetate only pills or injections) – were considered together. Secondly, we
8 classified contraceptives according to the hormonal content as progestin-only contraceptives,
9 and combined estrogen-progestin contraceptives. We classified women as having used
10 hormonal contraceptives before the first pregnancy, before second pregnancy (regardless if the
11 use was only before first pregnancy, both before first pregnancy and between first and second
12 pregnancy, or only between first and second pregnancy) and before third pregnancy (as for the
13 second pregnancy, but also including women using contraceptives between the second and third
14 pregnancies).

15 The statistical analyses were performed using the SAS statistical package version 8.12. Logistic
16 regression was used for the estimation prevalence of odds ratios (OR) with 95% confidence
17 intervals (CI). Analyses were done separately for each of the three first pregnancies.

18 In the multivariate analysis, besides use of hormonal contraceptives before each relevant
19 pregnancy, we included in the models the following co-variables hypothesized to be associated
20 with pregnancy-related pelvic pain: time elapsed since relevant birth, weight of the newborn in
21 each relevant pregnancy and age at menarche. In the analysis of pelvic pain in the first
22 pregnancy we also included indicator variables for potential risk factors in the multivariate
23 regression models, namely education, height of the mother and smoking habits during the first
24 pregnancy. However, since they did not affect the risk estimates meaningfully, they were
25 excluded in the multivariate analysis of the second and third pregnancies.

26 For the analysis of the second and third pregnancies we considered the occurrence of pelvic pain
27 in the previous pregnancy as potential determinants of pelvic pain in the following pregnancy.

1 **Results**

2

3 **Characteristics of the study participants**

4 Some characteristics of the women included in the study are shown in Table 1. The age
5 distribution in the study population was nearly uniform, while use of hormonal contraceptives
6 before first full-term pregnancy decreased with increasing age at enrolment. Women who
7 reached menarche before age 14 were more likely to have used hormonal contraceptives before
8 their first full-term pregnancy than women over 14 years of age at menarche ($p=0.001$). Age at
9 first birth, years of education, and interval between menarche and first birth were directly
10 associated with hormonal contraceptive use before first pregnancy (p values ≤ 0.001). The
11 inverse was observed with number of births ($p<0.001$). Use of hormonal contraceptives before
12 first pregnancy was unrelated with weight of the first newborn child ($p=0.60$). Nearly one-third
13 of the women smoked during their first pregnancy. The proportion of hormonal contraceptive
14 users before first pregnancy was similar among smokers and non-smokers.

15

16 **Pelvic pain in pregnancy**

17 Pregnancy-related pelvic pain – in the first, second or third pregnancy – was reported most often
18 in the youngest women in our study (data not shown). The proportion of women reporting
19 pregnancy-related pelvic pain increased with the number of pregnancies (22.9% in the first
20 pregnancy, 27.4% in the second pregnancy and 34.0% in the third pregnancy). Similar increase
21 in the prevalence of pelvic pain with increasing number of pregnancies was observed in all age
22 groups, irrespective of age at study enrolment (data not shown).

23

24 **Pelvic pain in the first pregnancy**

25 Women who reported having used hormonal contraceptives before their first pregnancy reported
26 a higher frequency of pelvic pain in the first pregnancy as compared with non-users (OR=1.6;
27 95% CI 1.2-2.1) (Table 2). Neither age at menarche, age at first birth, time elapsed since first

1 birth; weight of newborn child, years of education nor smoking during the first pregnancy
2 changed significantly the risk estimated in this analysis (Table 2).

3

4 **Pelvic pain in the second and third pregnancies**

5 Use of hormonal contraceptives before second and before third pregnancy was not associated
6 with risk of pregnancy-related pelvic pain in the second or third pregnancy (OR=1.0; 95% CI
7 0.7-1.5 and OR=1.2; 95% CI 0.7-1.9 respectively). The only important determinant of
8 pregnancy-related pelvic pain in the second or third pregnancy was the history of pregnancy-
9 related pelvic pain in the preceding pregnancy (OR=57.3; 95% CI 40.5-81.2 in second
10 pregnancy and OR=31.2; 95% CI 19.7-49.4 in third pregnancy) (Table 3). Pregnancy-related
11 pelvic pain in the second pregnancy (but not in the first) was a strong predictor of pelvic pain in
12 the third pregnancy (RR 18.0, 95% CI 8.2-39.6). Women who presented pregnancy-related pain
13 in the first two pregnancies had an extremely high risk of also suffering from it in the third
14 pregnancy (RR 232, 95% CI 82-658).

