ORIGINAL RESEARCH ARTICLE



Factors in early pregnancy predicting pregnancy-related pain in the second and third trimester

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Abstract

Introduction: Pain during pregnancy affects women's well-being, causes worry and is a risk factor for the child and the mother during labor. The aim was to investigate the relative importance of an extensive set of pregnancy-related physiological symptoms and psychosocial factors assessed in the first trimester compared with the occurrence of pregnancy-related pain symptoms later in the pregnancy.

Material and methods: Included were all women who booked an appointment for a first prenatal visit in one of 125 randomly selected general practitioner practices in Eastern Denmark from April 2015 to August 2016. These women answered an electronic questionnaire containing questions on the occurrence of five pregnancy-related pain symptoms: back pain, leg cramps, pelvic cavity pain, pelvic girdle pain and uterine contractions. The questionnaire also included sociodemographic questions and questions on chronic diseases, physical symptoms, mental health symptoms, lifestyle and reproductive background. The questionnaire was repeated in each trimester. The relative importance of this set of factors from the first trimester on the five pregnancy-related pain symptoms compared with the second and third trimesters was assessed in a dominance analysis.

Results: A total of 1491 women were included. The most important factor for pregnancy-related pain in the second trimester and third trimester is the presence of the corresponding pain in the first trimester. Parity was associated with pelvic cavity pain and uterine contractions in the following pregnancies. For back pain and pelvic cavity pain, the odds increased as the women's estimated low self-assessed fitness decreased and had low WHO-5 wellbeing scores.

Conclusions: When including physical risk factors, sociodemographic factors, psychological factors and clinical risk factors, women's experiences of pregnancy-related pain in the first trimester are the most important predictors for pain later in pregnancy. Beyond the expected positive effects of pregnancy-related pain, notably self-assessed fitness, age and parity were predictive for pain later in pregnancy.

Abbreviations: ASS, Anxiety Symptom Scale; GP, general practitioner; MDI, Major Depression Inventory.

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KEYWORDS

early complications, epidemiology, pain, patient-reported measures, pregnancy

1 | INTRODUCTION

Pain related to pregnancy, such as back pain, leg cramps, pelvic cavity pain, pelvic girdle pain and uterine contractions, is a major health concern because it affects well-being and causes worries for pregnant women.¹ Pain during pregnancy also constitutes a risk factor for the child and mother, particularly during labor^{2,3} and may also be associated with disability, recurrent pain and continuous pain as long as more than a year after delivery and has been shown to affect employment.^{4,5} Women who experience pain during pregnancy more often have depression and anxiety in the third trimester⁶ and have a higher risk for postnatal depression.^{7,8}

The estimated prevalence of pregnancy-related pain is 16%-54%. 9-11 Severity and pain location also vary considerably across studies. 4,9-11 Pregnancy-related pain appears to reach peak intensity between the 24th and 36th week of pregnancy. Pain in the first trimester has been shown to predict pain in the third trimester; 10.11 however, pregnancy-related pain is often only partly understood and may in some cases represent several underlying conditions. 11 The literature is fragmented and focuses either on back pain, pelvic girdle pain, pelvic cavity pain or combinations of these pain types. 6,8,10,12 Localization of pain may, however, be difficult. Some women also experience pain from uterine contractions and leg cramps. Due to the difficulty of pain localization and because of differences in pain perception between individuals, it is relevant to investigate each of these different types of pain. 13

The initial prenatal consultation with the woman's general practitioner (GP) during the first trimester of pregnancy provides an opportunity to discuss and address pain during pregnancy. This includes understanding the anticipated pain levels and exploring potential strategies to prevent or minimize it. In this consultation, a simple clinical assessment is performed and there is a broad inquiry into the health of the woman. Some of the information obtained in this consultation may be indicative of pain later in the pregnancy and may give leads on how to handle pain so that it will have the fewest consequences for the further pregnancy and thereafter. Therefore, it is important to identify elements in the first prenatal consultation, ie information that is naturally and routinely asked about, which are most predictive of pain later in the pregnancy.

This study aims to investigate the relative importance of an extensive set of pregnancy-related physiological symptoms and psychosocial factors assessed in the first trimester to the occurrence of pregnancy-related pain symptoms: back pain, leg cramps, pelvic cavity pain, pelvic girdle pain and uterine contractions in the second and third trimester.

Key message

Women experiencing back pain, leg cramps, pelvic cavity pain, pelvic girdle pain and uterine contractions in the first trimester have a higher risk of pain later on in the pregnancy. The back pain and pelvic cavity pain was increased for women with low self-assessed fitness and low scores on the WHO-5 wellbeingidex.

2 | MATERIAL AND METHODS

2.1 | Study design and setting

The study is a prospective cohort study comprising data from Pregnancy Health Records and from a series of questionnaires collected throughout the pregnancy.

