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Possible relationship between general and pregnancy-related anxiety during the first trimester of pregnancy and the birth process: a prospective cohort study

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ABSTRACT

Objectives The rate of interventions during childbirth has increased dramatically during the last decades. Maternal anxiety might play a role in the progress of the labour process and interventions during labour. This study aimed to identify associations between first trimester anxiety and the birth process, including any interventions required during labour. In addition, differences in the associations by parity and ethnicity were explored.

Design Prospective cohort study

Setting Primary care midwifery practices and secondary/tertiary care obstetric practices in Amsterdam, participating in the multi-ethnic ABCD study (participation rate 96%; response 8,266/12,373 (67%)).

Participants Included were women with singletons, alive at labour start, with a gestational age ≥24 weeks (n=6,443).

Independent variable General anxiety (STAI state) and pregnancy-related anxiety (PRAQ), were self-reported at the end of the first trimester.

Outcomes Associations between both forms of anxiety and several indicators of the birth process were analysed. Subgroup analyses were performed for parity and ethnicity.

Results The prevalence of high general anxiety (STAI score ≥ 43) and pregnancy-related anxiety (PRAQ score ≥P90) were 30.9% and 11.0%, respectively. After adjustment, both general and pregnancy-related anxiety were associated with pain relief and/or sedation (OR for general anxiety 1.27;95%-CI 1.07-1.50;OR for pregnancy-related anxiety 1.51;95%-CI 1.21-1.88). In multiparae, general anxiety was associated with induction of labour (OR 1.61;95%-CI 1.19-2.19), pregnancy-related anxiety was associated with primary caesarean section (OR

1.67;95%-CI 1.02-2.75). In nulliparae, pregnancy-related anxiety was associated with referral during labour (OR 1.38; 95%-CI 1.02-1.86). Associations were largely similar for all ethnicities.

Conclusions

High levels of general and pregnancy-related anxiety in early pregnancy contribute modestly to more interventions during the birth process with similar associations between ethnic groups, but with some differences between primiparae and multiparae.

Abbreviations: ABCD study = Amsterdam Born Children and their Development study, BMI = body mass index, PRN = Dutch Perinatal Registration, STAI = State Trait Anxiety Inventory, PRAQ = Pregnancy-Related Anxiety Questionnaire

ARTICLE SUMMARY

- We studied the possible relationship between pregnancy-related as well general anxiety with the progression of the process of labour, while most studies only studied pregnancy-related anxiety.

- We performed a prospective study in a large multi-ethnic cohort.

- We used validated questionnaires to assess both forms of anxiety.

- Anxiety was measured in the first trimester of pregnancy.

INTRODUCTION

The rate of interventions during childbirth has increased dramatically in recent decades. For example, in the Netherlands, from 1993-2002 the caesarean section rate rose from 8.1% to 13.6%.[1] The rate of labour induction increased during 2008-2013 from 15% to 21%.[2] A similar rise in caesarean sections occurred in other western countries.[3-6]

The progression of the birth process and concomitant interventions are associated with maternal characteristics such as age, parity, body mass index (BMI), ethnicity, illness, infant birth weight, as well as with organisational factors, such as existing guidelines, the availability of 24-h pain relief, the profession of the obstetric care provider (midwife versus physician), and the level of care (primary/secondary).[7-11] Moreover, maternal anxiety might play a role in the birth process. Although one review found no overall association between anxiety and obstetric complications, specific types of anxiety (such as fear of childbirth) may be associated with specific complications and interventions, such as prolonged labour and caesarean section.[12]

Several studies have shown a relationship between fear of childbirth and elective caesarean section [13-16], duration of labour [17-19], emergency caesarean section [18, 20] and epidural analgesia.[21] On the other hand, other studies reported no such relationships.[22-24] One explanation for these inconsistencies could be differences in cultural, social and organisational characteristics between countries. These factors can mediate or exacerbate the effect of anxiety on the birth process and on concomitant interventions. Inconsistencies might also be explained by differences in maternal characteristics influencing the association between anxiety and the birth process. For example, some ethnic groups are more

susceptible to stress-induced neuroendocrine and inflammatory pathways which could lead to adverse perinatal outcomes.[25-28] Also, cultural and social differences between ethnic groups (e.g. language barriers, unfamiliarity with the obstetric care organisation) may explain differences between ethnic groups regarding the influence of anxiety on the birth process.[29-32] In addition, parity and level of care (factors associated with the progression of birth) might influence the association between anxiety and the birth process.[7, 9-11] To our knowledge, no study has investigated the level of care and ethnicity in the association between general and pregnancy-related anxiety, and the progression of birth.

If anxiety does have a detrimental effect on the birth process, screening early in pregnancy for anxiety (and, where indicated, appropriate treatment) is desirable.

Therefore, this study investigates the association between general anxiety and/or pregnancy-related anxiety measured during the first trimester of pregnancy and the birth process, and the interaction of this association with parity, ethnicity and the level of care at the start of labour.

METHODS

Study design and participants

Data were derived from the Amsterdam Born Children and their Development (ABCD) study, a large multi-ethnic prospective cohort study.[33] The ABCD study is aimed at examining the relationship between maternal lifestyle and psychosocial conditions during pregnancy and the child's health at birth as well as later in life. Between January 2003 and March 2004,

participating obstetric care providers (midwives and hospital obstetricians; participation rate 96%) invited pregnant women in Amsterdam at their first antenatal visit to enroll in the ABCD. A total of 12,373 women were approached (99% of the target population). Within two weeks of this first contact, women who agreed to take part were sent a questionnaire, covering socio-demographic conditions, obstetric history and psychosocial conditions. Consent forms were also sent for the linkage of study data to medical records as well as to data from the Dutch Perinatal Registration (PRN).

A total of 8266 women (response rate 67%) filled in the pregnancy questionnaire at an average of 16 weeks gestation (IQR 14-18 weeks) and 7043 gave permission for perusal of their medical records. To facilitate participation by women unable to speak Dutch, questionnaires were also available in Turkish, Arabic and English, and women could also complete the questionnaire with the assistance of an interviewer. Participation of foreign-born women was lower (42-64%) than for Dutch-born women (77%) but comparable with response rates in other population-based, multi-ethnic studies in the Netherlands.[34] In the present study we included women with a singleton pregnancy, a gestational age ≥ 24 weeks, and a living foetus at the start of labour.

Approval for the study was obtained from the Medical Ethical Committees of the participating hospitals and the Registration Committee of the Municipality of Amsterdam. All women gave written informed consent.

Definition and measurement of variables

General and pregnancy-related anxiety

General anxiety was assessed using the Dutch version of the State-Trait Anxiety Inventory (STAI).[35-36] The 20 items regarding the state anxiety subscale were included in our questionnaire, with each item scored on a 4-point scale. The anxiety score was dichotomised in low-average (<43 points) and high anxiety (≥ 43 points).[37] In our sample, the internal consistency (Cronbach's alpha) of the scale was 0.94.

Pregnancy-related anxiety was assessed using an abbreviated 10-item version of the Pregnancy-Related Anxieties Questionnaire (PRAQ).[38-39] The internal consistency (Cronbach's alpha) was 0.79; each item was scored on a 4-point scale. Three aspects that can be distinguished in the PRAQ are 'fear of labour', 'fear of bearing a physically or mentally handicapped child' and 'concern about one's appearance'. In the present study we used the total score on pregnancy-related anxiety. One question was only applicable for nulliparous women ("I am scared of labour and birth because I have never experienced this"), resulting in a maximum score of 40 for nulliparous women and 36 for multiparous women. Because cut-off scores were not available for dichotomisation of the results from this instrument, we used the 90th percentile to identify women with a high level of pregnancy-related anxiety.[40] This resulted in cut-off scores of 28 and 24 for nulliparous and multiparous women, respectively.

Birth process

Outcome data on the birth process were obtained by linking our records with the PRN database. Validation of the PRN database has been described previously.[34] The outcome variables were determined from the records of the Registry of Midwives, the Registry of Obstetricians and the Registry of Paediatricians according to the decision rules of the PRN.[41]

We defined the following outcomes: primary caesarean (yes/no), induction of labour (yes/no), referral during labour [only in the group that started labour under primary care; (yes/no)], augmentation (yes/no), pain relief/sedation (yes/no), duration of first stage of labour (≤ 12 h/>12 h; only available in registry of midwives), secondary caesarean (yes/no), vaginal instrumental delivery [ventouse or forceps; (yes/no), duration of second stage (< 1.5 h/≥ 1.5 h)].

Covariates

The following covariates were included in the analyses: maternal age (years), ethnicity, education (years after primary school), pre-pregnancy BMI (kg/m^2), parity (nulliparae/multiparae), smoking during pregnancy (yes/no), alcohol use during pregnancy (yes/no), hypertensive disorders and diabetes (pre-existent or detected during pregnancy), gestational age at delivery (weeks), care at start of labour (primary/secondary), and birth weight (g). Ethnicity was based on the birth country of the participant's mother (self-reported) and included the following categories: Dutch, Turkish, Moroccan, Black (Antillean/Aruban, Surinamese, Ghanaian or other African descent), other non-Western and other Western countries. Pre-pregnancy weight and height, education, smoking and alcohol use during pregnancy were self-reported in the questionnaire. Parity, birth weight, gestational age, hypertension and diabetes were extracted from the PRN database.

Statistical analysis

Descriptive statistics were used to profile the sample characteristics according to the level of maternal general anxiety and of pregnancy-related anxiety. Categorical variables were

described by percentages per category. Continuous variables were described using the mean and 95% confidence intervals (CI), if normally distributed and, if not, with the median and minimum and maximum values. Risks were presented as odds ratios (OR) and 95% CI. Differences were tested with Student's t test or Mann-Whitney U test for continuous variables and Pearson's chi square test for categorical variables. Associations between high general and/or pregnancy-related anxiety compared to low anxiety were analysed for each outcome using multiple logistic regression analyses. All potential confounders were determined a priori and added to the regression model in two steps. In the first step we adjusted for general covariates: age, ethnicity, education, pre-pregnancy BMI, parity, smoking and alcohol use; in the second step hypertension, diabetes, gestational age and birth weight were added to the model to determine whether these pregnancy-related covariates confounded the association between anxiety and each of the outcomes. Subgroup analyses were performed according to parity (nulliparous versus multiparous women), ethnicity (Dutch, Turkish, Moroccan and Black) and care at start of labour (primary/secondary care). No subgroup analysis was performed in the ethnic groups 'other Western' and 'other non-Western' as each of these groups represented a diverse selection of ethnicities. To formally test whether different associations existed for the different subgroups (parity, ethnicity, and care at start of labour) between STAI or PRAQ and the birth process variables, interaction terms were added to the final model.

All analyses were performed with SPSS 21.0 (IBM Statistics, USA).

RESULTS

Response

Of the 8266 women who completed the pregnancy questionnaire, for 6616 women valid results for the STAI or PRAQ and outcome data, were available. After exclusion of 173 women (with a multiple foetus, a gestational age ≤ 24 weeks, or antenatal death), 6443 records were available for analysis (Figure 1). Most women completed both the STAI and the PRAQ (n=6335); 37 women completed only the STAI and 71 women only the PRAQ.

Covariates according to anxiety levels

A high STAI score (further referred to as 'high general anxiety') was found in 31.0% of the sample and a high score on the PRAQ (further referred to as 'high pregnancy-related anxiety') in 11.1% of the sample. The STAI score was moderately correlated with the PRAQ score (Pearson's r=0.36; p<0.001).

High general anxiety and high pregnancy-related anxiety were more frequently observed in younger women, in women with non-Dutch ethnicities, fewer years of education, higher pre-pregnancy BMIs, smoking women, women with less alcohol consumption, and in women who gave birth to babies with a lower birth weight. There were no differences in the rates of hypertension and gestational age between the high and low anxiety groups; however, diabetes and secondary care at the start of labour were more frequently observed in women with high general anxiety. Nulliparous women appeared to be at lower risk for high general

anxiety compared to multiparous women, but at an increased risk for high pregnancy-related anxiety (Table 1).

Table 1. Maternal characteristics according to first trimester general anxiety and pregnancy-related anxiety

		General anxiety			Pregnancy-related anxiety		
		Low n=4400[1]	High n=1972[1]	p-value[2]	Low n=5697[1]	High n=709[1]	p-value[2]
Anxiety score	-median (min-max)						
Nulliparae		33 (20-42)	49 (43-80)		21 (10-27)	30 (28-40)	
Multiparae		33 (20-42)	49 (43-74)		18 (9-23)	26 (34-36	
Age (years)	-mean (95% CI)	31.5 (31.4-31.7)	29.7 (29.5-30.0)	<.001	31.2 (31.1-31.4)	28.7 (28.3-29.2)	<.001
Ethnicity	-%			<.001			<.001
Dutch		63.5	38.9		58.8	30.1	
Turkish		2.6	8.6		3.6	12.9	
Moroccan		5.4	12.1		6.5	15.3	
Black		6.5	12.8		8.6	8.1	
Other Western		14.1	13.3		13.7	14.4	
Other non-Western		7.9	14.3		8.9	19.3	
Education (years)	-mean (95% CI)	9.6 (9.5-9.7)	7.5 (7.3-7.7)	<.001	9.2 (9.1-9.3)	7.1 (6.8-7.5)	<.001
Pre-pregnancy BMI (kg/m^2)	-mean (95% CI)	22.8 (22.7-22.9)	23.8 (23.6-24.0)	<.001	23.0 (22.9-23.1)	23.8 (23.5-24.1)	<.001
Nulliparae	-%	59.1	49.5	<.001	55.5	59.9	.025
Smoking in pregnancy	-%	7.3	15.2	<.001	9.0	15.0	<.001
Alcohol in pregnancy	-%	24.7	16.0	<.001	22.9	15.3	<.001
Hypertensive disorders	-%	12.2	12.5	.70	12.1	12.9	.54
Diabetes	-%	1.8	3.1	.001	2.1	3.1	.08
Gestational age	-%			.27			.87
<37 weeks		5.0	6.0		5.4	5.1	
37-41 weeks		85.7	84.7		85.4	85.2	
>=42 weeks		9.3	9.3		9.2	9.7	
Care start labour	-%			<.001			.29
primary care		60.1	54.6		58.6	56.6	
secondary care		39.9	45.4		41.4	43.4	
Birth weight (g)	-mean (95% CI)	3473 (3456-3490)	3379 (3354-3405)	<.001	3450 (3435-3465)	3391 (3351-3431)	.009

[1] Missing values were excluded (range 0-217). [2] Continuous variables: Student's t-test and/or Mann-Whitney U test; categorical variables Pearson's Chi square test

Outcome prevalences

The prevalences of the indicators of the birth process are shown in Table 2.

Table 2. Univariate and multivariate associations between first trimester general and pregnancy-related anxiety and labour process, overall and according to parity

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=4400 %	High n=1972 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=5697 %	High n=709 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Primary caesarean	5.5	5.6	0.99 (0.78-1.25)	1.01 (0.78-1.31)	5.4	5.8	1.10 (0.78-1.55)	1.32 (0.92-1.89)
Nulliparae	5.6	3.9	0.68 (0.47-0.99)	0.79 (0.53-1.18) [6]	5.2	4.3	0.80 (0.48-1.34)	1.05 (0.61-1.80)
Multiparae	5.4	7.2	1.31 (0.95-1.80)	1.32 (0.93-1.87) [6]	5.8	8.2	1.54 (0.97-2.44)	1.67 (1.02-2.75)
Induction[2]	10.3	12.8	1.31 (1.11-1.56)	1.25 (1.02-1.52)	10.8	13.3	1.27 (0.99-1.61)	1.07 (0.81-1.42)
Nulliparae	11.7	12.2	1.09 (0.86-1.38)	1.02 (0.78-1.35) [6]	11.8	12.4	1.03 (0.74-1.42)	0.91 (0.62-1.33)
Multiparae	8.2	13.4	1.74 (1.35-2.26)	1.61 (1.19-2.19) [6]	9.5	14.7	1.69 (1.16-2.47)	1.32 (0.85-2.06)
Referral during labour[3]	38.3	39.3	1.07 (0.92-1.24)	1.14 (0.96-1.36)	37.7	45.9	1.47 (1.18-1.83)	1.27 (0.99-1.62)
Nulliparae	52.0	53.2	1.11 (0.91-1.36)	1.13 (0.91-1.41)	51.7	57.5	1.38 (1.04-1.83)	1.38 (1.02-1.86)
Multiparae	18.8	23.6	1.33 (1.03-1.73)	1.18 (0.88-1.58)	19.8	25.9	1.43 (0.96-2.14)	1.03 (0.66-1.62)
Augmentation[2]	25.1	22.9	0.91 (0.79-1.03)	0.99 (0.85-1.14)	24.3	25.8	1.11 (0.92-1.34)	0.98 (0.80-1.21)
Nulliparae	34.5	32.5	0.94 (0.80-1.11)	0.97 (0.81-1.15)	34.4	33.4	1.00 (0.80-1.26)	0.98 (0.77-1.24)
Multiparae	11.7	13.1	1.18 (0.93-1.51)	1.05(0.81-1.36)	12.1	13.7	1.19 (0.81-1.74)	1.03 (0.69-1.54)
Pain relief/sedation[2]	14.9	16.9	1.18 (1.02-1.37)	1.27 (1.07-1.50)	14.7	21.8	1.68 (1.37-2.06)	1.51 (1.21-1.88)
Nulliparae	21.3	26.6	1.37 (1.15-1.64)	1.27 (1.05-1.54)	21.9	30.2	1.63 (1.29-2.06)	1.50 (1.17-1.92)
Multiparae	5.5	6.9	1.28 (0.92-1.79)	1.27 (0.88-1.82)	5.7	8.6	1.57 (0.97-2.54)	1.63 (0.98-2.72)
Secondary caesarean[2]	9.7	9.7	1.01 (0.84-1.22)	1.01 (0.82-1.24)	9.5	11.3	1.22 (0.94-1.59)	1.13 (0.85-1.49)
Nulliparae	12.4	13.1	1.09 (0.87-1.37)	1.02 (0.80-1.31)	12.3	14.7	1.26 (0.93-1.70)	1.22 (0.89-1.68)
Multiparae	5.8	6.2	1.08 (0.77-1.53)	1.00 (0.69-1.47)	5.9	5.9	0.92 (0.51-1.66)	0.90 (0.49-1.68)