15

16 We found no clear association between duration of use of hormonal contraceptives before first
17 pregnancy and pregnancy-related pelvic pain in the first pregnancy (Test for heterogeneity $p=$
18 0.23). There was no evidence of a differential effect according to the hormonal content of the
19 pill, i.e., progestin- only or combined estrogen-progestin pills (Test for heterogeneity $p=0.94$)
20 (Table 4).

21 We also performed an analysis classifying separately the 23 women that used both progestin-
22 only and combined estrogen-progestin contraceptives. In this analysis the estimates were equal
23 as those in the Table 4 for progestin-only and for combined estrogen-progestin contraceptives,
24 and the estimate for women who used both was OR=2.0 (95% CI: 0.8-5.0). Finally, we
25 excluded from the analysis these 23 women, and the results were not materially different than
26 those shown in Table 4.

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Discussion

In our study use of hormonal contraceptives was associated with the occurrence of pelvic pain in the first pregnancy, but not in the second and third pregnancies. Occurrence of pelvic pain in a previous pregnancy was strongly associated with occurrence of the symptoms in subsequent pregnancies.

During a fertile life, at least 20% of women experience pelvic pain in at least one pregnancy.

The prevalence of the symptoms increases with increasing parity [2,9,12]. Most of the published studies on determinants of pregnancy-related pelvic pain originate from Scandinavia, where this condition appears to be prevalent [2,3,9,10,13,18,19]. Only a few studies have looked into hormonal contraceptives as a possible risk factor for pregnancy-related pelvic pain [3,6,7,9,14].

All these studies were negative or non-conclusive, and most of them were too small to allow any conclusions. None of them have stratified the analysis on parity, analysing each pregnancy separately. Our strategy of analysing each pregnancy separately might explain why our results deviate from earlier studies. If hormonal contraceptives are an explanatory biological factor in the development of pelvic pain, it might be an advantage to study each pregnancy separately, because of the high recurrence of the condition in subsequent pregnancies. Endresen [2] emphasises that both age and parity are important explanatory variables, out of which parity is the more powerful. She also argues that adjustment for age would hardly be required if the data were stratified for parity.

Östgaard et al. [11] reported that back problems independent of pregnancy was an important factor when predicting back pain and pain intensity in a future pregnancy. We did not have information about back pain before pregnancy in our study, and thus we could not take this factor into consideration in our analyses.

1 The response rate in this study was around 60%, which might be considered low. The possible
2 problems with a low response rate, such as selection bias, have been discussed elsewhere [20]. It
3 is unlikely that the response rate introduced a selection bias that might cause major problems in
4 this study. The unique person-number given to all Norwegian inhabitants made it possible for us
5 to link a sub-sample of the women in the Norwegian Women and Cancer Study to the National
6 Register of Education and Fertility and compare the responses with the total invited group in the
7 same sub-cohort. This linkage uncovered no selection bias except that the response rate
8 increased with increased education. We have slightly better educated women in the cohort than
9 expected according to the Norwegian female population as a whole [16]. In addition, no
10 association between the proportion of women using hormonal contraceptives, parity or age at
11 first birth was revealed according to the response rate from an earlier analysis within our same
12 study cohort [21]. If ever users of hormonal contraceptives with pelvic pain were more likely to
13 answer the questionnaire than never users of hormonal contraceptives without pelvic pain,
14 selection bias could have occurred. We consider this to be rather unlikely, since a possible
15 association between hormonal contraceptive use and pregnancy-related pelvic pain was not a
16 known hypothesis in the general population at the time of the survey. Moreover, the questions
17 about pregnancy-related pelvic pain were not mentioned in the study's letter of introduction or
18 in the headings of the questionnaires used.