The healthcare system in Denmark is tax-funded and care is free of charge for the patient. The majority of Danes (99%) are affiliated with a GP, who functions as a gatekeeper to secondary care. All pregnant women are offered a minimum of three preventive prenatal assessments at the gestational age of 6–10 weeks, 25 weeks and 32 weeks, along with a postpartum assessment at 8 weeks postpartum at their GP. The first prenatal assessment is accepted by almost 100% of the women¹⁴ and, in this consultation, a structured record

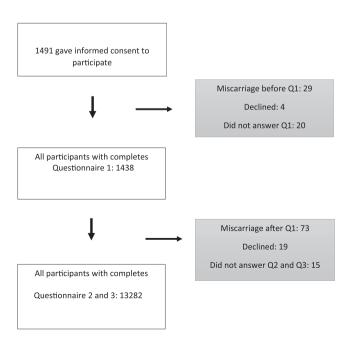


FIGURE 1 Flowchart of inclusion.



TABLE 1 Characteristics of the women in the present study, both total and stratified on the experience of pain in the second and third trimester, respectively. Values as n (%).

	Total <i>n</i> = 1328	No pain second trimester <i>n</i> =480	Pain second trimester n=848	No pain third trimester $n = 690$	Pain third trimester n=638
Nausea	1181 (88.93)	443 (92.29)	738 (87.03)	632 (91.59)	549 (86.05)
Vomiting	539 (40.59)	223 (46.46)	316 (37.26)	309 (44.78)	230 (36.05)
Back pain	493 (37.12)	243 (50.63)	250 (29.48)	320 (46.38)	173 (27.12)
Pelvic girdle pain	746 (56.17)	342 (71.25)	404 (47.64)	452 (65.51)	294 (46.08)
Pelvic cavity pain	442 (33.28)	225 (46.88)	217 (25.59)	295 (42.75)	147 (23.04)
Itching of vulva	253 (19.05)	100 (20.83)	153 (18.04)	146 (21.16)	107 (16.77)
Varicose veins	35 (2.64)	13 (2.71)	22 (2.59)	21 (3.04)	14 (2.19)
Leg cramps	133 (10.02)	63 (13.13)	70 (8.25)	77 (11.16)	56 (8.78)
Vaginal bleeding	222 (16.72)	94 (19.58)	128 (15.09)	136 (19.71)	86 (13.48)
Uterine contractions	62 (4.67)	37 (7.71)	25 (2.95)	41 (5.94)	21 (3.29)
Sleep complaints	278 (20.93)	130 (27.08)	148 (17.45)	175 (25.36)	103 (16.14)
Age (>30 years)	702 (52.86)	217 (45.21)	485 (57.19)	336 (48.70)	366 (57.37)
Marital status (not married or cohabiting)	67 (5.05)	28 (5.83)	39 (4.60)	36 (5.22)	31 (4.86)
Education (<4 years)	668 (50.30)	262 (54.58)	406 (47.88)	376 (54.49)	292 (45.77)
Occupation (not presently in work)	327 (24.62)	133 (27.71)	194 (22.88)	179 (25.94)	148 (23.20)
Income of household (<40,000 €)	740 (55.72)	290 (60.42)	450 (53.07)	411 (59.57)	329 (51.57)
Smoking in pregnancy	89 (6.70)	42 (8.75)	47 (5.54)	57 (8.26)	32 (5.02)
Drinking alcohol in pregnancy	10 (0.75)	5 (1.04)	5 (0.59)	8 (1.16)	2 (0.31)
Use of other drugs	4 (0.30)	3 (0.63)	1 (0.12)	3 (0.43)	1 (0.16)
Parity (no previous births)	589 (44.35)	195 (40.63)	394 (46.46)	290 (42.03)	299 (46.87)
Previous miscarriages/ abortions	491 (36.97)	208 (43.33)	283 (33.37)	277 (40.14)	214 (33.54)
In vitro fertilization	131 (9.86)	36 (7.50)	95 (11.20)	66 (9.57)	65 (10.19)
Self-rated health (fair, low, very low)	280 (21.08)	132 (27.50)	148 (17.45)	169 (24.49)	111 (17.40)
Self-assessed fitness (fair, low, very low)	945 (71.16)	360 (75.00)	585 (68.99)	512 (74.20)	433 (67.87)
Wellbeing (WHO-5 score ≤50)	1032 (77.71)	399 (83.13)	633 (74.65)	573 (83.04)	459 (71.94)
Heart disease	58 (4.37)	24 (5.00)	34 (4.01)	30 (4.35)	28 (4.39)
Lung disease	95 (7.15)	43 (8.96)	52 (6.13)	63 (9.13)	32 (5.02)
Thyroid disease	51 (3.84)	18 (3.75)	33 (3.89)	30 (4.35)	21 (3.29)
Diabetes	10 (0.75)	4 (0.83)	6 (0.71)	5 (0.72)	5 (0.78)
Epilepsy	14 (1.05)	6 (1.25)	8 (0.94)	9 (1.30)	5 (0.78)
Recurrent urinary tract infections	60 (4.52)	29 (6.04)	31 (3.66)	30 (4.35)	30 (4.70)
Psychiatric disorders	95 (7.15)	47 (9.79)	48 (5.66)	52 (7.54)	43 (6.74)
Previous psychological difficulties	656 (49.40)	280 (58.33)	376 (44.34)	374 (54.20)	282 (44.20)
Depression (MDI score 21 or more)	232 (17.47)	124 (25.83)	108 (12.74)	156 (22.61)	76 (11.91)
Anxiety (ASS score 10 or more)	95 (7.15)	57 (11.88)	38 (4.48)	68 (9.86)	27 (4.23)