Outcome			General anxiety				Pregnancy-related anxiety	
	Low n=440 %	High n=1972 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=5697 %	High n=709 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
First stage >12 hr[4]	19.5	20.1	1.05 (0.87-1.26)	1.09 (0.88-1.35)	19.4	21.9	1.21 (0.93-1.59)	0.96 (0.71-1.30)
Nulliparae	30.5	33.1	1.12 (0.90-1.39)	1.02 (0.80-1.29)	31.1	31.1	1.03 (0.76-1.40)	0.88 (0.64-1.22)
Multiparae	3.9	5.8	1.65 (0.99-2.74)	1.48 (0.86-2.56)	4.4	7.2	1.93 (0.96-3.89)	1.64 (0.78-3.45)
Second stage >=90 min[5]	11.1	7.1	0.60 (0.48-0.75)	0.88 (0.69-1.12)	10.0	8.9	0.86 (0.63-1.18)	0.96 (0.68-1.34)
Nulliparae	18.4	12.6	0.62 (0.49-0.80)	0.80 (0.62-1.03)[6]	17.2	14.5	0.79 (0.56-1.10)	0.95 (0.67-1.35)
Multiparae	1.3	2.0	1.53 (0.79-2.97)	1.86 (0.91-3.79)[6]	1.6	1.3	0.84 (0.26-2.77)	0.92 (0.26-3.23)
Instrumental delivery[5]	12.5	10.0	0.78 (0.64-0.94)	1.08 (0.87-1.33)	11.8	11.2	0.93 (0.70-1.23)	0.99 (0.73-1.34)
Nulliparae	19.6	17.1	0.86 (0.70-1.07)	1.07 (0.85-1.35)	19.1	17.5	0.89 (0.66-1.20)	1.04 (0.75-1.43)
Multiparae	3.0	3.3	1.02 (0.63-1.66)	1.16 (0.69-1.95)	3.2	2.1	0.68 (0.27-1.71)	0.80 (0.31-2.05)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol, diabetes, hypertension, gestational age, birth weight [2]Excluded women with primary caesarean section. [3]Only women under primary care at start of labour [4]Excluded women with caesarean section; data available for 3533 women (only recorded in perinatal registry of midwives) [5]Excluded women with caesarean section (primary/ secondary) [6]p-value interaction parity and anxiety <.05

Most prevalences were higher (p-values <0.05) in nulliparous than in multiparous women, except primary caesarean section (p=0.09). Most prevalences were similar in the different ethnicities, except for a higher prevalence of prolonged second stage of labour and instrumental delivery in the Dutch women (p<0.001).

Multivariate analyses

In all analyses, after adjustment for general covariates, there were no major changes in the models when, in the second step, also the pregnancy-related covariates (hypertension, diabetes, gestational age and birth weight) were added. Therefore, only the crude models and the fully adjusted models are presented.

General anxiety and parity

After full adjustment, women with high general anxiety were more likely to undergo induction of labour and receive pain relief/sedation. Subgroup analysis showed that the association with induction of labour was only significant in multiparous women (OR 1.61; 95% CI 1.19-2.19; p-value for interaction 0.025) (Table 2). Moreover, significant interactions between parity and general anxiety were found for primary caesarean section (p-value 0.045) and a second stage of ≥ 90 min (p-value 0.011): highly anxious multiparous women were more likely to experience these two outcomes than highly anxious nulliparous women.

Pregnancy-related anxiety and parity

After full adjustment, women with high pregnancy-related anxiety, both nulliparous and multiparous women, were more likely to receive pain relief/sedation. Subgroup analysis showed an increased risk for referral during labour in highly anxious nulliparous women and an increased risk for primary caesarean in highly anxious multiparous women; however, no significant interactions with parity were observed when formal interaction testing was completed (Table 2).

General and pregnancy-related anxiety and ethnicity

No significant interactions were found between general or pregnancy-related anxiety with ethnicity for any of the outcome measures (all p-values ≥ 0.12). However, subgroup analyses suggested a significant association between pregnancy-related anxiety and instrumental delivery in Turkish women (OR 3.47; 95% CI 1.03-11.6), which was not present in the total group (Table 3).

Table 3. Univariate and multivariate associations between first trimester general and pregnancy-related anxiety and labour process, according to ethnicity

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=3430 %	High n=1426 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=4404 %	High n=469 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Primary caesarean								
Dutch	5.6	7.0	1.29 (0.94-1.79)	1.23 (0.88-1.73)	5.9	6.1	1.05 (0.59-1.87)	1.09 (0.60-1.96)
Turkish	3.4	3.6	1.07 (0.30-3.88)	0.98 (0.23-4.19)	3.4	3.3	1.26 (0.30-5.20)	1.95 (0.39-9.82)
Moroccan	5.2	2.1	0.40 (0.14-1.15)	0.32 (0.10-1.09)	3.3	3.8	1.21 (0.38-3.58)	1.22 (0.33-4.48)
Black	6.5	4.4	0.65 (0.29-1.44)	0.80 (0.31-2.01)	6.1	1.8	0.33 (0.04-2.45)	0.44 (0.05-3.60)
Induction[2]								
Dutch	10.1	13.3	**1.39 (1.08-1.79)**	1.31 (0.98-1.75)	10.7	12.5	1.19 (0.77-1.84)	0.99 (0.61-1.63)
Turkish	10.7	13.5	1.29 (0.60-2.74)	1.13 (0.46-2.77)	12.8	13.8	1.05 (0.47-2.31)	0.97 (0.38-2.48)
Moroccan	9.5	10.3	1.11 (0.59-2.09)	0.91 (0.45-1.82)	9.9	9.8	0.96 (0.44-2.10)	*0.96 (0.42-2.21)*
Black	8.2	12.2	1.69 (0.92-3.08)	1.99 (0.96-4.12)	9.4	14.5	1.57 (0.66-3.74)	1.22 (0.41-3.58)
Referral during labour[3]								
Dutch	36.3	38.5	1.13 (0.90-1.42)	1.27 (0.98-1.64)	36.2	45.5	1.44 (0.99-2.10)	1.30 (0.86-1.96)
Turkish	44.9	34.0	0.63 (0.33-1.21)	0.59 (0.28-1.27)	33.3	47.4	2.13 (1.07-4.20)	1.68 (0.75-3.74)
Moroccan	41.5	47.4	1.15 (0.72-1.86)	1.37 (0.80-2.34)	43.2	51.6	1.35 (0.75-2.42)	1.21 (0.64-2.31)
Black	39.1	39.8	1.08 (0.65-1.79)	1.16 (0.65-2.08)	39.8	34.3	0.92 (0.42-2.00)	0.93 (0.39-2.20)
Augmentation[2]								
Dutch	24.2	22.4	0.91 (0.75-1.11)	0.95 (0.77-1.18)	23.5	28.6	1.31 (0.95-1.81)	1.09 (0.78-1.53)
Turkish	21.4	22.2	1.09 (0.61-1.96)	1.17 (0.62-2.22)	20.5	25.3	1.31 (0.70-2.43)	1.23 (0.62-2.43)
Moroccan	24.1	23.3	0.96 (0.62-1.49)	1.18 (0.73-1.92)	24.3	22.5	0.97 (0.57-1.66)	0.95 (0.53-1.69)
Black	22.6	21.0	0.95 (0.61-1.47)	1.04 (0.65-1.66)	21.9	20.8	1.01 (0.49-2.06)	0.96 (0.45-2.04)
Pain relief/ sedation[2]								
Dutch	13.8	17.7	1.35 (1.08-1.69)	1.31 (1.03-1.67)	14.0	25.1	2.08 (1.48-2.92)	1.69 (1.18-2.41)
Turkish	15.2	14.8	1.01 (0.51-1.98)	0.99 (0.45-2.17)	13.8	19.5	1.67 (0.83-3.34)	1.90 (0.84-4.27)
Moroccan	12.7	16.4	1.36 (0.80-2.33)	1.74 (0.96-3.13)	12.7	18.6	1.71 (0.94-3.11)	1.67 (0.87-3.23)
Black	15.1	13.7	0.91 (0.55-1.52)	0.98 (0.55-1.76)	13.7	22.6	2.02 (0.99-4.12)	2.05 (0.90-4.66)
Secondary caesarean[2]								
Dutch	8.6	10.1	1.19 (0.90-1.59)	1.17 (0.87-1.57)	8.7	12.1	1.37 (0.87-2.16)	1.21 (0.76-1.92)
Turkish	6.3	9.3	1.47 (0.57-3.77)	1.44 (0.51-4.07)	7.2	8.0	1.32 (0.50-3.44)	1.35 (0.47-3.82)
Moroccan	10.0	7.8	0.71 (0.37-1.38)	0.80 (0.43-1.48)	9.0	8.8	0.91 (0.40-2.07)	0.92 (0.38-2.19)
Black	15.1	10.3	0.67 (0.38-1.16)	0.80 (0.43-1.48)	12.1	15.1	1.44 (0.64-3.25)	1.68 (0.67-4.19)

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=3430 %	HIgh n=1426 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=4404 %	High n=469 %	Adjusted model[1] OR (95% CI)	Crude model OR (95% CI)
First stage >12 hr[4]								
Dutch	17.9	19.1	1.09 (0.82-1.44)	1.16 (0.86-1.58)	18.1	19.1	1.09 (0.67-1.78)	0.92 (0.55-1.54)
Turkish	14.5	19.1	1.47 (0.63-3.43)	1.15 (0.41-3.23)	17.5	16.7	1.02 (0.42-2.44)	0.52 (0.17-1.60)
Moroccan	21.8	19.0	0.86 (0.48-1.57)	0.98 (0.49-1.94)	20.1	21.0	1.11 (0.54-2.28)	0.91 (0.41-2.02)
Black	20.2	22.0	1.16 (0.59-2.29)	1.35 (0.61-2.95)	21.3	17.2	0.82 (0.29-2.31)	0.98 (0.31-3.10)
Second stage >=90 min[5]								
Dutch	12.6	**8.9**	0.68 (0.50-0.92)	0.81 (0.59-1.12)	11.7	13.0	1.12 (0.70-1.77)	1.02 (0.63-1.65)
Turkish	4.9	5.6	1.17 (0.37-3.70)	1.14 (0.34-3.86)	3.4	10.3	3.04 (0.98-9.39)	2.72 (0.81-9.15)
Moroccan	7.7	4.8	0.47 (0.19-1.17)	0.59 (0.23-1.54)	6.3	6.5	0.95 (0.34-2.63)	0.95 (0.33-2.80)
Black	2.9	3.6	1.26 (0.42-3.81)	1.46 (0.44-4.78)	3.3	2.4	0.75 (0.10-5.91)	0.76 (0.09-6.53)
Instrumental delivery[5]								
Dutch	13.6	12.0	0.88 (0.67-1.14)	0.99 (0.74-1.32)	13.3	12.6	0.93 (0.59-1.47)	0.79 (0.49-1.28)
Turkish	6.7	5.4	0.83 (0.29-2.36)	0.83 (0.27-2.56)	3.9	11.3	3.02 (1.05-8.69)	3.47 (1.03-11.6)
Moroccan	5.1	9.3	1.62 (0.72-3.63)	2.11 (0.89-4.98)	6.5	8.6	1.29 (0.52-3.17)	1.26 (0.49-3.24)
Black	5.1	4.3	0.85 (0.34-2.09)	1.15 (0.43-3.07)	4.7	4.4	1.00 (0.22-4.47)	1.26 (0.25-6.42)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol, diabetes, hypertension, gestational age, birth weight [2]Excluded women with primary caesarean section. [3]Only women under primary care at start of labour [4]Excluded women with caesarean section; data available for 3530 women (only recorded in perinatal registry of midwives) [5]Excluded women with caesarean section (primary/ secondary)

General and pregnancy-related anxiety and level of care

No significant interactions were found between general or pregnancy-related anxiety with the level at care at the start of labour for any of the outcome measures (all p-values ≥ 0.07). However, in the subgroup analyses, the risk for pain relief/sedation showed a greater increase in highly anxious women who started labour in secondary care (general anxiety: OR 1.30; 95% CI 1.03-1.63; pregnancy-related anxiety: OR 1.88; 95% CI 1.33-2.46) compared to those who began labour in primary care (general anxiety: OR 1.14; 95% CI 0.88-1.47; pregnancy-related anxiety: OR 1.23; 95% CI 0.88-1.73); however, the interactions were not significant (p-values 0.34 and 0.17, respectively) (supplemental Table).

DISCUSSION

Main findings

In this multi-ethnic cohort, general anxiety and pregnancy-related anxiety, as measured in the first trimester of pregnancy, were associated with an increased risk for interventions during labour, but not with the progression of birth. Pregnancy-related anxiety showed stronger associations than general anxiety. Some associations differed between primiparae and multiparae, whereas similar associations were found across all ethnic groups.

Strengths and limitations

A major strength of the present study is the prospective design in a large multi-ethnic cohort. Although the participation of non-Dutch women was lower than that of Dutch women, we collected data for ≥ 2800 non-Dutch women, making it possible to perform subgroup analyses in the four major ethnic groups in the Netherlands. However, the sample sizes were not large enough to prove a potential interaction effect of ethnicity and anxiety with less frequent outcomes. Although our sample might not be representative for all pregnant women in Amsterdam or in the Netherlands, there is no reason to assume that the association between anxiety and the birth process should be different in non-responders.

Another strength is the assessment of both general anxiety and pregnancy-related anxiety, using validated questionnaires, while most other studies only assessed pregnancy-related anxiety.

A limitation of the abbreviated 10-item version of the PRAQ that we used, is that this questionnaire has only been validated in nulliparous women. Because one item of the 3-item subscale 'fear of labour' was not applicable for multiparae, the assessment of this aspect in multiparae was limited. Therefore, we only used the total PRAQ score and could not distinguish between the different aspects of pregnancy-related anxiety. This is in agreement with other questionnaires, such as the Wijma Delivery Expectancy Questionnaire) (W-DEQ; a frequently used questionnaire) conceptualized as a uni-dimensional instrument to measure fear of childbirth.[42] Outcome data on the birth process and interventions were available from the PRN. A possible limitation of this might be that not all outcome data were completely registered. However, the amount of missing data was limited and there is no reason to assume that data were missing in a selective manner. Since the collection of our data in 2003-2004, the prevalence of interventions during labour has increased.[1-2, 43] Nevertheless, we think that the associations between anxiety and the birth process have remained similar.

Anxiety was measured in the first trimester of pregnancy, while other studies measured anxiety later in pregnancy.[19] Little evidence is available concerning how anxiety in the first trimester persists and evolves during pregnancy. However, assessment of anxiety in the first trimester allows provides the opportunity to perform an intervention to reduce anxiety, particularly pregnancy-related anxiety.

Comparison with other studies

Some studies found no association between general anxiety and the birth process [19,44] whereas Adams et al. were the only group to find a trend for increased risk for labour induction in general anxious women in a cohort of 2206 women.[17] To our knowledge, our study is the first to show a significant association between general anxiety and interventions during birth. The difference between our study and others might be explained by a lack of power in other studies (including 88 and 1515 women, respectively), as well as by different views on the management of labour, e.g. the use of pain relief. Moreover, the other studies did not investigate the association between anxiety and labour induction, as this is not considered to be an 'undesirable' outcome.

Our observed association between pregnancy-related anxiety and pain relief/sedation is in line with other studies reporting an association between fear of labour and epidural analgesia.[21, 45] Several studies found an association between fear of labour and elective caesarean section.[13-16] Although we found no association between general or pregnancy-related anxiety and primary caesarean, an interaction was seen between parity and general anxiety, suggesting a decreased risk for anxious nulliparae and an increased risk for multiparae. This might reflect the restraint of obstetricians in the Netherlands to perform an elective caesarean in nulliparae. In anxious multiparae with a complicated birth history, obstetric caregivers will be more willing to perform a caesarean section. Although others reported an association between fear of labour and emergency caesarean section this was not seen in our study.[18, 20]

Several studies found a longer duration of labour in women with high fear of labour.[17-19] We did not find such an association; unfortunately, however, in our study data on the duration of the first stage of labour were only available in categories of six hours.

Subgroup analyses showed some different effects in nulliparae and multiparae. Parity is known to be associated with the birth process, which was confirmed in the present study.[7, 9-10] The different effect of anxiety on the birth process in nulliparae and multiparae can be explained by physiological factors, and by the woman's experience during the previous labour and the information available for the care provider on the previous birth process. The increased risk for induction of labour in multiparae with high general anxiety may be due to greater confidence by obstetric caregivers that the induction will be successful in multiparae. An increased risk for referral during labour was only seen in nulliparous women with high pregnancy-related anxiety. This can be explained by the lower a priori risk for referral in multiparae and the subsequent greater confidence of primary care midwives in a successful delivery in primary care. To our knowledge, this is the first study to investigate possible interactions with parity with regard to the impact of anxiety on the birth process. More research is necessary to unravel the factors contributing to the different effects of anxiety in primiparous and multiparous women.