19 Differential misclassification of exposure [22] could have resulted in either an exaggerated or
20 underestimated effect. However, we have no reason to believe that women with a history of
21 pelvic pain systematically remembered their hormonal contraceptive use differently from
22 women without this condition.

23 Our study could have been affected by recall bias: women might remember in more detail recent
24 events (such as recent use of hormonal contraceptives or pain related to a recent pregnancy)
25 compared to past events. Time elapsed since first birth is correlated with the woman's birth year,
26 and we found a non-significant reduced risk of pregnancy-related pelvic pain with increasing
27 time elapsed since first birth. However, if pelvic pain incidence is increasing, younger women or

1 women who gave birth for the first time close to enrolment will be more likely to report having
2 suffered from the illness. Both the association between pelvic pain and women's birth year or
3 age have been reported earlier [2,9].

4 **Conclusions**

5 Our results suggest that use of hormonal contraceptives before the first pregnancy may cause an
6 increased risk of pregnancy-related pelvic pain in the first pregnancy. Pregnancy-related pelvic
7 pain in a preceding pregnancy is a very strong predictor of pelvic pain in a subsequent
8 pregnancy.

9 The association between use of hormonal contraceptives and pelvic pain in the first pregnancy is
10 this study was weak, but it might be of interest in a public health perspective since both the
11 prevalence of hormonal contraceptive use before first pregnancy, and the prevalence of pelvic
12 pain in pregnancy are high in Scandinavia.

13 **Competing interests**

14 None declared.

15 **Authors' contributions**

16 Merethe Kumle and Eiliv Lund conceived of the study and participated in its design and
17 coordination. Merethe Kumle, Elisabete Weiderpass and Eiliv Lund participated in the sequence
18 alignment and drafted the manuscript. Elin Alsaker performed the statistical analysis. All
19 authors read and approved the final manuscript.

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1 Tables

2 **Table 1 - Characteristics of the study population (n=1163)**

3

	Study cohort Number (%)	Used hormonal contraceptives before first birth	
		%	p value
Age			
35-36 years	320 (15.4)	49.1	
37-38 years	273 (13.1)	49.5	
39-40 years	276 (13.3)	42.4	
41-42 years	296 (14.2)	27.4	
43-44 years	260 (12.5)	20.4	
45-46 years	296 (14.2)	15.5	
49-49 years	357 (17.2)	10.9	p<0.0001
Age at menarche			
< = 12 year	538 (26.4)	30.1	
13 years	615 (30.2)	35.5	
> = 14 years	882 (43.3)	26.6	p=0.001
Age at first birth			
<= 20 years	503 (24.2)	6.4	
21-25 years	961 (46.3)	25.6	
> = 26 years	614 (29.5)	57.0	p<= 0.0001
Weight of newborn child			
<3000 g	360 (18.0)	31.4	
3000-3500 g	750 (37.4)	31.2	
3501-4000 g	617 (30.8)	28.4	
> = 4001 g	276 (13.8)	31.9	P=0.6
Education			
7-9 years	428 (20.9)	12.9	
10-12 years	759 (37.2)	24.2	
13-15 years	517 (25.3)	39.9	
> = 16 years	339 (16.6)	51.9	p<0.0001
Years between menarche and first birth			
0-5 years	215(10.6)	5.6	
6-10 years	926(45.5)	17.4	
11-15 years	628 (30.9)	43.0	
> = 16 years	266 (13.1)	64.7	p<0.0001
Number of births			
One	307(14.8)	46.3	
Two	1044 (50.2)	32.2	
Three	543 (26.1)	23.9	
> = Four	184(8.9)	10.9	p<0.0001
Smoking in the first pregnancy			
No	1396 (69.6)	30.5	
Yes	611 (30.4)	30.0	p=0.8

4

1 **Table 2 - Odds ratio (OR) with 95% confidence intervals (CI) for**
 2 **pregnancy-related pelvic pain in the first pregnancy**