Note: The pain was defined as at least one indication of one of the five pain items: back pain, leg cramps, pelvic cavity pain, pelvic girdle pain, and uterine contractions.

is established (the Pregnancy Health Record) and sent to hospital midwives.

Pregnant women were recruited from 125 randomly selected GP practices in two of five administrative Danish regions. A detailed description of the recruitment process is described elsewhere. 15

All pregnant women booking an appointment for the first prenatal assessment with one of the participating GPs were eligible for inclusion in the project and consecutively invited for the project. The women received oral and written information about the project and were included after signing a consent form granting access to their Pregnancy Health Records and allowing the researchers to contact them and send questionnaires. The inclusion period was from April 1, 2015 to August 15, 2016. Women were excluded if they did not complete each of the electronic questionnaires (all in Danish), if they withdrew consent, if the Pregnancy Health Record was missing or if the pregnancy ended in miscarriage.

Data were collected from the clinical interview conducted by the GPs during the first prenatal assessment, reported in the Pregnancy Health Record, and from electronic patient questionnaires. The Pregnancy Health Record is a two-page form completed between gestational weeks 6 and 10. The electronic questionnaires for this study were sent to the pregnant women by email after each of the three prenatal assessments, and could only be returned if fully completed. Questionnaires were re-sent to non-respondents after 2 weeks, and in the case of no response, reminders were sent by email and text message.

Outcomes were the experience of back pain, leg cramps, pelvic cavity pain, pelvic girdle pain, and uterine contractions in the second and third trimesters. These five pregnancy-related pain symptoms were explored in the electronic questionnaires with simple yes/no questions. For some of the symptoms, the questionnaires contained anatomic pictures with arrows pointing, for example, at the area of pelvic girdle pain (see Appendix S1).

The following describe the factors in the first trimester assessed for importance for the experience of pain in the second and third trimesters.

Pregnancy-related physical symptoms: nausea, vomiting, back pain, pelvic girdle pain, pelvic cavity pain, itching of the vulva, varicose

2nd trimester

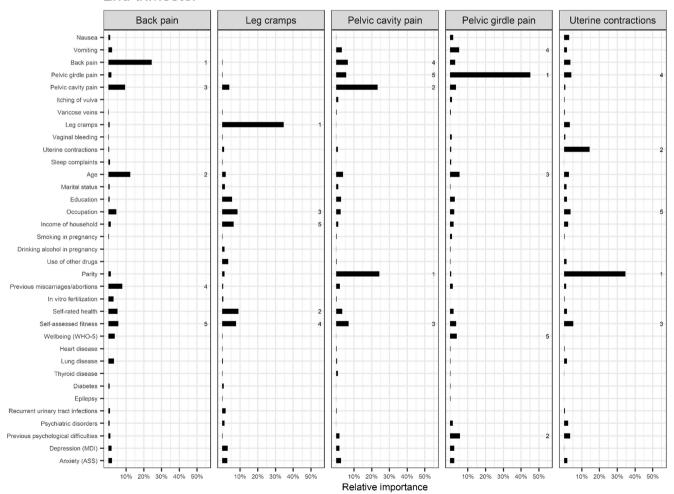


FIGURE 2 Relative importance of factors in the second trimester. The relative importance (%) of pregnancy-related factors is distributed among the five pain outcomes; back pain, leg cramps, pelvic cavity pain, pelvic girdle pain and uterine contractions. Larger bars indicate greater importance. The top five important factors are indicated in the right margin of each panel.

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veins, leg cramps, vaginal bleeding, uterine contractions and sleep complaints (yes/no).