In contrast to our expectation, we found no stronger associations between general or pregnancy-related anxiety in the non-Dutch groups compared to the Dutch group. However, some indication was found for an increased risk for instrumental delivery in Turkish women with high pregnancy-related anxiety. It is unlikely that this is explained by the lack of prenatal healthcare visits or language barriers, because these factors are also seen among Moroccan and Surinamese women.[46] However, this latter finding should be interpreted with caution as the subgroup was small; we recommend more studies in large multi-ethnic cohorts to address these questions. The large prevalence of high anxiety in non-Dutch women also justifies this research.

Some indications were found that the odds for pain relief/sedation were especially increased in anxious women who started labour in secondary care compared to primary care. This may reflect that primary caregivers use different strategies to support anxious women during labour.

It is reassuring that we found no association between general and pregnancy-related anxiety and the progression of birth, but only with interventions. Another Dutch study showed that referral during labour, a significant intervention within the Dutch context, was associated with a negative recall of labour three years late.[47] In 2013, the need for pain relief was the most frequent reason (18.5%) for referral during labour.[48] Therefore, it is worthwhile to investigate whether these interventions during labour can be managed by interventions during pregnancy in anxious women, to avoid the necessity of labour-related interventions. If effective interventions are identified, screening for anxiety (especially pregnancy-related anxiety showing the strongest associations) should be implemented in prenatal care, at least in subgroups with an increased risk for anxiety. The observed high prevalence of general and pregnancy-related anxiety in non-Dutch women underlines the relevance of screening and subsequent fear-reducing interventions, especially in this group.

Conclusion

General and pregnancy-related anxiety in the first trimester of pregnancy are not associated with prolonged or obstructed labour and artificial delivery and, therefore, do not appear to influence the progression of birth. However, high levels of anxiety contribute to greater use of interventions during labour, especially pain relief/sedation, induction of labour and referral during labour. Although we found similar associations between ethnic groups, the

high prevalence of anxiety symptoms in pregnant women with a migrant background justifies more research on the effect of interventions to reduce anxiety symptoms in ethnic groups.

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COMPETING INTERESTS

None declared. Completed disclosure of interests form available to view online as supporting information.

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CONTRIBUTION TO AUTHORSHIP

The study was designed by JMK and TGV. JMK performed the statistical analysis and drafted the manuscript. TGV rendered and provided the ABCD Study data. JMK, TGV and AMS interpreted the results of the analysis. TGV and AMS made substantial contributions in revising the manuscript. The final manuscript was read and approved by all authors.

DETAILS OF ETHICAL APPROVAL

Approval for the ABCD study was obtained from the Central Committee on Research involving Human Subjects in the Netherlands, the Medical Ethical Committees of participating hospitals, and from the Registration Committee of Amsterdam.

DATA SHARING

Data of the ABCD study can be shared for specific research questions. Please contact t.vrijkotte@amc.uva.nl.

LEGENDS OF FIGURES

Figure 1. Flowchart of the ABCD study and inclusion in the current analyses

STAI = State Trait Anxiety Inventory

PRAQ = Pregnancy-Related Anxiety Questionnaire

PRN=Dutch Perinatal Registration

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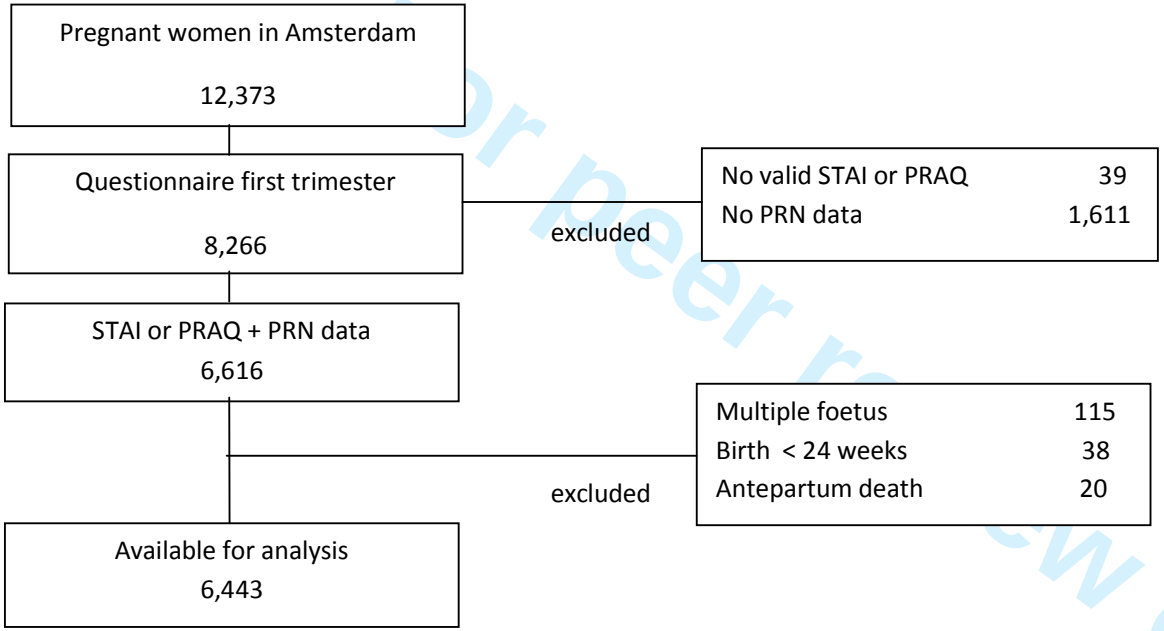
Figure 1. Flowchart of the ABCD study and inclusion in the current analyses



STAI = State Trait Anxiety Inventory

PRAQ = Pregnancy-Related Anxiety Questionnaire

PRN=Dutch Perinatal Registration

Supplemental Table I. Univariate and multivariate associations between first trimester general and pregnancy related anxiety and labour process, according to care at start of labour

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=4126 %	High n=1850 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=5348 %	High n=662 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Augmentation[2]								
primary care	19.7	19.4	1.01 (0.85-1.22)	1.07 (0.87-1.31)	19.4	21.8	1.20 (0.93-1.55)	1.01 (0.76-1.34)
secondary care	34.7	27.7	0.74 (0.61-0.89)	0.84 (0.68-1.04)	32.4	31.8	0.99 (0.75-1.31)	0.95 (0.70-1.29)
Pain relief/sedation[2]								
primary care	10.5	11.3	1.12 (0.89-1.41)	1.14 (0.88-1.47)	10.4	13.9	1.47 (1.08-2.01)	1.23 (0.88-1.73)
secondary care	22.6	24.6	1.12 (0.91-1.38)	1.30 (1.03-1.63)	21.9	33.7	1.87(1.41-2.48)	1.81 (1.33-2.46)
Secondary caesarean[2]								
primary care	4.9	4.6	0.98 (0.70-1.37)	0.95 (0.66-1.38)	4.7	5.8	1.24 (0.78-1.97)	1.01 (0.62-1.65)
secondary care	19.2	16.6	0.90 (0.72-1.14)	0.95 (0.74-1.22)	17.4	19.5	1.17 (0.84-1.63)	1.16 (0.81-1.64)
First stage >12 hr[3]								
primary care	19.4	19.8	1.03 (0.85-1.25)	1.07 (0.86-1.34)	19.2	22.1	1.24 (0.95-1.63)	1.00 (0.74-1.35)
secondary care	21.2	28.6	1.55 (0.65-3.68)	1.62 (0.56-4.73)	23.6	12.5	0.48 (0.06-4.03)	0.24 (0.02-3.03)
Second stage >=90 min[4]								
primary care	11.3	8.0	0.67 (0.57-0.81)	0.91 (0.68-1.23)	10.4	10.3	0.93 (0.64-1.36)	0.96 (0.64-1.45)
secondary care	10.7	5.8	0.51 (0.35-0.75)	0.82 (0.54-1.24)	9.3	6.7	0.73 (0.41-1.29)	0.94 (0.51-1.74)
Instrumental delivery[4]								
primary care	9.7	8.2	0.84 (0.65-1.10)	1.10 (0.82-1.47)	9.1	10.2	1.11 (0.77-1.61)	1.10 (0.73-1.63)
secondary care	18.4	12.8	0.65 (0.49-0.86)	0.98 (0.72-1.32)	16.7	12.9	0.73 (0.47-1.12)	0.86 (0.54-1.36)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol, diabetes, hypertension, gestational age, birth weight [2]Excluded women with primary caesarean section
[3]Excluded women with caesarean section; data available for 3530 women (only recorded in perinatal registry of midwives) [4]Excluded women with caesarean section (primary/secondary)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

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

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	Suppl file
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, p 11
		(b) Indicate number of participants with missing data for each variable of interest	All tables
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	Table 2 and 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2 and 3
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	19
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-23
Generalisability	21	Discuss the generalisability (external validity) of the study results	23
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Possible relationship between general and pregnancy-related anxiety during the first half of pregnancy and the birth process: a prospective cohort study

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Possible relationship between general and pregnancy-related anxiety during the first half of pregnancy and the birth process: a prospective cohort study

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Word count: 3731

ABSTRACT

Objectives The rate of interventions during childbirth has increased dramatically during the last decades. Maternal anxiety might play a role in the progress of the labour process and interventions during labour. This study aimed to identify associations between anxiety in the first half of pregnancy and the birth process, including any interventions required during labour. In addition, differences in the associations by parity and ethnicity were explored.

Design Prospective cohort study

Setting Primary care midwifery practices and secondary/tertiary care obstetric practices in Amsterdam, participating in the multi-ethnic ABCD study (participation rate 96%; response 8,266/12,373 (67%)).

Participants Included were women with singletons, alive at labour start, with a gestational age ≥24 weeks (n=6,443).

Independent variable General anxiety (STAI state) and pregnancy-related anxiety (PRAQ), were self-reported in the first half of pregnancy.

Outcomes Associations between both forms of anxiety and several indicators of the birth process were analysed. Subgroup analyses were performed for parity and ethnicity.

Results The prevalence of high general anxiety (STAI score ≥ 43) and pregnancy-related anxiety (PRAQ score ≥P90) were 30.9% and 11.0%, respectively. After adjustment, both general and pregnancy-related anxiety were associated with pain relief and/or sedation (OR for general anxiety 1.27;95%-CI 1.07-1.50;OR for pregnancy-related anxiety 1.51;95%-CI 1.21-1.88). In multiparae, general anxiety was associated with induction of labour (OR 1.61;95%-CI 1.19-2.19), pregnancy-related anxiety was associated with primary caesarean section (OR

1.67;95%-CI 1.02-2.75). In nulliparae, pregnancy-related anxiety was associated with referral during labour (OR 1.38; 95%-CI 1.02-1.86). Associations were largely similar for all ethnicities.

Conclusions

High levels of general and pregnancy-related anxiety in early pregnancy contribute modestly to more interventions during the birth process with similar associations between ethnic groups, but with some differences between primiparae and multiparae.

Abbreviations: ABCD study = Amsterdam Born Children and their Development study, BMI = body mass index, PRN = Dutch Perinatal Registration, STAI = State Trait Anxiety Inventory, PRAQ = Pregnancy-Related Anxiety Questionnaire

STRENGTH AND LIMITATIONS

Strengths

- We performed a prospective study in a large multi-ethnic cohort.
- We used validated questionnaires to assess both forms of anxiety.
- Anxiety was measured in the first half of pregnancy.

Limitations

- The subscale for Fear of Childbirth (FOC) within the Pregnancy-Related Anxiety Inventory was not suitable to measure FOC in multiparous women. Therefore, we only reported the total score on pregnancy-related anxiety and not on the subscales.

- Our data are collected in 2003 and 2004. Since 2004 the intervention rate has increased, but there is no reason to assume that the association between anxiety and (interventions in) the birth process has changed.

INTRODUCTION

The rate of interventions during childbirth has increased dramatically in recent decades. For example, in the Netherlands, from 1993-2002 the caesarean section rate rose from 8.1% to 13.6%. and 16.7% in 2010.[1,2] The rate of labour induction increased during 2008-2013 from 15% to 21%.[3] Although the absolute incidence of caesarean section is higher in other western countries compared to the Netherland, a similar rise in caesarean sections occurred in other western countries.[4-7]

The progression of the birth process and concomitant interventions are associated with maternal characteristics such as age, parity, body mass index (BMI), ethnicity, illness, infant birth weight, as well as with organisational factors, such as existing guidelines, the availability of 24-h pain relief, the profession of the obstetric care provider (midwife versus physician), and the level of care (primary/secondary).[8-12] Moreover, maternal anxiety might play a role in the birth process. Although one review found no overall association between anxiety and obstetric complications, specific types of anxiety (such as fear of childbirth) may be associated with specific complications and interventions, such as prolonged labour and caesarean section.[13]

Several studies have shown a relationship between fear of childbirth and duration of labour [14-16], epidural analgesia [17] and elective [18-22] and emergency caesarean. [15,23]

On the other hand, other studies reported no such relationships.[24-26] One explanation for these inconsistencies could be differences in cultural, social and organisational characteristics between countries. These factors can mediate or exacerbate the effect of anxiety on the birth process and on concomitant interventions. For example, some ethnic groups are more

susceptible to stress-induced neuroendocrine and inflammatory pathways which could lead to adverse perinatal outcomes.[27-30] Also, cultural and social differences between ethnic groups (e.g. language barriers, unfamiliarity with the obstetric care organisation) may explain differences between ethnic groups regarding the influence of anxiety on the birth process.[31-34] In addition, it is unknown whether the association between anxiety and the birth process differs between nulliparous and multiparous women as well as between women giving birth in primary and secondary care. To our knowledge, no study has investigated the level of care and ethnicity in the association between general and pregnancy-related anxiety, and the progression of birth.

Anxiety in pregnancy is associated with shorter gestational age and has negative implications for fetal neurodevelopment and child outcomes. Women with high fear of childbirth in pregnancy are at risk for psychiatric problems postpartum, for example postpartum depression and even posttraumatic stress syndrome (PTSS). [35-37] To lower the risk for those serious consequences, appropriate treatment is desirable. If anxiety does also have a detrimental effect on the birth process, there is all the more reason for screening early in pregnancy for anxiety. Screening for anxiety early in pregnancy, provides sufficient time for treatment or therapy for women with high anxiety levels.

Therefore, this study investigates the association between general anxiety and/or pregnancy-related anxiety measured during the first half of pregnancy and the birth process, and the interaction of this association with parity, ethnicity and the level of care at the start of labour.

METHODS

Study design and participants

Data were derived from the Amsterdam Born Children and their Development (ABCD) study, a large multi-ethnic prospective cohort study.[38] The ABCD study is aimed at examining the relationship between maternal lifestyle and psychosocial conditions during pregnancy and the child's health at birth as well as later in life. Between January 2003 and March 2004, participating obstetric care providers (midwives and hospital obstetricians; participation rate 96%) invited pregnant women in Amsterdam at their first antenatal visit to enroll in the ABCD. A total of 12,373 women were approached (99% of the target population). Within two weeks of this first contact, women who agreed to take part were sent a questionnaire, covering socio-demographic conditions, obstetric history and psychosocial conditions, including general and pregnancy-related anxiety. Consent forms were also sent for the linkage of study data to medical records as well as to data from the Dutch Perinatal Registration (PRN).

A total of 8266 women (response rate 67%) filled in the pregnancy questionnaire at an average of 16 weeks gestation (IQR 14-18 weeks) and 7043 gave permission for perusal of their medical records. To facilitate participation by women unable to speak Dutch, questionnaires were also available in Turkish, Arabic and English, and women could also complete the questionnaire with the assistance of an interviewer. Participation of foreign-born women was lower (42-64%) than for Dutch-born women (77%) but comparable with response rates in other population-based, multi-ethnic studies in the Netherlands.[39] In the present study we included women with a singleton pregnancy, a gestational age ≥ 24 weeks, and a living foetus at the start of labour.

Approval for the study was obtained from the Medical Ethical Committees of the participating hospitals and the Registration Committee of the Municipality of Amsterdam. All women gave written informed consent.

Definition and measurement of variables

General and pregnancy-related anxiety

General anxiety was assessed using the Dutch version of the State-Trait Anxiety Inventory (STAI).[40-41] The 20 items regarding the state anxiety subscale were included in our questionnaire, with each item scored on a 4-point scale. The anxiety score was dichotomised in low-average (<43 points) and high anxiety (≥ 43 points).[42] In our sample, the internal consistency (Cronbach's alpha) of the scale was 0.94.

Pregnancy-related anxiety was assessed using an abbreviated 10-item version of the Pregnancy-Related Anxieties Questionnaire (PRAQ).[43-44] The internal consistency (Cronbach's alpha) was 0.79; each item was scored on a 4-point scale. Three aspects that can be distinguished in the PRAQ are 'fear of labour', 'fear of bearing a physically or mentally handicapped child' and 'concern about one's appearance'. In the present study we used the total score on pregnancy-related anxiety. One question was only applicable for nulliparous women ("I am scared of labour and birth because I have never experienced this"), resulting in a maximum score of 40 for nulliparous women and 36 for multiparous women. Because cut-off scores were not available for dichotomisation of the results from this instrument, we used the 90th percentile to identify women with a high level of pregnancy-related anxiety.[45] This resulted in cut-off scores of 28 and 24 for nulliparous and multiparous women, respectively.