3

Characteristic		Pregnancy-related pelvic pain in first pregnancy
		OR (95% CI) *
Use of hormonal contraceptives before first birth		
	No	1.0 (ref.)
	Yes	1.6 (1.2-2.1)
Age at menarche		
	<= 12 years	1.0 (ref.)
	13 years	0.9 (0.7-1.2)
	14 + years	0.8 (0.6-1.1)
Age at first birth		
	<=20 years	1.0 (ref.)
	21-25 years	1.2 (0.9-1.5)
	26 + years	0.8 (0.5-1.1)
Time elapsed since first birth (per 3 years)**		0.9 (0.8-1.0)
Weight of newborn child (per 500g)		1.0 (0.95-1.1)
Years of education		
	7-9	1.0 (ref.)
	10-12	1.0 (0.7-1.3)
	13-15	0.9 (0.7-1.3)
	16+	1.1 (0.7-1.7)
Smoking during first pregnancy		
	No	1.0 (ref.)
	Yes	0.9 (0.7-1.1)

4

5 * All variables are mutually adjusted. Analysis includes women with valid information for listed
 6 variables, i.e. 437 women with and 1424 women without pregnancy-related pelvic pain during
 7 their first pregnancy.

8

9 ** Years between first birth and enrolment in the study cohort.

10

1 **Table 3 - Relative risk (RR) with 95% confidence intervals (CI) for pregnancy-related**
 2 **pelvic pain in the second and third pregnancies according to history of previous**
 3 **pregnancy (ies)**
 4

Characteristic	Pregnancy-related pelvic pain in second pregnancy	Pregnancy-related pelvic pain in third pregnancy
	RR (95% CI)*	RR (95% CI)**
Pregnancy-related pelvic pain in first pregnancy		
No	1.0 (ref.)	-
Yes	57.3 (40.5-81.2)	-
Pregnancy-related pelvic pain in at least one of the first two pregnancies		
No	-	1.0 (ref.)
Yes	-	31.2 (19.7-49.4)
Not suffered from Pregnancy-related pelvic pain in the previous two pregnancies		1.0 (ref)
Pregnancy-related pelvic pain	-	
in the first but not in the second pregnancy	-	1.4 (0.5-4.0)
not in the first but in the second pregnancy	-	18.0 (8.2-39.6)
both in the first and the second pregnancy	-	232 (82-659)

5
 6 * Adjusted for use of hormonal contraceptives, age at second birth, weight of newborn and time
 7 since second birth (years between second birth and enrolment in the study cohort). Analysis
 8 includes women with valid information for listed variables, i.e., 467 women with and 1221
 9 women without pregnancy-related pelvic pain in second pregnancy.

10
 11 ** Adjusted for use of hormonal contraceptives, age at third birth, weight newborn and time
 12 since third birth (years between third birth and enrolment in the study cohort). Analysis includes
 13 women with valid information for listed variables, altogether 233 women with and 449 women
 14 without pregnancy-related pelvic pain during their second pregnancy.
 15

1 Table 4 –Odds ratio (OR) with 95% confidence intervals (CI) for pregnancy-related
 2 pelvic pain in the first pregnancy
 3

Characteristic	N	Pregnancy-related pelvic pain in first pregnancy OR (95 % CI)*
No use	1290	1.0 (ref.)
Duration of hormonal contraceptives before first pregnancy**		
1-29 months	245	1.8 (1.3-2.5)
30-59 months	135	1.2 (0.8-1.9)
60 months or more	135	1.6 (1.0-2.5)
Type of hormonal contraceptives used before first pregnancy***		
Progestin-only contraceptives	71	1.7 (0.97-2.8)
Combined estrogen-progestin contraceptives****	323	1.7 (1.2-2.3)

4
 5 * Adjusted for age at menarche, years of education, smoking during first pregnancy, age at first
 6 birth, weight of newborn and time since first birth (years between first birth and enrolment in the
 7 study cohort).
 8

9 **Analysis includes women with valid information for duration and adjustment variables, i.e.
 10 421 women with and 1384 without pregnancy related pelvic pain in first pregnancy.
 11

12 ***Analysis includes women with valid information for brand name and adjustment variables,
 13 i.e. 387 women with and 1297 without pregnancy related pelvic pain in first pregnancy.
 14

15 **** Includes 23 women who used both progestin-only and combined contraceptives before
 16 first pregnancy.
 17