Sociodemographic factors: Age (<25 years, 26–30 years, 31–35 years, 36+ years), marital status (married or cohabiting, others, alone), education (none, 3 years, 4 or 5 years, >5 years), occupation (employed, unemployed, student, other, sick leave) and income of household (≤39,999 €, 40,000–79,999 €, 80,000–119,999 €, ≥120,000 €, do not want to answer). 16,17

Lifestyle: Smoking in pregnancy, drinking in pregnancy, and use of other drugs yes/no).¹⁷

Reproductive background: Parity (no, yes once, yes multiple times), previous miscarriages/abortions (no, yes one miscarriage, yes >1 – last was a miscarriage, yes one abortion, yes >1 – last was abortion) and in vitro fertilization (yes/no).¹⁷

Physical health: Self-rated health (very good, good, fair, poor), ¹⁸ self-assessed fitness (very good, good, fair, poor, very poor), ¹⁹ well-being measured by the World Health Organization five wellbeing index, where low scores express low wellbeing (WHO-5 score ≤50, WHO-5 score >50). Low score is associated with risk of early death. ²⁰

Chronic physical diseases: Heart disease, lung disease, thyroid disease, diabetes, epilepsy and recurrent urinary tract infections (yes/no).¹⁷

Mental health: Psychiatric disorders (yes/no)¹⁷ previous psychological difficulties (no, yes but I did not seek treatment, yes and I did seek treatment), depression (Major Depression Inventory (MDI) score 21 or more),²¹ and anxiety (Anxiety Symptom Scale (ASS) score 10 or more).²¹

2.2 | Statistical analyses

The relative importance of each factor in a set of factors was computed in a dominance analysis as the mean increase in a pseudo R^2 -value when the factor was added to a logistic regression model across all possible logistic regression models including the remaining variables. ²² McFadden's pseudo R^2 has similar properties to the ordinary coefficient of determination, R^2 , and is useful as a substitute for the ordinary R^2 for this purpose. The mean increases were normalized to add up to one so that for each factor we obtained the fraction



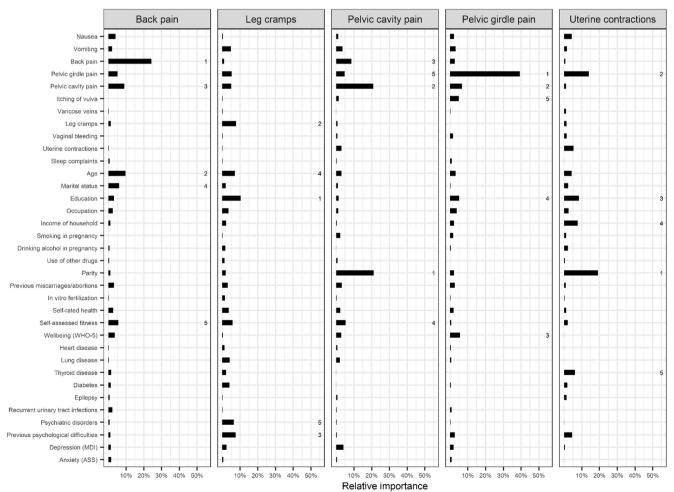


FIGURE 3 Relative importance of factors in the third trimester. The relative importance (%) of pregnancy-related factors is distributed among the five pain outcomes; back pain, leg cramps, pelvic cavity pain, pelvic girdle pain and uterine contractions. Larger bars indicate greater importance. The top five important factors are indicated in the right margin of each panel.



TABLE 2 Multivariable logistic regression analysis for the most important factors for each pain symptom.

	Second trimester								
	Back pain		Leg cramps		Pelvic cavity pair	1	Pelvic girdle pain	Uterine contractions	
	OR (95% CI)	Р	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)
Vomiting							1.48 (1.16-1.88)	0.0015	
Back pain	2.77 (2.07-3.76)	<0.0001			1.55 (1.19-2.02)	0.0011			
Pelvic girdle pain					1.58 (1.23-2.03)	<0.0001	3.16 (2.48-4.05)	<0.0001	1.59 (1.25-2.0
Pelvic cavity pain	1.76 (1.31-2.37)	0.0002			2.54 (1.92-3.40)	<0.0001			
Itching of vulva									
Leg cramps			3.58 (2.32-5.72)	<0.0001					
Uterine contractions									6.39 (2.53-21
Age									
<25 years	ref	-					ref	-	
26-30 years	0.51 (0.30-0.84)	0.0104					0.60 (0.41-0.88)	0.0097	
31-35 years	0.34 (0.20-0.55)	<0.0001					0.51 (0.35-0.76)	0.0008	
36+ years	0.34 (0.20-0.59)	0.0001					0.57 (0.37-0.87)		
Marital status	,								
Married or cohabiting									
Others									
Alone									
Education									
None									
3 years									
4 or 5 years									
>5 years									
Occupation									
Employed			ref	_					ref
			0.63 (0.37-1.06)						
Unemployed									0.60 (0.36-1.0
Student			0.93 (0.65-1.32)						1.09 (0.78-1.5
Other			1.68 (0.90-3.27)						0.52 (0.29-0.9
Sick leave			1.03 (0.45-2.49)	0.9380					1.01 (0.41-2.7
Income of household									
≤39,999€			ref	-					
40,000-79,999 €			1.05 (0.71-1.56)						
80,000-119,999 €			1.07 (0.72-1.61)						
≥120,000€			0.76 (0.46-1.25)						
Do not want to answer			1.42 (0.90-2.23)	0.1320					
Parity									
No					ref	-			ref
Yes once					2.05 (1.57-2.68)				1.88 (1.44-2.4
Yes multiple times					2.93 (2.06-4.20)	<0.0001			3.91 (2.67-5.8
Previous miscarriages/ abortions									
No	ref	-							
Yes one miscarriage	1.00 (0.69-1.47)	0.9950							
Yes>1 – last was miscarriage	0.94 (0.58-1.53)	0.7870							
Yes one abortion	2.16 (1.39-3.47)	0.0009							
Yes>1 -last was abortion	0.62 (0.34-1.16)	0.1300							