Birth process and interventions

Outcome data on the birth process and interventions were obtained by linking our records with the PRN database. Validation of the PRN database has been described previously.[39] The outcome variables were determined from the records of the Registry of Midwives, the Registry of Obstetricians and the Registry of Paediatricians according to the decision rules of the PRN.[46]

We defined the following outcomes:

Birth process: duration of first stage of labour (≤ 12 h/>12 h; only available in registry of midwives), duration of second stage (< 1.5 h/≥ 1.5 h)].

Interventions: primary caesarean (yes/no), induction of labour (yes/no), referral during labour [only in the group that started labour under primary care; (yes/no)], augmentation (yes/no), pain relief/sedation (yes/no), secondary caesarean (yes/no), vaginal instrumental delivery [ventouse or forceps; (yes/no)

Covariates

The following covariates were included in the analyses: maternal age (years), ethnicity, education (years after primary school), pre-pregnancy BMI (kg/m^2), parity (nulliparae/multiparae), smoking during pregnancy (yes/no), alcohol use during pregnancy (yes/no), hypertensive disorders and diabetes (pre-existent or detected during pregnancy), gestational age at delivery (weeks), care at start of labour (primary/secondary), and birth weight (g). Ethnicity was based on the birth country of the participant's mother (self-reported) and included the following categories: Dutch, Turkish, Moroccan, Black (Antillean/Aruban, Surinamese, Ghanaian or other African descent), other non-Western and

other Western countries. Pre-pregnancy weight and height, education, smoking and alcohol use during pregnancy were self-reported in the questionnaire. Parity, birth weight, gestational age, hypertension and diabetes were extracted from the PRN database.

Statistical analysis

Descriptive statistics were used to profile the sample characteristics according to the level of maternal general anxiety and of pregnancy-related anxiety. Categorical variables were described by percentages per category. Continuous variables were described using the mean and 95% confidence intervals (CI), if normally distributed and, if not, with the median and minimum and maximum values. Risks were presented as odds ratios (OR) and 95% CI. Differences were tested with Student's t test or Mann-Whitney U test for continuous variables and Pearson's chi square test for categorical variables. Associations between high general and/or pregnancy-related anxiety compared to low anxiety were analysed for each outcome using multiple logistic regression analyses. All potential confounders were determined a priori and added to the regression model in two steps. In the first step we adjusted for general covariates: age, ethnicity, education, pre-pregnancy BMI, parity, smoking and alcohol use; in the second step hypertension, diabetes, gestational age and birth weight were added to the model to determine whether these pregnancy-related covariates confounded the association between anxiety and each of the outcomes. Subgroup analyses were performed according to parity (nulliparous versus multiparous women), ethnicity (Dutch, Turkish, Moroccan and Black) and care at start of labour (primary/secondary care). No subgroup analysis was performed in the ethnic groups 'other Western' and 'other non-Western' as each of these

groups represented a diverse selection of ethnicities. To formally test whether different associations existed for the different subgroups (parity, ethnicity, and care at start of labour) between STAI or PRAQ and the birth process variables, interaction terms (between parity, ethnicity respectively care at start of labour with general and pregnancy-related anxiety) were added to the final model.

All analyses were performed with SPSS 21.0 (IBM Statistics, USA).

RESULTS

Response

Of the 8266 women who completed the pregnancy questionnaire, for 6616 women valid results for the STAI or PRAQ and outcome data, were available. The mean STAI-score was significantly higher in the group of women with missing outcome data (39.5 versus 38.2); the PRAQ-scores were comparable. After exclusion of 173 women (with a multiple foetus, a gestational age ≤ 24 weeks, or antenatal death), 6443 records were available for analysis (Figure 1). Most women completed both the STAI and the PRAQ (n=6335); 37 women completed only the STAI and 71 women only the PRAQ.

Covariates according to anxiety levels

A high STAI score (further referred to as 'high general anxiety') was found in 30.9% of the sample and a high score on the PRAQ (further referred to as 'high pregnancy-related anxiety') in 11.1% of the sample. The STAI score was moderately correlated with the PRAQ score (Pearson's r=0.36; p<0.001).

High general anxiety and high pregnancy-related anxiety were more frequently observed in younger women, in women with non-Dutch ethnicities, fewer years of education, higher pre-pregnancy BMIs, smoking women, women with less alcohol consumption, and in women who gave birth to babies with a lower birth weight. There were no differences in the rates of hypertension and gestational age between the high and low anxiety groups; however, diabetes and secondary care at the start of labour were more frequently observed in women

with high general anxiety. Nulliparous women appeared to be at lower risk for high general anxiety compared to multiparous women. (Table 1)

Table 1. Maternal characteristics according to general anxiety in the first half of pregnancy and pregnancy-related anxiety

		General anxiety			Pregnancy-related anxiety		
		Low n=4400[1]	High n=1972[1]	p-value[2]	Low n=5697[1]	High n=709[1]	p-value[2]
Anxiety score	-median (min-max)						
Nulliparae		33 (20-42)	49 (43-80)		21 (10-27)	30 (28-40)	
Multiparae		33 (20-42)	49 (43-74)		18 (9-23)	26 (24-36)	
Age (years)	-mean (95% CI)	31.5 (31.4-31.7)	29.7 (29.5-30.0)	<.001	31.2 (31.1-31.4)	28.7 (28.3-29.2)	<.001
Ethnicity	-%			<.001			<.001
Dutch		63.5	38.9		58.8	30.1	
Turkish		2.6	8.6		3.6	12.9	
Moroccan		5.4	12.1		6.5	15.3	
Black		6.5	12.8		8.6	8.1	
Other Western		14.1	13.3		13.7	14.4	
Other non-Western		7.9	14.3		8.9	19.3	
Education (years)	-mean (95% CI)	9.6 (9.5-9.7)	7.5 (7.3-7.7)	<.001	9.2 (9.1-9.3)	7.1 (6.8-7.5)	<.001
Pre-pregnancy BMI (kg/m^2)	-mean (95% CI)	22.8 (22.7-22.9)	23.8 (23.6-24.0)	<.001	23.0 (22.9-23.1)	23.8 (23.5-24.1)	<.001
Nulliparae	-%	59.1	49.5	<.001	[3]	[3]	
Smoking in pregnancy	-%	7.3	15.2	<.001	9.0	15.0	<.001
Alcohol in pregnancy	-%	24.7	16.0	<.001	22.9	15.3	<.001
Hypertensive disorders	-%	12.2	12.5	.70	12.1	12.9	.54
Diabetes	-%	1.8	3.1	.001	2.1	3.1	.08
Gestational age	-%			.27			.87
<37 weeks		5.0	6.0		5.4	5.1	
37-41 weeks		85.7	84.7		85.4	85.2	
>=42 weeks		9.3	9.3		9.2	9.7	
Care start labour	-%			<.001			.29
primary care		60.1	54.6		58.6	56.6	
secondary care		39.9	45.4		41.4	43.4	
Birth weight (g)	-mean (95% CI)	3473 (3456-3490)	3379 (3354-3405)	<.001	3450 (3435-3465)	3391 (3351-3431)	.009

[1] Missing values were excluded (range 0-217). [2] Continuous variables: Student's t-test and/or Mann-Whitney U test; categorical variables Pearson's Chi square test [3] No comparison possible between nulliparous and multiparous women because in each group the P90 was used as cut-off for high pregnancy-related anxiety

Outcome prevalences

The prevalences of the indicators of the birth process are shown in Table 2.

Table 2. Univariable and multivariable associations between general and pregnancy-related anxiety in the first half of pregnancy and (interventions in) the birth process, overall and according to parity

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=4400 %	High n=1972 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=5697 %	High n=709 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Primary caesarean	5.5	5.6	0.99 (0.78-1.25)	1.01 (0.78-1.31)	5.4	5.8	1.10 (0.78-1.55)	1.32 (0.92-1.89)
Nulliparae	5.6	3.9	0.68 (0.47-0.99)	0.79 (0.53-1.18) [6]	5.2	4.3	0.80 (0.48-1.34)	1.05 (0.61-1.80)
Multiparae	5.4	7.2	1.31 (0.95-1.80)	1.32 (0.93-1.87) [6]	5.8	8.2	1.54 (0.97-2.44)	1.67 (1.02-2.75)
Induction[2]	10.3	12.8	1.31 (1.11-1.56)	1.25 (1.02-1.52)	10.8	13.3	1.27 (0.99-1.61)	1.07 (0.81-1.42)
Nulliparae	11.7	12.2	1.09 (0.86-1.38)	1.02 (0.78-1.35) [6]	11.8	12.4	1.03 (0.74-1.42)	0.91 (0.62-1.33)
Multiparae	8.2	13.4	1.74 (1.35-2.26)	1.61 (1.19-2.19) [6]	9.5	14.7	1.69 (1.16-2.47)	1.32 (0.85-2.06)
Referral during labour[3]	38.3	39.3	1.07 (0.92-1.24)	1.14 (0.96-1.36)	37.7	45.9	1.47 (1.18-1.83)	1.27 (0.99-1.62)
Nulliparae	52.0	53.2	1.11 (0.91-1.36)	1.13 (0.91-1.41)	51.7	57.5	1.38 (1.04-1.83)	1.38 (1.02-1.86)
Multiparae	18.8	23.6	1.33 (1.03-1.73)	1.18 (0.88-1.58)	19.8	25.9	1.43 (0.96-2.14)	1.03 (0.66-1.62)
Augmentation[2]	25.1	22.9	0.91 (0.79-1.03)	0.99 (0.85-1.14)	24.3	25.8	1.11 (0.92-1.34)	0.98 (0.80-1.21)
Nulliparae	34.5	32.5	0.94 (0.80-1.11)	0.97 (0.81-1.15)	34.4	33.4	1.00 (0.80-1.26)	0.98 (0.77-1.24)
Multiparae	11.7	13.1	1.18 (0.93-1.51)	1.05(0.81-1.36)	12.1	13.7	1.19 (0.81-1.74)	1.03 (0.69-1.54)
Pain relief/sedation[2]	14.9	16.9	1.18 (1.02-1.37)	1.27 (1.07-1.50)	14.7	21.8	1.68 (1.37-2.06)	1.51 (1.21-1.88)
Nulliparae	21.3	26.6	1.37 (1.15-1.64)	1.27 (1.05-1.54)	21.9	30.2	1.63 (1.29-2.06)	1.50 (1.17-1.92)
Multiparae	5.5	6.9	1.28 (0.92-1.79)	1.27 (0.88-1.82)	5.7	8.6	1.57 (0.97-2.54)	1.63 (0.98-2.72)
Secondary caesarean[2]	9.7	9.7	1.01 (0.84-1.22)	1.01 (0.82-1.24)	9.5	11.3	1.22 (0.94-1.59)	1.13 (0.85-1.49)
Nulliparae	12.4	13.1	1.09 (0.87-1.37)	1.02 (0.80-1.31)	12.3	14.7	1.26 (0.93-1.70)	1.22 (0.89-1.68)

Multiparae	5.8	6.2	1.08 (0.77-1.53)	1.00 (0.69-1.47)	5.9	5.9	0.92 (0.51-1.66)	0.90 (0.49-1.68)

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=440 %	High n=1972 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=5697 %	High n=709 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
First stage >12 hr[4]	19.5	20.1	1.05 (0.87-1.26)	1.09 (0.88-1.35)	19.4	21.9	1.21 (0.93-1.59)	0.96 (0.71-1.30)
Nulliparae	30.5	33.1	1.12 (0.90-1.39)	1.02 (0.80-1.29)	31.1	31.1	1.03 (0.76-1.40)	0.88 (0.64-1.22)
Multiparae	3.9	5.8	1.65 (0.99-2.74)	1.48 (0.86-2.56)	4.4	7.2	1.93 (0.96-3.89)	1.64 (0.78-3.45)
Second stage >=90 min[5]	11.1	7.1	0.60 (0.48-0.75)	0.88 (0.69-1.12)	10.0	8.9	0.86 (0.63-1.18)	0.96 (0.68-1.34)
Nulliparae	18.4	12.6	0.62 (0.49-0.80)	0.80 (0.62-1.03)[6]	17.2	14.5	0.79 (0.56-1.10)	0.95 (0.67-1.35)
Multiparae	1.3	2.0	1.53 (0.79-2.97)	1.86 (0.91-3.79)[6]	1.6	1.3	0.84 (0.26-2.77)	0.92 (0.26-3.23)
Instrumental delivery[5]	12.5	10.0	0.78 (0.64-0.94)	1.08 (0.87-1.33)	11.8	11.2	0.93 (0.70-1.23)	0.99 (0.73-1.34)
Nulliparae	19.6	17.1	0.86 (0.70-1.07)	1.07 (0.85-1.35)	19.1	17.5	0.89 (0.66-1.20)	1.04 (0.75-1.43)
Multiparae	3.0	3.3	1.02 (0.63-1.66)	1.16 (0.69-1.95)	3.2	2.1	0.68 (0.27-1.71)	0.80 (0.31-2.05)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol, diabetes, hypertension, gestational age, birth weight [2]Excluded women with primary caesarean section. [3]Only women under primary care at start of labour [4]Excluded women with caesarean section; data available for 3533 women (only recorded in perinatal registry of midwives) [5]Excluded women with caesarean section (primary/ secondary) [6]p-value interaction parity and anxiety <.05

Most prevalences were higher (p-values <0.05) in nulliparous than in multiparous women, except primary caesarean section (p=0.09). Most prevalences were similar in the different ethnicities, except for a higher prevalence of prolonged second stage of labour and instrumental delivery in the Dutch women (p<0.001).

Multivariable analyses

In all analyses, after adjustment for general covariates, there were no major changes in the models when, in the second step, also the pregnancy-related covariates (hypertension, diabetes, gestational age and birth weight) were added. Therefore, only the crude models and the fully adjusted models are presented.

General anxiety and parity

After full adjustment, women with high general anxiety were more likely to undergo induction of labour and receive pain relief/sedation. Subgroup analysis showed that the association with induction of labour was only statistically significant in multiparous women (OR 1.61; 95% CI 1.19-2.19; p-value for interaction 0.025) (Table 2). Moreover, statistically significant interactions between parity and general anxiety were found for primary caesarean section (p-value 0.045) and a second stage of ≥ 90 min (p-value 0.011): highly anxious multiparous women were more likely to experience these two outcomes than highly anxious nulliparous women.

Pregnancy-related anxiety and parity

After full adjustment, women with high pregnancy-related anxiety, both nulliparous and multiparous women, were more likely to receive pain relief/sedation. Subgroup analysis showed an increased risk for referral during labour in highly anxious nulliparous women and an increased risk for primary caesarean in highly anxious multiparous women; however, no statistically significant interactions with parity were observed when formal interaction testing was completed (Table 2).

General and pregnancy-related anxiety and ethnicity

No statistically significant interactions were found between general or pregnancy-related anxiety with ethnicity for any of the outcome measures (all p-values ≥ 0.12). However, subgroup analyses suggested a statistically significant association between pregnancy-related anxiety and instrumental delivery in Turkish women (OR 3.47; 95% CI 1.03-11.6), which was not present in the total group (Table 3).