	Back pain		Leg cramps		Pelvic cavity pain		Pelvic girdle pain		Uterine contractions		
P	OR (95% CI)	P	OR (95% CI)	Р	OR (95% CI)	Р	OR (95% CI)	Р	OR (95% CI)	Р	
	2.73 (1.99-3.80)	<0.0001			1.68 (1.27-2.23)	0.0003					
0.0002					1.48 (1.14-1.90)	0.0032	2.58 (2.04-3.27)	<0.0001	2.07 (1.51-2.85)	<0.000	
	1.75 (1.28-2.42)	0.0006			2.18 (1.61-2.97)	<0.0001	1.52 (1.19-1.95)	0.0010			
							1.56 (1.16-2.09)	0.0030			
			1.95 (1.29-3.02)	0.0022							
0.0005											
	ref	-	ref	-							
	0.44 (0.24-0.77) 0.31 (0.17-0.53)	0.0052 <0.0001	1.05 (0.70-1.55) 0.75 (0.50-1.13)	0.8240 0.1750							
	0.31 (0.17-0.55)	0.0001	1.00 (0.63–1.56)	0.9860							
	0.01 (0.17 0.33)	0.0001	1.00 (0.00 1.00)	0.7000							
	ref	-									
	0.24 (0.07-0.80)	0.0169									
	0.62 (0.33-1.22)	0.1560									
			ref	-			ref	-	ref	-	
			1.08 (0.77-1.52)	0.6620			1.01 (0.72-1.41)	0.9450	0.91 (0.59-1.40)	0.6730	
			1.48 (1.03-2.13)	0.0328			0.82 (0.59-1.15)	0.2530	1.05 (0.66-1.66)	0.8420	
			0.97 (0.65-1.45)	0.8670			0.59 (0.40-0.87)	0.0078	1.69 (0.94-3.08)	0.0839	
-											
0.0532											
0.6350											
0.0373											
0.9860											
									ref	-	
									1.43 (0.87-2.32)	0.1490	
									1.46 (0.88-2.39)	0.1400	
									1.87 Don't1-4.04)	0.0995	
									1.16 (0.67-2.01)	0.6000	
-					ref	_			ref	-	
<0.0001					1.89 (1.43-2.50)	<0.0001			1.60 (1.14-2.27)	0.0069	
<0.0001					2.69 (1.86-3.97)	<0.0001			3.20 (1.91-5.65)	<0.000	



TABLE 2 (Continued)

	Second trimester								
	Back pain		Leg cramps	Leg cramps		Pelvic cavity pain		Pelvic girdle pain	
	OR (95% CI)	Р	OR (95% CI)	Р	OR (95% CI)	P	OR (95% CI)	Р	OR (95% CI)
Self-rated health									
Very good			ref	-					
Good			1.79 (1.26-2.55)	0.0014					
Fair			1.97 (1.26-3.07)	0.0029					
Poor			2.40 (1.03-5.76)	0.0455					
Self-assessed fitness									
Very good	ref	-	ref	-	ref	-			ref
Good	1.95 (0.99-3.88)	0.0550	0.70 (0.35-1.38)	0.2970	3.12 (1.54-6.64)	0.0021			0.94 (0.46-0.19)
Fair	2.82 (1.45-5.55)	0.0023	0.89 (0.45-1.77)	0.7400	3.04 (1.52-6.37)	0.0022			0.80 (0.39-1.55
Poor	3.33 (1.66-6.78)	0.0008	0.73 (0.35-1.51)	0.3920	3.08 (1.50-6.61)	0.0028			0.63 (0.30-1.26
Very poor	3.46 (1.16-11.5)	0.0318	0.52 (0.18-1.46)	0.2130	7.87 (2.36-32.2)	0.0017			0.62 (0.21-1.85)
Wellbeing (WHO-5)							1.60 (1.19-2.16)	0.0020	
Thyroid disease									
Psychiatric disorders									
Previous psychological difficulties									
No							ref	-	
Yes but I did not seek treatment							1.29 (0.94-1.76)	0.1090	
Yes and I did seek treatment							1.71 (1.31-2.24)	0.0001	

Note: The table shows the distribution of the factors and the directions of their effects. The null hypothesis claims no association between pregnancy-related factors and pregnancy-related pain in the second or third trimester. A P-value \leq 0.05 is considered significant.

of the total R^2 attributable to that factor. This allows easy comparison of the importance of the factors. For each of the 10 analyses, the five most important factors were indicated.

For each of the outcomes, the five factors with the largest relative importance among all selected factors were assessed with odds ratios (ORs) and 95% confidence intervals (95% CI) from multivariable logistic regression models in order to determine the size and direction of the effects of these factors.

2.3 | Ethics statement

All procedures were in accordance with the Declaration of Helsinki II and Danish law. Approval from the Danish Data Protection Agency was obtained (Journal 2014-41-3018) on March 31, 2014. According to Danish Law, studies based entirely on data collected from registers and questionnaires do not need approval from an ethics committee.

3 | RESULTS

A total of 1491 pregnant women gave informed consent to participate in the study (Figure 1). In all, 96% (1438 women) responded to

the first questionnaire and, of these, 1328 (92%) women returned the second and third questionnaires. The most common reason to leave the study was miscarriage (n = 102, 7%); 58 women (4%) withdrew their consent or did not answer all the questionnaires.

Characteristics of the women in the present study, both total and stratified by the experience of pain in the second and third trimesters, respectively, are presented in Table 1. There were 848 women who experienced pain in the second trimester (480 without pain) and 638 in the third trimester (690 without pain). The most frequent pain types were the same in the second and third trimesters: back pain (29% and 27%, respectively), pelvic girdle pain (47% and 46%, respectively), and pelvic cavity pain (25% and 23%, respectively). Pain was more frequent among women who were more than 30 years old, had not given birth before, and had in vitro fertilization.

The most visible results in Figures 2 and 3, in which the relative importance of a set of pregnancy-related factors for each of the five pain outcomes in the second and third trimester, respectively, are shown, are the autoregressive effects, ie the most important predictor for a type of pain in later trimesters is the presence of the corresponding pain in the first trimester. In addition to these, there are several other important factors such as age, parity as well as so-cioeconomic factors such as education, occupation, and income of household. Further, psychological factors such as self-rated health,



	Third trimester									
	Back pain		Leg cramps	Leg cramps		Pelvic cavity pain		n	Uterine contract	ions
P	OR (95% CI)	P	OR (95% CI)	Р	OR (95% CI)	Р	OR (95% CI)	Р	OR (95% CI)	P

ef	-			ref	-				
.08 (0.53-2.14)	0.8330			2.28 (1.16-4.57)	0.0182				
.51 (0.75-2.94)	0.2370			2.68 (1.38-5.29)	0.0038				
.32 (1.10-4.77)	0.0233			2.80 (1.40-5.70)	0.0039				
.39 (0.46-4.59)	0.5670			3.44 (1.12;12.3)	0.0400				
						1.71 (1.30-2.27)	0.0002		
								0.41 (0.22-0.81)	0.0075
		0.60 (0.38-0.95)	0.0284						
		ref	-						
		0.80 (0.59-1.08)	0.1430						
		1.29 (0.97–1.72)	0.0789						
.(08 (0.53-2.14) 51 (0.75-2.94) 32 (1.10-4.77)	08 (0.53-2.14) 0.8330 51 (0.75-2.94) 0.2370 32 (1.10-4.77) 0.0233	08 (0.53-2.14)	08 (0.53-2.14)	0.8330 2.28 (1.16-4.57) 0.8330 2.28 (1.16-4.57) 0.10.75-2.94) 0.2370 2.68 (1.38-5.29) 0.23 2 (1.10-4.77) 0.0233 2.80 (1.40-5.70) 0.39 (0.46-4.59) 0.5670 3.44 (1.12;12.3) 0.60 (0.38-0.95) 0.0284 ref - 0.80 (0.59-1.08) 0.1430	0.8330	2.28 (1.16-4.57) 0.0182 51 (0.75-2.94) 0.2370 2.68 (1.38-5.29) 0.0038 32 (1.10-4.77) 0.0233 2.80 (1.40-5.70) 0.0039 39 (0.46-4.59) 0.5670 3.44 (1.12;12.3) 0.0400 1.71 (1.30-2.27) 0.60 (0.38-0.95) 0.0284 ref - 0.80 (0.59-1.08) 0.1430	2.28 (1.16-4.57) 0.0182 51 (0.75-2.94) 0.2370 2.68 (1.38-5.29) 0.0038 32 (1.10-4.77) 0.0233 2.80 (1.40-5.70) 0.0039 39 (0.46-4.59) 0.5670 3.44 (1.12;12.3) 0.0400 1.71 (1.30-2.27) 0.0002 0.60 (0.38-0.95) 0.0284	2.28 (1.16-4.57) 0.0182 51 (0.75-2.94) 0.2370 2.68 (1.38-5.29) 0.0038 52 (1.10-4.77) 0.0233 2.80 (1.40-5.70) 0.0039 53 (0.46-4.59) 0.5670 3.44 (1.12;12.3) 0.0400 1.71 (1.30-2.27) 0.0002 0.41 (0.22-0.81) ref - 0.80 (0.59-1.08) 0.1430