Table 3. Univariable and multivariable associations between general and pregnancy-related anxiety in the first half of pregnancy and (interventions in) the birth process, according to ethnicity

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=3430 %	High n=1426 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=4404 %	High n=469 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Primary caesarean								
Dutch	5.6	7.0	1.29 (0.94-1.79)	1.23 (0.88-1.73)	5.9	6.1	1.05 (0.59-1.87)	1.09 (0.60-1.96)
Turkish	3.4	3.6	1.07 (0.30-3.88)	0.98 (0.23-4.19)	3.4	3.3	1.26 (0.30-5.20)	1.95 (0.39-9.82)
Moroccan	5.2	2.1	0.40 (0.14-1.15)	0.32 (0.10-1.09)	3.3	3.8	1.21 (0.38-3.58)	1.22 (0.33-4.48)
Black	6.5	4.4	0.65 (0.29-1.44)	0.80 (0.31-2.01)	6.1	1.8	0.33 (0.04-2.45)	0.44 (0.05-3.60)
Induction[2]								
Dutch	10.1	13.3	**1.39 (1.08-1.79)**	1.31 (0.98-1.75)	10.7	12.5	1.19 (0.77-1.84)	0.99 (0.61-1.63)
Turkish	10.7	13.5	1.29 (0.60-2.74)	1.13 (0.46-2.77)	12.8	13.8	1.05 (0.47-2.31)	0.97 (0.38-2.48)
Moroccan	9.5	10.3	1.11 (0.59-2.09)	0.91 (0.45-1.82)	9.9	9.8	0.96 (0.44-2.10)	*0.96 (0.42-2.21)*
Black	8.2	12.2	1.69 (0.92-3.08)	1.99 (0.96-4.12)	9.4	14.5	1.57 (0.66-3.74)	1.22 (0.41-3.58)
Referral during labour[3]								
Dutch	36.3	38.5	1.13 (0.90-1.42)	1.27 (0.98-1.64)	36.2	45.5	1.44 (0.99-2.10)	1.30 (0.86-1.96)
Turkish	44.9	34.0	0.63 (0.33-1.21)	0.59 (0.28-1.27)	33.3	47.4	2.13 (1.07-4.20)	1.68 (0.75-3.74)
Moroccan	41.5	47.4	1.15 (0.72-1.86)	1.37 (0.80-2.34)	43.2	51.6	1.35 (0.75-2.42)	1.21 (0.64-2.31)
Black	39.1	39.8	1.08 (0.65-1.79)	1.16 (0.65-2.08)	39.8	34.3	0.92 (0.42-2.00)	0.93 (0.39-2.20)
Augmentation[2]								
Dutch	24.2	22.4	0.91 (0.75-1.11)	0.95 (0.77-1.18)	23.5	28.6	1.31 (0.95-1.81)	1.09 (0.78-1.53)
Turkish	21.4	22.2	1.09 (0.61-1.96)	1.17 (0.62-2.22)	20.5	25.3	1.31 (0.70-2.43)	1.23 (0.62-2.43)
Moroccan	24.1	23.3	0.96 (0.62-1.49)	1.18 (0.73-1.92)	24.3	22.5	0.97 (0.57-1.66)	0.95 (0.53-1.69)
Black	22.6	21.0	0.95 (0.61-1.47)	1.04 (0.65-1.66)	21.9	20.8	1.01 (0.49-2.06)	0.96 (0.45-2.04)
Pain relief/ sedation[2]								
Dutch	13.8	17.7	1.35 (1.08-1.69)	1.31 (1.03-1.67)	14.0	25.1	2.08 (1.48-2.92)	1.69 (1.18-2.41)
Turkish	15.2	14.8	1.01 (0.51-1.98)	0.99 (0.45-2.17)	13.8	19.5	1.67 (0.83-3.34)	1.90 (0.84-4.27)
Moroccan	12.7	16.4	1.36 (0.80-2.33)	1.74 (0.96-3.13)	12.7	18.6	1.71 (0.94-3.11)	1.67 (0.87-3.23)
Black	15.1	13.7	0.91 (0.55-1.52)	0.98 (0.55-1.76)	13.7	22.6	2.02 (0.99-4.12)	2.05 (0.90-4.66)
Secondary caesarean[2]								
Dutch	8.6	10.1	1.19 (0.90-1.59)	1.17 (0.87-1.57)	8.7	12.1	1.37 (0.87-2.16)	1.21 (0.76-1.92)
Turkish	6.3	9.3	1.47 (0.57-3.77)	1.44 (0.51-4.07)	7.2	8.0	1.32 (0.50-3.44)	1.35 (0.47-3.82)
Moroccan	10.0	7.8	0.71 (0.37-1.38)	0.80 (0.43-1.48)	9.0	8.8	0.91 (0.40-2.07)	0.92 (0.38-2.19)
Black	15.1	10.3	0.67 (0.38-1.16)	0.80 (0.43-1.48)	12.1	15.1	1.44 (0.64-3.25)	1.68 (0.67-4.19)

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=3430 %	HIgh n=1426 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=4404 %	High n=469 %	Adjusted model[1] OR (95% CI)	Crude model OR (95% CI)
First stage >12 hr[4]								
Dutch	17.9	19.1	1.09 (0.82-1.44)	1.16 (0.86-1.58)	18.1	19.1	1.09 (0.67-1.78)	0.92 (0.55-1.54)
Turkish	14.5	19.1	1.47 (0.63-3.43)	1.15 (0.41-3.23)	17.5	16.7	1.02 (0.42-2.44)	0.52 (0.17-1.60)
Moroccan	21.8	19.0	0.86 (0.48-1.57)	0.98 (0.49-1.94)	20.1	21.0	1.11 (0.54-2.28)	0.91 (0.41-2.02)
Black	20.2	22.0	1.16 (0.59-2.29)	1.35 (0.61-2.95)	21.3	17.2	0.82 (0.29-2.31)	0.98 (0.31-3.10)
Second stage >=90 min[5]								
Dutch	12.6	**8.9**	0.68 (0.50-0.92)	0.81 (0.59-1.12)	11.7	13.0	1.12 (0.70-1.77)	1.02 (0.63-1.65)
Turkish	4.9	5.6	1.17 (0.37-3.70)	1.14 (0.34-3.86)	3.4	10.3	3.04 (0.98-9.39)	2.72 (0.81-9.15)
Moroccan	7.7	4.8	0.47 (0.19-1.17)	0.59 (0.23-1.54)	6.3	6.5	0.95 (0.34-2.63)	0.95 (0.33-2.80)
Black	2.9	3.6	1.26 (0.42-3.81)	1.46 (0.44-4.78)	3.3	2.4	0.75 (0.10-5.91)	0.76 (0.09-6.53)
Instrumental delivery[5]								
Dutch	13.6	12.0	0.88 (0.67-1.14)	0.99 (0.74-1.32)	13.3	12.6	0.93 (0.59-1.47)	0.79 (0.49-1.28)
Turkish	6.7	5.4	0.83 (0.29-2.36)	0.83 (0.27-2.56)	3.9	11.3	3.02 (1.05-8.69)	3.47 (1.03-11.6)
Moroccan	5.1	9.3	1.62 (0.72-3.63)	2.11 (0.89-4.98)	6.5	8.6	1.29 (0.52-3.17)	1.26 (0.49-3.24)
Black	5.1	4.3	0.85 (0.34-2.09)	1.15 (0.43-3.07)	4.7	4.4	1.00 (0.22-4.47)	1.26 (0.25-6.42)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol, diabetes, hypertension, gestational age, birth weight [2]Excluded women with primary caesarean section. [3]Only women under primary care at start of labour [4]Excluded women with caesarean section; data available for 3530 women (only recorded in perinatal registry of midwives) [5]Excluded women with caesarean section (primary/ secondary)

General and pregnancy-related anxiety and level of care

No statistically significant interactions were found between general or pregnancy-related anxiety with the level at care at the start of labour for any of the outcome measures (all p-values ≥ 0.07). However, in the subgroup analyses, the risk for pain relief/sedation showed a greater increase in highly anxious women who started labour in secondary care (general anxiety: OR 1.30; 95% CI 1.03-1.63; pregnancy-related anxiety: OR 1.88; 95% CI 1.33-2.46) compared to those who began labour in primary care (general anxiety: OR 1.14; 95% CI 0.88-1.47; pregnancy-related anxiety: OR 1.23; 95% CI 0.88-1.73); however, the interactions were not statistically significant (p-values 0.34 and 0.17, respectively) (Supplemental Table 1).

DISCUSSION

Main findings

In this multi-ethnic cohort, general anxiety and pregnancy-related anxiety, as measured in the first half of pregnancy, were not associated with the progress of the birth process, but were associated with an increased risk for interventions during labour. Pregnancy-related anxiety showed stronger associations than general anxiety. Some associations differed between primiparae and multiparae, whereas similar associations were found across all ethnic groups.

Strengths and limitations

A major strength of the present study is the prospective design in a large multi-ethnic cohort. Although the participation of non-Dutch women was lower than that of Dutch women, we collected data for ≥ 2800 non-Dutch women, making it possible to perform subgroup analyses in the four major ethnic groups in the Netherlands. However, the sample sizes were not large enough to prove a potential interaction effect of ethnicity and anxiety with less frequent outcomes. Although our sample might not be representative for all pregnant women in Amsterdam or in the Netherlands, there is no reason to assume that the association between anxiety and the birth process should be different in non-responders or in women with missing outcome data.

Another strength is the assessment of both general anxiety and pregnancy-related anxiety, using validated questionnaires, while most other studies only assessed pregnancy-related anxiety.

A limitation of the abbreviated 10-item version of the PRAQ that we used, is that this questionnaire has only been validated in nulliparous women. Because one item of the 3-item subscale 'fear of labour' was not applicable for multiparae, the assessment of this aspect in multiparae was limited. Therefore, we only used the total PRAQ score and could not distinguish between the different aspects of pregnancy-related anxiety. This is in agreement with other questionnaires, such as the Wijma Delivery Expectancy Questionnaire) (W-DEQ; a frequently used questionnaire) conceptualized as a uni-dimensional instrument to measure fear of childbirth.[47] Outcome data on the birth process and interventions were available from the PRN. A possible limitation of this might be that not all outcome data were completely registered. However, the amount of missing data within the group with outcome data available was limited and there is no reason to assume that data were missing in a selective manner. Since the collection of our data in 2003-2004, the prevalence of interventions during labour has increased.[1-3, 48] Nevertheless, we think that the associations between anxiety and the birth process have remained similar.

Anxiety was measured in the first half of pregnancy, while other studies measured anxiety later in pregnancy.[16] Little evidence is available concerning how anxiety in the first half of pregnancy persists and evolves during pregnancy, but in case of fear of childbirth it is likely that fear will increase during pregnancy, because the event that is feared is unavoidable and slowly coming closer. Moreover, assessment of anxiety in the first half of pregnancy provides the opportunity to perform an intervention to reduce anxiety, particularly pregnancy-related anxiety.

Comparison with other studies

The prevalence of high general anxiety was higher in our study than in other Dutch studies. [49,50] This can be explained by the large proportion of women of non-Dutch origine in our study.

Some studies found no association between general anxiety and (interventions in) the birth process [16,51] whereas Adams et al. were the only group to find a trend for increased risk for labour induction in general anxious women in a cohort of 2206 women.[14] To our knowledge, our study is the first to show a statistically significant association between general anxiety and interventions during birth. The difference between our study and others might be explained by a lack of power in other studies (including 88 and 1515 women, respectively), as well as by different views on the management of labour, e.g. the use of pain relief. Moreover, the other studies did not investigate the association between anxiety and labour induction, as this is not considered to be an 'undesirable' outcome.

Our observed association between pregnancy-related anxiety and pain relief/sedation is in line with other studies reporting an association between fear of labour and epidural analgesia.[17, 52] Several studies found an association between fear of labour and elective caesarean section.[18-21] Unfortunately, in our data elective caesarean was not coded, but only primary caesarean. Although we found no association between general or pregnancy-related anxiety and primary caesarean, an interaction was seen between parity and general anxiety, suggesting a decreased risk for primary caesarean in anxious nulliparae and an increased risk for anxious multiparae. This might reflect the restraint of obstetricians in the

Netherlands to perform an elective caesarean in nulliparae. In anxious multiparae with a complicated birth history, obstetric caregivers will be more willing to perform a caesarean section. Although others reported an association between fear of labour and emergency caesarean section this was not seen in our study.[15, 23]

Several studies found a longer duration of labour in women with high fear of labour.[14-16] We did not find such an association; unfortunately, however, in our study data on the duration of the first stage of labour were only available in categories of six hours. Since we also did not find an association with augmentation during labour or artificial delivery, we think that an association with the process of birth in our population is very unlikely.

Subgroup analyses showed some different effects in nulliparae and multiparae. Parity is known to be associated with the birth process, which was confirmed in the present study.[8, 10-11] The different effect of anxiety on interventions in the birth process in nulliparae and multiparae can be explained by physiological factors, by by the woman's experience during the previous labour, resulting in more anxiety in women with a complicated previous labour, and also by the information available for the care provider on the previous birth process. The increased risk for induction of labour in multiparae with high general anxiety may be due to greater confidence by obstetric caregivers that the induction will be successful in multiparae. [53,54] An increased risk for referral during labour was only seen in nulliparous women with high pregnancy-related anxiety. This can be explained by the lower a priori risk for referral in multiparae and the subsequent greater confidence of primary care midwives in a successful delivery in primary care. To our knowledge, this is the first study to investigate possible interactions with parity with regard to the impact of anxiety on the birth process. More

research is necessary to unravel the factors contributing to the different effects of anxiety in primiparous and multiparous women.

In contrast to our expectation, we found no stronger associations between general or pregnancy-related anxiety in the non-Dutch groups compared to the Dutch group. However, some indication was found for an increased risk for instrumental delivery in Turkish women with high pregnancy-related anxiety. It is unlikely that this is explained by the lack of prenatal healthcare visits or language barriers, because these factors are also seen among Moroccan and Surinamese women.[55] However, this latter finding should be interpreted with caution as the subgroup was small; we recommend more studies in large multi-ethnic cohorts to address these questions. The large prevalence of high anxiety in non-Dutch women also justifies this research.

Some indications were found that the odds for pain relief/sedation were especially increased in anxious women who started labour in secondary care compared to primary care. This may reflect that primary caregivers use different strategies to support anxious women during labour.

It is reassuring that we found no association between general and pregnancy-related anxiety and the progression of birth, but only with interventions. Another Dutch study showed that referral during labour, a significant intervention within the Dutch context, was associated with a negative recall of labour three years late.[56] In 2013, the need for pain relief was the most frequent reason (18.5%) for referral during labour.[57] Therefore, it is worthwhile to investigate whether these interventions during labour can be managed by treatment or therapy during pregnancy in anxious women, to avoid the necessity of labour-related interventions. If effective treatments are identified, screening for anxiety (especially

pregnancy-related anxiety showing the strongest associations) should be implemented in prenatal care, at least in subgroups with an increased risk for anxiety. The observed high prevalence of general and pregnancy-related anxiety in non-Dutch women underlines the relevance of screening and subsequent fear-reducing interventions, especially in this group.

Conclusion

General and pregnancy-related anxiety in the first half of pregnancy are not associated with prolonged or obstructed labour and artificial delivery and, therefore, do not appear to influence the progression of birth. However, high levels of anxiety contribute to greater use of interventions during labour, especially pain relief/sedation, induction of labour and referral during labour. Although we found similar associations between ethnic groups, the high prevalence of anxiety symptoms in pregnant women with a migrant background justifies more research on the effect of interventions to reduce anxiety symptoms in ethnic groups.

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COMPETING INTERESTS

None declared. Completed disclosure of interests form available to view online as supporting information.

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CONTRIBUTION TO AUTHORSHIP

The study was designed by JMK and TGV. JMK performed the statistical analysis and drafted the manuscript. TGV rendered and provided the ABCD Study data. JMK, TGV and AMS interpreted the results of the analysis. TGV and AMS made substantial contributions in revising the manuscript. The final manuscript was read and approved by all authors.

DETAILS OF ETHICAL APPROVAL

Approval for the ABCD study was obtained from the Central Committee on Research involving Human Subjects in the Netherlands, the Medical Ethical Committees of participating hospitals, and from the Registration Committee of Amsterdam.

DATA SHARING

Data of the ABCD study can be shared for specific research questions. Please contact t.vrijkotte@amc.uva.nl.

LEGENDS OF FIGURES

Figure 1. Flowchart of the ABCD study and inclusion in the current analyses

STAI = State Trait Anxiety Inventory

PRAQ = Pregnancy-Related Anxiety Questionnaire

PRN=Dutch Perinatal Registration

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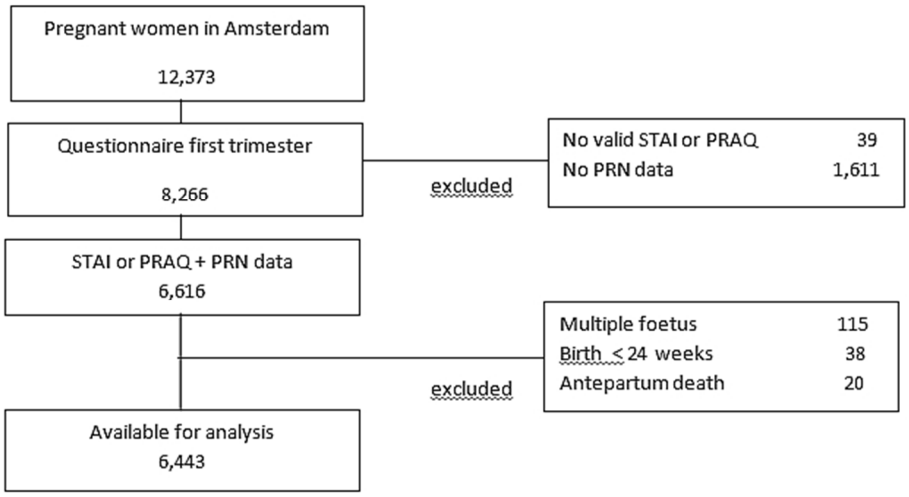
Figure 1. Flowchart of the ABCD study and inclusion in the current analyses



STAI = State Trait Anxiety Inventory

PRAQ = Pregnancy-Related Anxiety Questionnaire

PRN=Dutch Perinatal Registration

Supplemental Table I. Univariate and multivariate associations between first trimester general and pregnancy related anxiety and (interventions in) the birth process, according to care at start of labour

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=4126 %	High n=1850 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=5348 %	High n=662 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Augmentation[2]								
primary care	19.7	19.4	1.01 (0.85-1.22)	1.07 (0.87-1.31)	19.4	21.8	1.20 (0.93-1.55)	1.01 (0.76-1.34)
secondary care	34.7	27.7	0.74 (0.61-0.89)	0.84 (0.68-1.04)	32.4	31.8	0.99 (0.75-1.31)	0.95 (0.70-1.29)
Pain relief/sedation[2]								
primary care	10.5	11.3	1.12 (0.89-1.41)	1.14 (0.88-1.47)	10.4	13.9	1.47 (1.08-2.01)	1.23 (0.88-1.73)
secondary care	22.6	24.6	1.12 (0.91-1.38)	1.30 (1.03-1.63)	21.9	33.7	1.87(1.41-2.48)	1.81 (1.33-2.46)
Secondary caesarean[2]								
primary care	4.9	4.6	0.98 (0.70-1.37)	0.95 (0.66-1.38)	4.7	5.8	1.24 (0.78-1.97)	1.01 (0.62-1.65)
secondary care	19.2	16.6	0.90 (0.72-1.14)	0.95 (0.74-1.22)	17.4	19.5	1.17 (0.84-1.63)	1.16 (0.81-1.64)
First stage >12 hr[3]								
primary care	19.4	19.8	1.03 (0.85-1.25)	1.07 (0.86-1.34)	19.2	22.1	1.24 (0.95-1.63)	1.00 (0.74-1.35)
secondary care	21.2	28.6	1.55 (0.65-3.68)	1.62 (0.56-4.73)	23.6	12.5	0.48 (0.06-4.03)	0.24 (0.02-3.03)
Second stage >=90 min[4]								
primary care	11.3	8.0	0.67 (0.57-0.81)	0.91 (0.68-1.23)	10.4	10.3	0.93 (0.64-1.36)	0.96 (0.64-1.45)
secondary care	10.7	5.8	0.51 (0.35-0.75)	0.82 (0.54-1.24)	9.3	6.7	0.73 (0.41-1.29)	0.94 (0.51-1.74)
Instrumental delivery[4]								
primary care	9.7	8.2	0.84 (0.65-1.10)	1.10 (0.82-1.47)	9.1	10.2	1.11 (0.77-1.61)	1.10 (0.73-1.63)
secondary care	18.4	12.8	0.65 (0.49-0.86)	0.98 (0.72-1.32)	16.7	12.9	0.73 (0.47-1.12)	0.86 (0.54-1.36)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol, diabetes, hypertension, gestational age, birth weight [2]Excluded women with primary caesarean section
[3]Excluded women with caesarean section; data available for 3530 women (only recorded in perinatal registry of midwives) [4]Excluded women with caesarean section (primary/secondary)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

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

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	Suppl file
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, p 11
		(b) Indicate number of participants with missing data for each variable of interest	All tables
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	Table 2 and 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2 and 3
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	19
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-23
Generalisability	21	Discuss the generalisability (external validity) of the study results	23
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Possible relationship between general and pregnancy-related anxiety during the first half of pregnancy and the birth process: a prospective cohort study

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Possible relationship between general and pregnancy-related anxiety during the first half of pregnancy and the birth process: a prospective cohort study

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Word count: 4033

ABSTRACT

Objectives The rate of interventions during childbirth has increased dramatically during the last decades. Maternal anxiety might play a role in the progress of the labour process and interventions during labour. This study aimed to identify associations between anxiety in the first half of pregnancy and the birth process, including any interventions required during labour. In addition, differences in the associations by parity and ethnicity were explored.

Design Prospective cohort study

Setting Primary care midwifery practices and secondary/tertiary care obstetric practices in Amsterdam, participating in the multi-ethnic ABCD study (participation rate 96%; response 8,266/12,373 (67%)).

Participants Included were women with singletons, alive at labour start, with a gestational age ≥24 weeks (n=6,443).

Independent variable General anxiety (STAI state) and pregnancy-related anxiety (PRAQ), were self-reported in the first half of pregnancy.

Outcomes Associations between both forms of anxiety and several indicators of the birth process were analysed. Subgroup analyses were performed for parity and ethnicity.

Results The prevalence of high general anxiety (STAI score ≥ 43) and pregnancy-related anxiety (PRAQ score ≥P90) were 30.9% and 11.0%, respectively. After adjustment, in nulliparae, both general and pregnancy-related anxiety were associated with pain relief and/or sedation (OR for general anxiety 1.23;95%-CI 1.02-1.48;OR for pregnancy-related anxiety 1.45;95%-CI 1.14-1.85). In multiparae, general anxiety was associated with induction of labour (OR 1.53;95%-CI 1.16-2.03), pregnancy-related anxiety was associated with primary

caesarean section (OR 1.66;95%-CI 1.02-2.70). Associations were largely similar for all ethnicities.

Conclusions

High levels of general and pregnancy-related anxiety in early pregnancy contribute modestly to more interventions during the birth process with similar associations between ethnic groups, but with some differences between nulliparae and multiparae.

Abbreviations: ABCD study = Amsterdam Born Children and their Development study, BMI = body mass index, PRN = Dutch Perinatal Registration, STAI = State Trait Anxiety Inventory, PRAQ = Pregnancy-Related Anxiety Questionnaire

STRENGTH AND LIMITATIONS

Strengths

- We performed a prospective study in a large multi-ethnic cohort.
- We used validated questionnaires to assess both forms of anxiety.
- Anxiety was measured in the first half of pregnancy.

Limitations

- The subscale for Fear of Childbirth (FOC) within the Pregnancy-Related Anxiety Inventory was not suitable to measure FOC in multiparous women. Therefore, our focus was on the total score on pregnancy-related anxiety and not on the subscales.

- Our data are collected in 2003 and 2004. Since 2004 the intervention rate has increased, but there is no reason to assume that the association between anxiety and (interventions in) the birth process has changed.

INTRODUCTION

The rate of interventions during childbirth has increased dramatically in recent decades. For example, in the Netherlands, from 1993-2002 the caesarean section rate rose from 8.1% to 13.6%. and 16.7% in 2010.[1,2] The rate of labour induction increased during 2008-2013 from 15% to 21%.[3] Although the absolute incidence of caesarean section is higher in other western countries compared to the Netherland, a similar rise in caesarean sections occurred in other western countries.[4-7]

The progression of the birth process and concomitant interventions are associated with maternal characteristics such as age, parity, body mass index (BMI), ethnicity, illness, infant birth weight, as well as with organisational factors, such as existing guidelines, the availability of 24-h pain relief, the profession of the obstetric care provider (midwife versus physician), and the level of care (primary/secondary).[8-12] Moreover, maternal anxiety might play a role in the birth process. Although one review found no overall association between anxiety and obstetric complications, specific types of anxiety (such as fear of childbirth) may be associated with specific complications and interventions, such as prolonged labour and caesarean section.[13]

Several studies have shown a relationship between fear of childbirth and duration of labour [14-16], epidural analgesia [17] and elective [18-22] and emergency caesarean. [15,23]

On the other hand, other studies reported no such relationships.[24-26] One explanation for these inconsistencies could be differences in cultural, social and organisational characteristics between countries. These factors can mediate or exacerbate the effect of anxiety on the birth process and on concomitant interventions. For example, some ethnic groups are more

susceptible to stress-induced neuroendocrine and inflammatory pathways which could lead to adverse perinatal outcomes.[27-30] Also, cultural and social differences between ethnic groups (e.g. language barriers, unfamiliarity with the obstetric care organisation) may explain differences between ethnic groups regarding the influence of anxiety on the birth process.[31-34] In addition, it is unknown whether the association between anxiety and the birth process differs between nulliparous and multiparous women as well as between women giving birth in primary and secondary care. To our knowledge, no study has investigated the level of care and ethnicity in the association between general and pregnancy-related anxiety, and the progression of birth.

Anxiety in pregnancy is associated with shorter gestational age and has negative implications for fetal neurodevelopment and child outcomes.[35] Women with high fear of childbirth in pregnancy are at risk for psychiatric problems postpartum, for example postpartum depression and even posttraumatic stress syndrome (PTSS). [35-37] To lower the risk for those serious consequences, appropriate treatment is desirable. If anxiety does also have a detrimental effect on the birth process, there is all the more reason for screening early in pregnancy for anxiety. Screening for anxiety early in pregnancy, provides sufficient time for treatment or therapy for women with high anxiety levels.

Therefore, this study investigates the association between general anxiety and/or pregnancy-related anxiety measured during the first half of pregnancy and the birth process, and the interaction of this association with parity, ethnicity and the level of care at the start of labour.

METHODS

Study design and participants

Data were derived from the Amsterdam Born Children and their Development (ABCD) study, a large multi-ethnic prospective cohort study.[38] The ABCD study is aimed at examining the relationship between maternal lifestyle and psychosocial conditions during pregnancy and the child's health at birth as well as later in life. Between January 2003 and March 2004, participating obstetric care providers (midwives and hospital obstetricians; participation rate 96%) invited pregnant women in Amsterdam at their first antenatal visit to enroll in the ABCD. A total of 12,373 women were approached (99% of the target population). Within two weeks of this first contact, women who agreed to take part were sent a questionnaire, covering socio-demographic conditions, obstetric history and psychosocial conditions, including general and pregnancy-related anxiety. Consent forms were also sent for the linkage of study data to medical records as well as to data from the Dutch Perinatal Registration (PRN).

A total of 8266 women (response rate 67%) filled in the pregnancy questionnaire at an average of 16 weeks gestation (IQR 14-18 weeks) and 7043 gave permission for perusal of their medical records. Three months after birth, the women who gave permission for follow-up (n=6854) received a questionnaire concerning, amongst other things, the course of pregnancy and delivery. A total of 5218 mothers filled out this questionnaire. [38] To facilitate participation by women unable to speak Dutch, questionnaires were also available in Turkish, Arabic and English, and women could also complete the questionnaire with the assistance of an interviewer. Participation of foreign-born women was lower (42-64%) than for Dutch-born women (77%) but comparable with response rates in other population-based, multi-ethnic studies in the Netherlands.[39] In the present study we included women with a singleton pregnancy, a gestational age ≥ 24 weeks, and a living foetus at the start of labour.

Approval for the study was obtained from the Medical Ethical Committees of the participating hospitals and the Registration Committee of the Municipality of Amsterdam. All women gave written informed consent.

Definition and measurement of variables

General and pregnancy-related anxiety

General anxiety was assessed using the Dutch version of the State-Trait Anxiety Inventory (STAI).[40-41] The 20 items regarding the state anxiety subscale were included in our questionnaire, with each item scored on a 4-point scale. The anxiety score was dichotomised in low-average (<43 points) and high anxiety (≥ 43 points).[42] In our sample, the internal consistency (Cronbach's alpha) of the scale was 0.94.

Pregnancy-related anxiety was assessed using an abbreviated 10-item version of the Pregnancy-Related Anxieties Questionnaire (PRAQ).[43-44] The internal consistency (Cronbach's alpha) was 0.79; each item was scored on a 4-point scale. Three aspects that can be distinguished in the PRAQ are 'fear of labour', 'fear of bearing a physically or mentally handicapped child' (hereafter 'fear of child') and 'concern about one's appearance'. In the present study our focus was on the total score on pregnancy-related anxiety. One question was only applicable for nulliparous women ("I am scared of labour and birth because I have never experienced this"), resulting in a maximum score of 40 for nulliparous women and 36 for multiparous women. Because cut-off scores were not available for dichotomisation of the results from this instrument, we used the 90th percentile to identify women with a high level of pregnancy-related anxiety.[45] This resulted in cut-off scores of 28 and 24 for nulliparous

and multiparous women, respectively. We performed additional explorative analyses, using the PRAQ subscales 'fear of labour' (only for nulliparous women) and 'fear of child' These were dichotomised based on the 10th percentile, the cut-offs for 'fear of labour' and 'fear of child' were 10 and 12, respectively.

Birth process and interventions

Outcome data on the birth process and interventions were obtained by linking our records with the PRN database. Validation of the PRN database has been described previously.[39] The outcome variables were determined from the records of the Registry of Midwives, the Registry of Obstetricians and the Registry of Paediatricians according to the decision rules of the PRN.[46]

We defined the following outcomes:

Birth process: duration of first stage of labour (≤ 12 h/>12 h; only available in registry of midwives), duration of second stage (< 1.5 h/≥ 1.5 h)].

Interventions: primary caesarean (yes/no), induction of labour (yes/no), referral during labour [only in the group that started labour under primary care; (yes/no)], augmentation (yes/no), pain relief/sedation (yes/no), secondary caesarean (yes/no), vaginal instrumental delivery [ventouse or forceps; (yes/no)

Covariates

The following covariates were included in the analyses: maternal age (years), ethnicity, education (years after primary school), pre-pregnancy BMI (kg/m^2), parity (nulliparae/multiparae), smoking during pregnancy (yes/no), alcohol use during pregnancy

(yes/no), hypertensive disorders and diabetes (pre-existent or detected during pregnancy), gestational age at delivery (weeks), care at start of labour (primary/secondary), and birth weight (g). Ethnicity was based on the birth country of the participant's mother (self-reported) and included the following categories: Dutch, Turkish, Moroccan, Black (Antillean/Aruban, Surinamese, Ghanaian or other African descent), other non-Western and other Western countries. Pre-pregnancy weight and height, education, smoking and alcohol use during pregnancy were self-reported in the questionnaire. Parity, birth weight, gestational age, hypertension and diabetes were extracted from the PRN database. Missing data concerning parity, birth weight and gestational age were extracted from the three months questionnaire; hypertension and diabetes were encoded as 'yes' if these diseases were reported in the PRN database and/or in the three months questionnaire.

Statistical analysis

Descriptive statistics were used to profile the sample characteristics according to the level of maternal general anxiety and of pregnancy-related anxiety. Categorical variables were described by percentages per category. Continuous variables were described using the mean and 95% confidence intervals (CI), if normally distributed and, if not, with the median and minimum and maximum values. Risks were presented as odds ratios (OR) and 95% CI. Differences were tested with Student's t test or Mann-Whitney U test for continuous variables and Pearson's chi square test for categorical variables. Associations between high general and/or pregnancy-related anxiety compared to low anxiety were analysed for each outcome using multiple logistic regression analyses. All potential confounders were determined a priori

and added to the regression model. We adjusted for general covariates: age, ethnicity, education, pre-pregnancy BMI, parity, smoking and alcohol use. To avoid overadjustment, we did not adjust for potential intermediate variables, such as hypertension, diabetes, gestational age and birth weight. Subgroup analyses were performed according to parity (nulliparous versus multiparous women), ethnicity (Dutch, Turkish, Moroccan and Black) and care at start of labour (primary/secondary care). No subgroup analysis was performed in the ethnic groups 'other Western' and 'other non-Western' as each of these groups represented a diverse selection of ethnicities. To formally test whether different associations existed for the different subgroups (parity, ethnicity, and care at start of labour) between STAI or PRAQ and the birth process variables, interaction terms (between parity, ethnicity respectively care at start of labour with general and pregnancy-related anxiety) were added to the final model. We performed additional explorative analyses, using the PRAQ subscales 'fear of labour' (only for nulliparous women) and 'fear of child' following the same procedure.

All analyses were performed with SPSS 21.0 (IBM Statistics, USA).

RESULTS

Response

Of the 8266 women who completed the pregnancy questionnaire, for 6616 women valid results for the STAI or PRAQ and outcome data, were available. The mean STAI-score was significantly higher in the group of women with missing outcome data (39.5 versus 38.2); the PRAQ-scores were comparable. After exclusion of 173 women (with a multiple foetus, a gestational age ≤ 24 weeks, or antenatal death), 6443 records were available for analysis (Figure 1). Most women completed both the STAI and the PRAQ (n=6335); 37 women completed only the STAI and 71 women only the PRAQ.

Covariates according to anxiety levels

A high STAI score (further referred to as 'high general anxiety') was found in 30.9% of the sample and a high score on the PRAQ (further referred to as 'high pregnancy-related anxiety') in 11.1% of the sample. The STAI score was moderately correlated with the PRAQ score (Pearson's r=0.36; p<0.001).

High general anxiety and high pregnancy-related anxiety were more frequently observed in younger women, in women with non-Dutch ethnicities, fewer years of education, higher pre-pregnancy BMIs, smoking women, women with less alcohol consumption, and in women who gave birth to babies with a lower birth weight. There were no differences in the rates of hypertension and gestational age between the high and low anxiety groups; however, diabetes and secondary care at the start of labour were more frequently observed in women

with high general anxiety. Nulliparous women appeared to be at lower risk for high general anxiety compared to multiparous women. (Table 1)

Table 1. Maternal characteristics according to general anxiety in the first half of pregnancy and pregnancy-related anxiety

		General anxiety			Pregnancy-related anxiety		
		Low n=4400[1]	High n=1972[1]	p-value[2]	Low n=5697[1]	High n=709[1]	p-value[2]
Anxiety score	-median(min-max)						
Nulliparae		33 (20-42)	49 (43-80)		21 (10-27)	30 (28-40)	
Multiparae		33 (20-42)	49 (43-74)		18 (9-23)	26 (24-36)	
Age (years)	-mean (95% CI)	31.5 (31.4-31.7)	29.7 (29.5-30.0)	<.001	31.2 (31.1-31.4)	28.7 (28.3-29.2)	<.001
Ethnicity	-%			<.001			<.001
Dutch		63.5	38.9		58.8	30.1	
Turkish		2.6	8.6		3.6	12.9	
Moroccan		5.4	12.1		6.5	15.3	
Black		6.5	12.8		8.6	8.1	
Other Western		14.1	13.3		13.7	14.4	
Other non-Western		7.9	14.3		8.9	19.3	
Education (years)	-mean (95% CI)	9.6 (9.5-9.7)	7.5 (7.3-7.7)	<.001	9.2 (9.1-9.3)	7.1 (6.8-7.5)	<.001
Pre-pregnancy BMI (kg/m^2)	-mean (95% CI)	22.8 (22.7-22.9)	23.8 (23.6-24.0)	<.001	23.0 (22.9-23.1)	23.8 (23.5-24.1)	<.001
Nulliparae	-%	59.1	49.5	<.001	[3]	[3]	
Smoking in pregnancy	-%	7.3	15.2	<.001	9.0	15.0	<.001
Alcohol in pregnancy	-%	24.7	16.0	<.001	22.9	15.3	<.001
Hypertensive disorders	-%	12.2	12.5	.70	12.1	12.9	.54
Diabetes	-%	1.8	3.1	.001	2.1	3.1	.08
Gestational age	-%			.27			.87
<37 weeks		5.0	6.0		5.4	5.1	
37-41 weeks		85.7	84.7		85.4	85.2	
>=42 weeks		9.3	9.3		9.2	9.7	
Care start labour	-%			<.001			.29
primary care		60.1	54.6		58.6	56.6	
secondary care		39.9	45.4		41.4	43.4	
Birth weight (g)	-mean (95% CI)	3473 (3456-3490)	3379 (3354-3405)	<.001	3450 (3435-3465)	3391 (3351-3431)	.009

[1] Missing values were excluded (range 0-217). [2] Continuous variables: Student's t-test and/or Mann-Whitney U test; categorical variables Pearson's Chi square test [3] No comparison possible between nulliparous and multiparous women because in each group the P90 was used as cut-off for high pregnancy-related anxiety

Outcome prevalences

The prevalences of the indicators of the birth process are shown in Table 2.