self-assessed fitness, psychiatric disorders, previous psychological difficulties and well-being were important to some degree for all pain outcomes.

Table 2 reports the size and direction of the effects for each of the five pregnancy-related pain symptoms for the five most important factors in the second and the third trimester. Pain in the first trimester was related to pain in the second and third trimester; not only the same type of pain but across pain types as well. Higher age was associated with lower odds of back pain in the second and third trimesters and lower odds of pelvis girdle pain in the second trimester. Parity of one or more was associated with having pelvic cavity pain and uterine contractions in the second and third trimesters compared with nulliparity, and the association was strongest for parities >1. There were increasing odds for leg cramps in the second trimester according to decreasing self-rated health. For back pain in the second and third trimesters and pelvic cavity pain in the second trimester, the odds increased as the women's estimated self-assessed fitness decreased. Low WHO-5 wellbeing score was associated with pelvis girdle pain in the second and third trimesters. We did not explore the correlations between WHO-5 and fitness, but did find that both self-assessed fitness and WHO-5 score were individually important for the experience of pain during pregnancy.

4 | DISCUSSION

This study found that the most important factor for pregnancy-related pain in the second and third trimesters is the presence of the corresponding pain in the first trimester. Age, socioeconomic factors (education, occupation and income of household), self-rated health, self-assessed fitness, wellbeing (WHO-5 score), previous psychological difficulties, and parity were also important factors.

The ethology of pelvic girdle pain and back pain remains unclear, and reports on risk factors other than anamneses of pelvic girdle pain and back pain provide conflicting results. ¹¹ In line with our results, several physical and psychosocial factors have been shown to increase the risk of pregnancy-related pain, but no single, dominant risk factor has been identified. ^{23,24} Our results are supported by a recent scoping review exploring 24 papers. The heterogeneity was high and the studies used a total of 148 risk factors among which only 14 factors were examined in more than one study. Moreover, the following factors have proven to be associated with pregnancy-related back pain beyond a history of back pain or pelvic girdle pain: overweight/obesity, parity, younger age, lower educational level, no pre-pregnancy exercise, physically demanding work, previous back trauma/disease, progestin-intrauterine device use, stress, depression and anxiety. ¹²

As pregnancy progresses, the risk of experiencing pain increases. Pelvic girdle pain and back pain are common and occur often in the 18th week, reaching peak intensity between the 24th and 36th week of pregnancy, and pain in the first trimester is a strong predictor of pain in the third trimester. ^{10,11} This corresponds well with the results of this study. Further, pelvic girdle pain has previously been demonstrated to increase from 11% in first-time pregnancies to 18%–21% in later pregnancies, which supports our finding of increasing parity as a risk factor in pregnancy-related pain. ²⁵

Depression and anxiety have previously been identified as risk factors to pelvic pain; ¹² this was not found in the present study. Our women completed a depression (MDI) and anxiety (ASS) questionnaire in the first, second and third trimesters, but we did not find that depression or anxiety was among the important factors for experiences of back pain and pelvic cavity pain. A previous study within the same group of women found that a high depression score (MDI>20) at 8 weeks postpartum (6.6% of the women) was only associated with back pain and pelvic cavity pain in the first trimester. ⁷ Another study investigating back pain, pelvic girdle pain, functional disability and depression/anxiety also only found this association. ⁶ If the woman has previously had psychological difficulties, this was found to be a factor associated with experiencing pelvic girdle pain, particularly for those who seek treatment.