Most prevalences were higher (p-values <0.05) in nulliparous than in multiparous women, except primary caesarean section (p=0.09). Most prevalences were similar in the different ethnicities, except for a higher prevalence of prolonged second stage of labour and instrumental delivery in Dutch women (p<0.001).

Table 2. Univariable and multivariable associations between general and pregnancy-related anxiety in the first half of pregnancy and (interventions in) the birth process, according to parity

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=4400 %	High n=1972 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=5697 %	High n=709 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Primary caesarean								
Nulliparae	5.6	3.9	0.69 (0.47-0.99)	0.82 (0.56-1.20) [6]	5.2	4.3	0.85 (0.51-1.39)	1.07 (0.64-1.79)
Multiparae	5.4	7.2	1.33 (0.97-1.83)	1.37 (0.97-1.93) [6]	5.8	8.2	1.53 (0.96-2.42)	**1.66 (1.02-2.70)**
Induction[2]								
Nulliparae	11.7	12.2	1.07 (0.85-1.35)	1.06 (0.83-1.36) [6]	11.8	12.4	1.01 (0.73-1.40)	1.03 (0.74-1.45)
Multiparae	8.2	13.4	**1.74 (1.34-2.25)**	**1.53 (1.16-2.03)** [6]	9.5	14.7	**1.68 (1.15-2.44)**	1.38 (0.92-2.07)
Referral during labour[3]								
Nulliparae	52.0	53.2	1.10 (0.90-1.34)	1.10 (0.89-1.35)	51.7	57.5	1.30 (0.99-1.71)	1.26 (0.95-1.67)
Multiparae	18.8	23.6	**1.33 (1.03-1.72)**	1.07 (0.81-1.41)	19.8	25.9	1.48 (0.99-1.20)	1.17 (0.78-1.78)
Augmentation[2]								
Nulliparae	34.5	32.5	0.93 (0.80-1.10)	0.94 (0.79-1.11)	34.4	33.4	0.98 (0.79-1.23)	0.96 (0.76-1.21)
Multiparae	11.7	13.1	1.17 (0.91-1.49)	1.10 (0.78-1.31)	12.1	13.7	1.18 (0.81-1.73)	1.02 (0.68-1.52)
Pain relief/sedation[2]								
Nulliparae	21.3	26.6	**1.35 (1.14-1.61)**	**1.23 (1.02-1.48)**	21.9	30.2	**1.59 (1.26-2.01)**	**1.45 (1.14-1.85)**
Multiparae	5.5	6.9	1.27 (0.91-1.77)	1.26 (0.88-1.79)	5.7	8.6	1.56 (0.97-2.53)	1.61 (0.97-2.68)
Secondary caesarean[2]								
Nulliparae	12.4	13.1	1.09 (0.87-1.37)	1.02 (0.80-1.30)	12.3	14.7	1.24 (0.92-1.67)	1.22 (0.89-1.67)

Multiparae	5.8	6.2	1.07 (0.76-1.51)	1.03 (0.71-1.49)	5.9	5.9	0.92 (0.51-1.65)	0.93 (0.50-1.71)
First stage >12 hr[4]								
Nulliparae	30.5	33.1	1.12 (0.90-1.39)	1.00 (0.79-1.26)	31.1	31.1	1.04 (0.77-1.41)	0.89 (0.64-1.22)
Multiparae	3.9	5.8	1.59 (0.96-2.63)	1.43 (0.84-2.45)	4.4	7.2	1.85 (0.92-3.71)	1.63 (0.78-3.38)
Second stage >=90 min[5]								
Nulliparae	18.4	12.6	**0.64 (0.50-0.82)**	0.79 (0.61-1.01)[7]	17.2	14.5	0.80 (0.58-1.12)	0.95 (0.67-1.35)
Multiparae	1.3	2.0	1.51 (0.78-2.94)	1.74 (0.85-3.55)[7]	1.6	1.3	0.82 (0.25-2.71)	0.95 (0.28-3.24)
Instrumental delivery[5]								
Nulliparae	19.6	17.1	0.87 (0.70-1.07)	1.03 (0.82-1.29)	19.1	17.5	0.89 (0.66-1.20)	1.03 (0.75-1.41)
Multiparae	3.0	3.3	1.05 (0.65-1.70)	1.16 (0.69-1.93)	3.2	2.1	0.67 (0.27-1.68)	0.75 (0.29-1.93)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol [2]Excluded women with primary caesarean section. [3]Only women under primary care at start of labour [4]Excluded women with caesarean section; data available for 3533 women (only recorded in perinatal registry of midwives) [5]Excluded women with caesarean section (primary/ secondary) [6]p-value interaction parity and anxiety 0.018 [7]p-value interaction parity and anxiety 0.017

Multivariable analyses

General anxiety and parity

After adjustment, women with high general anxiety were more likely to receive pain relief/sedation, which association was only significant in nulliparous women. Multiparous women were more likely to undergo induction of labour, which was not seen in nulliparae. (Table 2). Moreover, statistically significant interactions between parity and general anxiety were found for primary caesarean section and a second stage of ≥ 90 min: highly anxious multiparous women were more likely to experience these two outcomes, compared to non-anxious women, while highly anxious nulliparous women were at decreased risk for these outcomes.

Pregnancy-related anxiety and parity

After adjustment, women with high pregnancy-related anxiety were more likely to receive pain relief/sedation, which association was only significant in nulliparous women. Subgroup analysis showed an increased risk for primary caesarean in highly anxious multiparous women; however, no statistically significant interactions with parity were observed when formal interaction testing was completed (Table 2).

Analyses with the subscales showed similar trends with one exception: fear of labour was associated with an increased risk for pain relief/sedation in (nulliparous) women, which was not the case for high 'fear of child'.

General and pregnancy-related anxiety and ethnicity

After adjustment, no statistically significant interactions were found between general or pregnancy-related anxiety with ethnicity for any of the outcome measures (all p-values ≥ 0.12). The increased risk for pain relief/sedation was only significant in Dutch women with high general or pregnancy-related anxiety.

However, subgroup analyses suggested a statistically significant lower risk for primary caesarean in Moroccon women with high general anxiety, an increased risk for instrumental delivery in Moroccon women with high general anxiety and in Turkish women with high pregnancy-related anxiety. (Table 3).

Analyses with the subscales showed similar trends. However, in Dutch women with high 'fear of labour' the risk for a first stage of labour longer than 12 hours and for a second stage of labour longer than 1,5 hour was increased. High 'fear of child' was not associated with an increased risk for any of the outcome parameters. (Supplemental table 3a).

Table 3. Univariable and multivariable associations between general and pregnancy-related anxiety in the first half of pregnancy and (interventions in) the birth process, according to ethnicity

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=3430 %	High n=1426 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=4404 %	High n=469 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Primary caesarean								
Dutch	5.6	7.0	1.28 (0.93-1.77)	1.26 (0.90-1.75)	5.9	6.1	1.05 (0.59-1.88)	1.01 (0.56-1.81)
Turkish	3.4	3.6	1.05 (0.29-3.80)	0.97 (0.24-3.84)	3.4	3.3	1.18 (0.29-4.84)	1.63 (0.35-7.52)
Moroccan	5.2	2.1	0.39 (0.14-1.13)	0.31 (0.10-0.94)	3.3	3.8	1.16 (0.37-3.67)	1.29 (0.40-4.20)
Black	6.5	4.4	0.64 (0.29-1.43)	0.77 (0.33-1.78)	6.1	1.8	0.31 (0.04-2.30)	0.41 (0.05-3.12)
Induction[2]								
Dutch	10.1	13.3	**1.37 (1.06-1.76)**	1.29 (0.99-1.67)	10.7	12.5	1.20 (0.78-1.85)	1.05 (0.68-1.64)
Turkish	10.7	13.5	1.26 (0.59-2.67)	1.21 (0.55-2.63)	12.8	13.8	1.03 (0.47-2.28)	1.09 (0.48-2.47)
Moroccan	9.5	10.3	1.08 (0.58-2.01)	1.08 (0.57-2.03)	9.9	9.8	0.91 (0.42-1.97)	0.92 (0.42-2.03)
Black	8.2	12.2	1.67 (0.92-3.04)	1.81 (0.96-3.43)	9.4	14.5	1.49 (0.63-3.53)	1.44 (0.58-3.54)
Referral during labour[3]								
Dutch	36.3	38.5	1.10 (0.88-1.37)	1.19 (0.93-1.52)	36.2	45.5	1.44 (0.99-2.09)	1.25 (0.84-1.86)
Turkish	44.9	34.0	0.65 (0.34-1.22)	0.60 (0.30-1.22)	33.3	47.4	**2.02 (1.04-3.94)**	1.79 (0.87-3.69)
Moroccan	41.5	47.4	1.25 (0.79-2.00)	1.54 (0.92-2.57)	43.2	51.6	1.41 (0.80-2.49)	1.39 (0.75-2.56)
Black	39.1	39.8	1.06 (0.64-1.73)	1.10 (0.64-1.87)	39.8	34.3	0.82 (0.39-1.73)	0.84 (0.38-1.87)
Augmentation[2]								
Dutch	24.2	22.4	0.91 (0.74-1.10)	0.93 (0.76-1.15)	23.5	28.6	1.32 (0.96-1.81)	1.11 (0.80-1.55)
Turkish	21.4	22.2	1.07 (0.60-1.92)	1.04 (0.56-1.92)	20.5	25.3	1.27 (0.69-2.36)	1.16 (0.60-2.22)
Moroccan	24.1	23.3	0.96 (0.62-1.49)	1.16 (0.73-1.84)	24.3	22.5	0.96 (0.57-1.64)	0.91 (0.52-1.59)
Black	22.6	21.0	0.94 (0.61-1.45)	1.03 (0.65-1.64)	21.9	20.8	0.95 (0.47-1.93)	0.87 (0.42-1.83)
Pain relief/ sedation[2]								
Dutch	13.8	17.7	**1.35 (1.08-1.68)**	**1.30 (1.02-1.65)**	14.0	25.1	**2.08 (1.49-2.91)**	**1.70 (1.20-2.41)**
Turkish	15.2	14.8	0.99 (0.50-1.95)	1.05 (0.49-2.25)	13.8	19.5	1.63 (0.82-3.25)	1.74 (0.79-3.82)
Moroccan	12.7	16.4	1.32 (0.78-2.24)	1.59 (0.90-2.79)	12.7	18.6	1.62 (0.89-2.93)	1.52 (0.81-2.86)
Black	15.1	13.7	0.90 (0.54-1.50)	1.05 (0.60-1.85)	13.7	22.6	1.89 (0.94-3.83)	1.89 (0.87-4.12)
Secondary caesarean[2]								
Dutch	8.6	10.1	1.20 (0.91-1.59)	1.19 (0.89-1.59)	8.7	12.1	1.38 (0.88-2.16)	1.20 (0.75-1.90)
Turkish	6.3	9.3	1.44 (0.56-3.70)	1.39 (0.52-3.68)	7.2	8.0	1.29 (0.50-3.37)	1.31 (0.48-3.57)
Moroccan	10.0	7.8	0.75 (0.39-1.43)	0.89 (0.45-1.78)	9.0	8.8	0.88 (0.39-1.99)	0.90 (0.39-2.11)
Black	15.1	10.3	0.66 (0.38-1.16)	0.78 (0.43-1.41)	12.1	15.1	1.36 (0.60-3.05)	1.47 (0.63-3.47)

Outcome			General anxiety				Pregnancy-related anxiety	
	Low n=3430 %	High n=1426 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=4404 %	High n=469 %	Adjusted model[1] OR (95% CI)	Crude model OR (95% CI)
First stage >12 hr[4]								
Dutch	17.9	19.1	1.09 (0.82-1.44)	1.16 (0.85-1.57)	18.1	19.1	1.08 (0.66-1.76)	0.92 (0.55-1.53)
Turkish	14.5	19.1	1.44 (0.62-3.34)	1.01 (0.38-2.68)	17.5	16.7	1.03 (0.43-2.46)	0.57 (0.20-1.58)
Moroccan	21.8	19.0	0.89 (0.50-1.59)	1.06 (0.56-2.03)	20.1	21.0	1.09 (0.54-2.19)	0.96 (0.45-2.06)
Black	20.2	22.0	1.16 (0.59-2.27)	1.27 (0.60-2.69)	21.3	17.2	0.80 (0.29-2.25)	0.80 (0.26-2.45)
Second stage >=90 min[5]								
Dutch	12.6	8.9	0.68 (0.50-0.92)	0.79 (0.57-1.08)	11.7	13.0	1.12 (0.71-1.78)	1.02 (0.63-1.66)
Turkish	4.9	5.6	1.16 (0.37-3.65)	1.06 (0.32-3.51)	3.4	10.3	2.30 (0.97-9.20)	3.01 (0.91-9.93)
Moroccan	7.7	4.8	0.59 (0.26-1.34)	0.79 (0.33-1.91)	6.3	6.5	1.07 (0.41-2.75)	1.04 (0.39-2.80)
Black	2.9	3.6	1.26 (0.42-3.83)	1.34 (0.42-4.26)	3.3	2.4	0.74 (0.09-5.82)	0.64 (0.08-5.28)
Instrumental delivery[5]								
Dutch	13.6	12.0	0.87 (0.66-1.13)	0.96 (0.72-1.27)	13.3	12.6	0.93 (0.59-1.48)	0.80 (0.49-1.28)
Turkish	6.7	5.4	0.82 (0.29-2.32)	0.83 (0.28-2.50)	3.9	11.3	**2.95 (1.03-8.48)**	**3.70 (1.16-11.8)**
Moroccan	5.1	9.3	1.91 (0.87-4.18)	**2.51 (1.09-5.75)**	6.5	8.6	1.34 (0.57-3.13)	1.33 (0.55-3.20)
Black	5.1	4.3	0.84 (0.34-2.07)	1.11 (0.42-2.93)	4.7	4.4	0.94 (0.21-4.20)	0.87 (0.18-4.09)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol [2]Excluded women with primary caesarean section. [3]Only women under primary care at start of labour
[4]Excluded women with caesarean section; data available for 3530 women (only recorded in perinatal registry of midwives) [5]Excluded women with caesarean section (primary/ secondary)

General and pregnancy-related anxiety and level of care

No statistically significant interactions were found between general or pregnancy-related anxiety with the level at care at the start of labour for any of the outcome measures (all p-values ≥ 0.07). However, in the subgroup analyses, the risk for pain relief/sedation was increased in highly anxious women who started labour in secondary care, only (general anxiety: OR 1.26; 95% CI 1.004-1.58; pregnancy-related anxiety: OR 1.81; 95% CI 1.33-2.45) compared to those who began labour in primary care (general anxiety: OR 1.09; 95% CI 0.84-1.40; pregnancy-related anxiety: OR 1.17; 95% CI 0.84-1.63). (Supplemental Table 1).

The subscale analyses showed that fear of labour was associated with pain relief/sedation, which was not the case of high 'fear of child'. (Supplemental table 4).

DISCUSSION

Main findings

In this multi-ethnic cohort, general anxiety and pregnancy-related anxiety, as measured in the first half of pregnancy, were not associated with the progress of the birth process, but were associated with an increased risk for interventions during labour. Pregnancy-related anxiety showed stronger associations than general anxiety. Some associations differed between nulliparous and multiparous women, whereas largely similar associations were found across all ethnic groups.

Strengths and limitations

A major strength of the present study is the prospective design in a large multi-ethnic cohort. Although the participation of non-Dutch women was lower than that of Dutch women, we collected data for ≥ 2800 non-Dutch women, making it possible to perform subgroup analyses in the four major ethnic groups in the Netherlands. However, the sample sizes were not large enough to prove a potential interaction effect of ethnicity and anxiety with less frequent outcomes. Although our sample might not be representative for all pregnant women in Amsterdam or in the Netherlands, there is no reason to assume that the association between anxiety and the birth process should be different in non-responders or in women with missing outcome data.

Another strength is the assessment of both general anxiety and pregnancy-related anxiety, using validated questionnaires, while most other studies only assessed pregnancy-related anxiety.

A limitation of the abbreviated 10-item version of the PRAQ that we used, is that this questionnaire has only been validated in nulliparous women. Because one item of the 3-item subscale 'fear of labour' was not applicable for multiparae, the assessment of this aspect in multiparae was limited. Therefore, we used the total PRAQ score, but also performed additional analyses to explore the aspects 'fear of labour' (only in nulliparous women) and 'fear of getting a handicapped child'. The use of the total PRAQ score is in agreement with other questionnaires, such as the Wijma Delivery Expectancy Questionnaire) (W-DEQ; a frequently used questionnaire) conceptualized as a uni-dimensional instrument to measure fear of childbirth.[47] Outcome data on the birth process and interventions were available from the PRN, as well as from a questionnaire filled out three months after birth by the mother. Combination of these two data sources resulted in a limited amount of missing data within the group with outcome data available and there is no reason to assume that data were missing in a selective manner. Since the collection of our data in 2003-2004, the prevalence of interventions during labour has increased.[1-3, 48] Nevertheless, we think that the associations between anxiety and the birth process have remained similar.