Lastly, the analysis in this paper included some factors combining physical and mental health; self-rated health and self-assessed fitness. Self-rated health is defined as a person's subjective assessment of their general health status and is widely used as a health marker. Few studies have explored self-rated health among pregnant women and our new findings of low self-rated health as a risk factor for experiencing pain in late pregnancy has not, to our knowledge, been described elsewhere. One study found that selfrated health can induce feelings of being normal but also increase perceptions of pregnant-related risk and concerns of being judged by the midwife.²⁶ Furthermore, poor self-rated health before pregnancy has been largely characterized by a history of psychiatric care and was associated with small-for-gestational-age children and preterm birth. 27 Studies of poor self-rated health among pregnant women found symptoms of depression and stress, health diagnoses, high body mass index, 28 low birthweight or preterm infants.²⁹ Conversely, higher self-rated health in pregnancy predicted fewer childbirth complications and lower odds of cesarean delivery.30

Self-assessed fitness is not as well described in the literature as self-rated health but several validity and reliability studies found that self-assessed fitness is a practical and cost-effective alternative to performance-based fitness tests. 19,31,32 In our study, low self-assessed fitness was associated with experiences of different types of pain during the second and third trimesters. Those women may have been inactive before pregnancy, and it is known that the level of physical activity before pregnancy affects the insensitivity of physical activity during pregnancy. 33 Physical activity before and during pregnancy may not reduce the odds of pregnant-related low back pain and pelvic girdle pain but it is an effective treatment to

decrease the severity and alleviate the pain.^{34,35} A correlation between physical activity and the quality of life has previously been documented.³⁶

Previous studies of pain in pregnancy have mainly focused on back pain and or pelvic girdle pain. The present study is novel because it includes all common types of pain, pregnancy-related discomfort and psychosocial factors measured in the first trimester. Great effort was put into recruiting and obtaining responses from the pregnant women, but GPs may to some degree have recruited only a subset of pregnant women for various reasons (such as convenience, eg women who did speak Danish) and participation in the longitudinal questionnaire survey was voluntary. 15 However, this pregnancy study offered a unique opportunity to identify the source population because almost all pregnant women in Denmark contact their GP in early pregnancy. There were very few non-responders among those who agreed to participate and complete data were obtained from almost all recruited participants. No exclusion criteria were used in recruitment, thus our sample of women can be perceived as being fairly representative of the general population of pregnant women in Denmark.

Conventional approaches to assess the importance of factors use sequential hypothesis testing which is sensitive to correlations between the factors assessed. In short, these approaches arrive at a set of important factors, but not an overview of the importance of all variables; some important factors may not be identified because of correlations with other factors. Instead, we use an analysis approach that directly addresses the relative importance of a set of possible predictive factors. This approach may not be commonly used in clinical research but it has been used more often, eg in organizational research. We pragmatically limited the set of factors investigated to those found in The Pregnancy Health record of the women, along with some clinical questions easily asked by the GP. Consequently, the mode of inquiry may be affected by the GP's questioning style or the woman's reporting style, but this is the way most of the information about the pregnant woman is obtained by GPs.

The use of a questionnaire instead of direct observation in the prenatal consultations to gather the data, and the scope of the analyses, limits our conclusions. The broad definition of pain as a simple yes/no answer to the question of whether there is pain ignores aspects of the pain such as severity and function limitation that are important in the woman's perception of the pain. 37,38 We did not pursue narrower definitions of pain in the present analyses, as we aimed to focus not on the acute meanings of the pain but more on the pain as a risk factor for the further pregnancy and thereafter. Moreover, severe or worrisome pain symptoms were rare and typically handled as acute conditions outside the prenatal consultations, thereby limiting their usefulness as outcome.

The electronic questionnaire was not validated against physical measures of pain. However, the questionnaire was meant to mimic elements of a prenatal consultation and assessed the women's comprehension of the pain, which may differ from the clinical definition. The differentiation between anatomic locations of pain may be difficult and, in our questionnaire, it was not possible to distinguish low

back pain from pelvic girdle pain, or pelvic cavity pain by means of a physical test. 13 Although localization of pelvic girdle pain and back pain was improved by the addition of illustrations, the pain indications should still be viewed as subjective measures of pain.

Notably, factors related to overall wellbeing - physical and mental - may be important and some interventions instituted. A way of improving pregnant women's self-rated health and selfassessed fitness could be the GP talking about the importance of preconception of health to women before pregnancy. Preconception interventions are described in a paper series in The Lancet. 39-41 The paper highlights the pregnancy-planning period as a highly motivated time for lifestyle changes, eg improving diet, reducing/ quitting smoking and/or alcohol, and increasing exercise to reduce the risk of developing pain during pregnancy.⁴² Lastly, women with back pain and pelvic girdle pain should be referred to educational programs and exercise early in the pregnancy. 43-45 Women with severe low back pain with neurological symptoms should be referred to neurology.46

CONCLUSION

When including physical risk factors, sociodemographic factors, psychological factors and the clinical risk factors, women's experiences of pregnancy-related pain in the first trimester are the most important predictors for pain later in pregnancy. Beyond the expected autoregressive positive effects of pregnancy-related pain, notably self-assessed fitness, age and parity, were predictive of pain later in pregnancy.

AUTHOR CONTRIBUTIONS

RE designed the study. RE and DN collected and RE, FG and VS analyzed the data. RE, GO, SV, ML and VS drafted the paper. All authors read, discussed and approved the article.

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CONFLICT OF INTEREST STATEMENT

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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