Anxiety was measured in the first half of pregnancy, while other studies measured anxiety later in pregnancy.[16] Little evidence is available concerning how anxiety in the first half of pregnancy persists and evolves during pregnancy, but in case of fear of childbirth/labour it might be possible that fear will increase during pregnancy, because the event that is feared is unavoidable and slowly coming closer. Moreover, assessment of anxiety in the first half of

pregnancy provides the opportunity to perform an intervention to reduce anxiety, particularly pregnancy-related anxiety.

Comparison with other studies

The prevalence of high general anxiety was higher in our study than in other Dutch studies. [49,50] This can be explained by the large proportion of women of non-Dutch origine in our study.

Some studies found no association between general anxiety and (interventions in) the birth process [16,51] whereas Adams et al. were the only group to find a trend for increased risk for labour induction in general anxious women in a cohort of 2206 women.[14] To our knowledge, our study is the first to show a statistically significant association between general anxiety and interventions during birth. The difference between our study and others might be explained by a lack of power in other studies (including 88 and 1515 women, respectively), as well as by different views on the management of labour, e.g. the use of pain relief. Moreover, the other studies did not investigate the association between anxiety and labour induction, as this is not considered to be an 'undesirable' outcome.

Our observed association between pregnancy-related anxiety and pain relief/sedation is in line with other studies reporting an association between fear of labour and epidural analgesia.[17, 52] Several studies found an association between fear of labour and elective caesarean section.[18-21] Unfortunately, in our data elective caesarean was not coded, but only primary caesarean. Although we found no association between general or pregnancy-related anxiety and primary caesarean, except in the subgroup of Moroccon women, an

interaction was seen between parity and general anxiety, suggesting a decreased risk for primary caesarean in anxious nulliparae and an increased risk in anxious multiparae. This might reflect the restraint of obstetricians in the Netherlands to perform an elective caesarean in nulliparae. In anxious multiparae with a complicated birth history, obstetric caregivers will be more willing to perform a caesarean section. Although others reported an association between fear of labour and emergency caesarean section this was not seen in our study.[15, 23]

Several studies found a longer duration of labour in women with high fear of labour.[14-16] We did not find such an association with general or pregnancy-related anxiety, but we did find an association with the PRAQ subscale 'fear of labour' within the subgroup of nulliparous Dutch women. However, this result from an explorative analysis should be interpreted with caution. Unfortunately, in our study, data on the duration of the first stage of labour were only available in categories of six hours. Since we did not find an association with augmentation during labour or artificial delivery, we think that an association with the process of birth in our population is very unlikely.

Subgroup analyses showed some different effects in nulliparae and multiparae. Parity is known to be associated with the birth process, which was confirmed in the present study.[8, 10-11] The different effect of anxiety on interventions in the birth process in nulliparae and multiparae can be explained by physiological factors, by the woman's experience during the previous labour, resulting in more anxiety in women with a complicated previous labour, and also by the information available for the care provider on the previous birth process. The increased risk for induction of labour in multiparae with high general anxiety may be due to greater confidence by obstetric caregivers that the induction will be successful in multiparae.

[53,54] An increased risk for referral during labour was only seen in nulliparous women with high 'fear of labour', an aspect of pregnancy-related anxiety. This can be explained by the lower a priori risk for referral in multiparae and the subsequent greater confidence of primary care midwives in a successful delivery in primary care. To our knowledge, this is the first study to investigate possible interactions with parity with regard to the impact of anxiety on the birth process. More research is necessary to unravel the factors contributing to the different effects of anxiety in nulliparous and multiparous women.

In contrast to our expectation, we found no stronger associations between general or pregnancy-related anxiety in the non-Dutch groups compared to the Dutch group. However, some indication was found for an increased risk for instrumental delivery in Turkish women with high pregnancy-related anxiety, for Moroccon women with high general anxiety, and for a lower risk for primary caesarean in highly anxious Moroccon women. It is unlikely that these findings are explained by the lack of prenatal healthcare visits or language barriers, because these factors are also seen among Moroccan and Surinamese women.[55] However, these latter findings should be interpreted with caution as the subgroups were small; we recommend more studies in large multi-ethnic cohorts to address these questions. The large prevalence of high anxiety in non-Dutch women also justifies this research.
Some indications were found that the odds for pain relief/sedation were especially increased in anxious women who started labour in secondary care compared to primary care. This may reflect that primary caregivers use different strategies to support anxious women during labour.

It is reassuring that we found no association between general and pregnancy-related anxiety and the progression of birth, but only with interventions. Another Dutch study showed that

referral during labour, a significant intervention within the Dutch context, was associated with a negative recall of labour three years late.[56] In 2013, the need for pain relief was the most frequent reason (18.5%) for referral during labour.[57] Therefore, it is worthwhile to investigate whether these interventions during labour can be managed by treatment or therapy during pregnancy in anxious women, to avoid the necessity of labour-related interventions. If effective treatments are identified, screening for anxiety (especially pregnancy-related anxiety showing the strongest associations) should be implemented in prenatal care, at least in subgroups with an increased risk for anxiety. The observed high prevalence of general and pregnancy-related anxiety in non-Dutch women underlines the relevance of screening and subsequent fear-reducing interventions, especially in this group.

Conclusion

General and pregnancy-related anxiety in the first half of pregnancy are not associated with prolonged or obstructed labour and artificial delivery and, therefore, do not appear to influence the progression of birth. However, high levels of anxiety contribute to greater use of interventions during labour, especially pain relief/sedation, induction of labour and possibly referral during labour. Although we found similar associations between ethnic groups, the high prevalence of anxiety symptoms in pregnant women with a migrant background justifies more research on the effect of interventions to reduce anxiety symptoms in ethnic groups.

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COMPETING INTERESTS

None declared. Completed disclosure of interests form available to view online as supporting information.

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CONTRIBUTION TO AUTHORSHIP

The study was designed by JMK and TGV. JMK performed the statistical analysis and drafted the manuscript. TGV rendered and provided the ABCD Study data. JMK, TGV and AMS interpreted the results of the analysis. TGV and AMS made substantial contributions in revising the manuscript. The final manuscript was read and approved by all authors.

DETAILS OF ETHICAL APPROVAL

Approval for the ABCD study was obtained from the Central Committee on Research involving Human Subjects in the Netherlands, the Medical Ethical Committees of participating hospitals, and from the Registration Committee of Amsterdam.

DATA SHARING

Data of the ABCD study can be shared for specific research questions. Please contact t.vrijkotte@amc.uva.nl.

LEGENDS OF FIGURES

Figure 1. Flowchart of the ABCD study and inclusion in the current analyses

STAI = State Trait Anxiety Inventory

PRAQ = Pregnancy-Related Anxiety Questionnaire

PRN=Dutch Perinatal Registration

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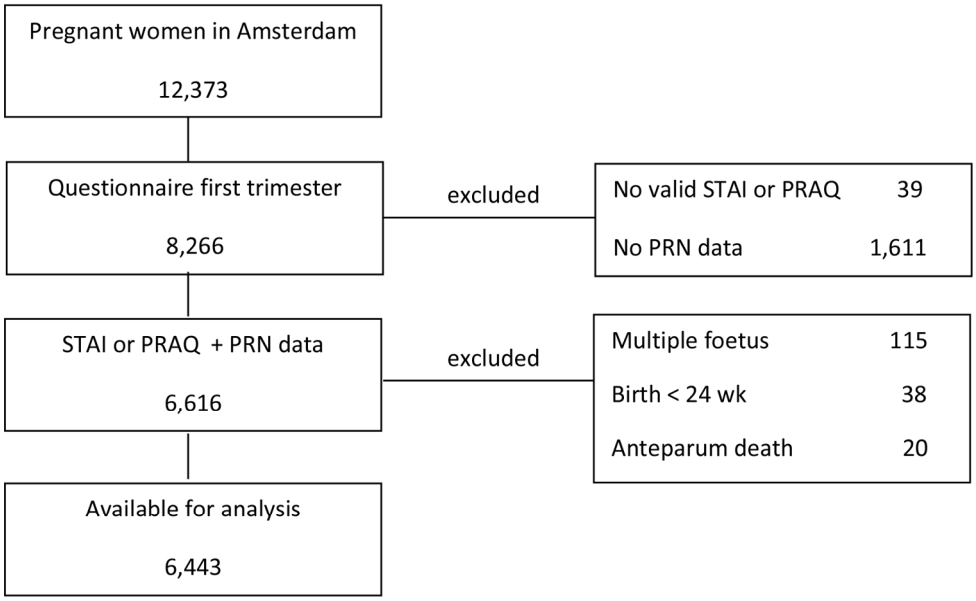
Figure 1. Flowchart of the ABCD study and inclusion in the current analyses



STAI = State Trait Anxiety Inventory

PRAQ = Pregnancy-Related Anxietye Questionnaire

PRN = Dutch Perinatal Registration

153x141mm (300 x 300 DPI)

Supplemental Table 1. Univariable and multivariable associations between first trimester general and pregnancy related anxiety and (interventions in) the birth process, according to care at start of labour

Outcome	General anxiety				Pregnancy-related anxiety			
	Low n=4126 %	High n=1850 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low n=5348 %	High n=662 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Augmentation[2]								
primary care	19.7	19.4	1.00 (0.84-1.20)	1.01 (0.83-1.24)	19.4	21.8	1.17 (0.91-1.52)	0.96 (0.73-1.27)
secondary care	34.7	27.7	0.73 (0.61-0.89)	0.83 (0.67-1.02)	32.4	31.8	0.98 (0.74-1.30)	0.95 (0.70-1.28)
Pain relief/sedation[2]								
primary care	10.5	11.3	1.10 (0.88-1.38)	1.09 (0.84-1.40)	10.4	13.9	**1.45 (1.06-1.98)**	1.17 (0.84-1.63)
secondary care	22.6	24.6	1.12 (0.91-1.37)	**1.26 (1.004-1.58)**	21.9	33.7	**1.85 (1.40-2.45)**	**1.81 (1.33-2.45)**
Secondary caesarean[2]								
primary care	4.9	4.6	0.96 (0.68-1.34)	0.91 (0.63-1.31)	4.7	5.8	1.23 (0.78-1.95)	0.97 (0.60-1.58)
secondary care	19.2	16.6	0.91 (0.72-1.15)	0.94 (0.73-1.21)	17.4	19.5	1.16 (0.83-1.61)	1.16 (0.82-1.65)
First stage >12 hr[3]								
primary care	19.4	19.8	1.03 (0.85-1.24)	1.04 (0.84-1.29)	19.2	22.1	1.23 (0.94-1.62)	0.99 (0.73-1.33)
secondary care	21.2	28.6	1.55 (0.65-3.68)	1.80 (0.65-5.02)	23.6	12.5	0.48 (0.06-4.03)	0.30 (0.03-3.43)
Second stage >=90 min[4]								
primary care	11.3	8.0	0.69 (0.53-0.90)	0.90 (0.67-1.21)	10.4	10.3	0.95 (0.65-1.37)	0.97 (0.65-1.45)
secondary care	10.7	5.8	0.51 (0.34-0.74)	0.77 (0.51-1.16)	9.3	6.7	0.72 (0.41-1.28)	0.93 (0.51-1.70)
Instrumental delivery[4]								
primary care	9.7	8.2	0.85 (0.65-1.10)	1.05 (0.78-1.39)	9.1	10.2	1.13 (0.78-1.62)	1.08 (0.73-1.59)
secondary care	18.4	12.8	0.66 (0.50-0.87)	0.97 (0.71-1.30)	16.7	12.9	0.72 (0.47-1.11)	0.87 (0.55-1.38)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol [2]Excluded women with primary caesarean section [3]Excluded women with caesarean section; data available for 3530 women (only recorded in perinatal registry of midwives) [4]Excluded women with caesarean section (primary/secondary)

Supplemental table 2a. Univariable and multivariable associations between PRAQ fear of labour and PRAQ fear of child in the first half of pregnancy and (interventions in) the birth process, according to parity

Outcome	Pregnancy Related Anxiety, according to Pregnancy Related Anxiety Questionnaire (PRAQ)							
	Fear of labour, only in nullparae				Fear of handicapped child			
	Low (3-9) n=3021 %	High (10-12) n=574 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low (4-11) n=5727* %	High (12-16) n=683* %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Primary caesarean								
Nulliparae	5.2	4.6	0.89 (0.58-1.37)	1.26 (0.79-2.01)	5.0	5.4	1.05 (0.65-1.69)	1.16 (0.72-1.88)
Multiparae					5.7	8.7	**1.58 (1.00-2.48)**	**1.69 (1.06-2.69)**
Induction[2]								
Nulliparae	11.6	13.3	1.18 (0.90-1.56)	1.27 (0.93-1.72)	11.6	13.8	1.16 (0.84-1.61)	1.19 (0.86-1.66)
Multiparae					9.7	13.0	1.40 (0.95-2.07)	1.33 (0.88-2.00)
Referral during labour[3]								
Nulliparae	51.3	57.6	1.36 (1.07-1.74)	**1.39 (1.06-1.81)**	51.7	57.5	1.31 (0.98-1.75)	1.31 (0.98-1.76)
Multiparae					20.7	16.7	0.79 (0.50-1.25)	0.71 (0.45-1.14)
Augmentation[2]								
Nulliparae	33.5	36.2	1.15 (0.95-1.40)	1.15 (0.93-1.43)	34.1	32.6	0.94 (0.74-1.19)	0.94 (0.74-1.19)
Multiparae					12.4	11.2	0.90 (0.59-1.35)	0.85 (0.56-1.30)
Pain relief/sedation[2]								
Nulliparae	21.4	30.8	1.70 (1.38-2.09)	**1.58 (1.26-1.99)**	22.5	25.8	1.22 (0.95-1.57)	1.14 (0.88-1.47)
Multiparae					6.0	6.2	0.93 (0.53-1.65)	0.94 (0.53-1.67)
Secondary caesarean[2]								
Nulliparae	12.5	13.4	1.12 (0.85-1.47)	1.02 (0.75-1.37)	12.3	14.8	1.27 (0.93-1.73)	1.30 (0.95-1.79)
Multiparae					5.9	5.8	0.98 (0.56-1.73)	1.03 (0.58-1.84)

First stage >12 hr[4]								
Nulliparae	30.3	36.1	**1.34 (1.03-1.73)**	1.14 (0.86-1.53)	31.0	32.2	1.10 (0.81-1.51)	1.03 (0.75-1.42)
Multiparae					4.9	2.1	0.45 (0.14-1.45)	0.44 (0.14-1.43)
Second stage >=90 min[5]								
Nulliparae	17.3	14.4	0.83 (0.62-1.10)	1.14 (0.83-1.57)	17.3	12.8	0.71 (0.50-1.01)	0.77 (0.54-1.11)
Multiparae					1.6	0.8	0.53 (0.13-2.20)	0.53 (0.13-2.23)
Instrumental delivery[5]								
Nulliparae	19.2	17.3	0.90 (0.69-1.17)	1.17 (0.88-1.57)	19.3	15.4	0.74 (0.54-1.03)	0.80 (0.57-1.11)
Multiparae					3.2	2.0	0.66 (0.26-1.65)	0.69 (0.28-1.75)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol [2]Excluded women with primary caesarean section. [3]Only women under primary care at start of labour
[4]Excluded women with caesarean section; data available for 3535 women (only recorded in perinatal registry of midwives) [5]Excluded women with caesarean section (primary/ secondary)

*Including four respondents how did not complete the total PRAQ, but who completed the subscale 'fear of child'.

Supplemental table 3a. Univariable and multivariable associations between PRAQ fear of labour and PRAQ fear of child in the first half of pregnancy and (interventions in) the birth process, according to ethnicity

Outcome	Fear of labour, only in nulliparae				Fear of handicapped child			
	Low (3-9)	High (10-12)	Crude model	Adjusted model[1]	Low (4-11)	High (12-16)	Crude model	Adjusted model[1]
	n=3021	n=574			n=5727*	n=683*		
	%	%	OR (95% CI)	OR (95% CI)	%	%	OR (95%-CI)	OR (95%-CI)
Primary caesarean								
Dutch	5.9	5.2	0.91 (0.44-1.91)	0.98 (0.46-2.06)	5.8	7.1	1.25 (0.79-1.97)	1.20 (0.75-1.90)
Turkish	0.0	3.4	p=0.19	p=1.00	3.8	1.8	0.56 (0.07-4.59)	0.59 (0.06-5.33)
Moroccan	2.3	3.2	1.40 (0.28-7.09)	1.33 (0.26-6.82)	3.3	3.8	1.16 (0.32-4.18)	1.34 (0.37-4.92)
Black	6.9	1.4	0.25 (0.03-1.97)	0.50 (0.06-4.33)	5.7	4.7	0.43 (0.06-3.27)	0.61 (0.08-4.69)
Induction[2]								
Dutch	11.7	14.5	1.33 (0.82-2.17)	1.29 (0.78-2.13)	10.5	13.8	1.37 (0.96-1.94)	1.31 (0.91-1.90)
Turkish	13.3	14.3	1.01 (0.35-2.91)	1.08 (0.36-3.27)	12.3	16.1	1.24 (0.51-3.06)	1.31 (0.51-3.35)
Moroccan	7.1	14.4	2.20 (0.89-5.39)	2.41 (0.96-6.05)	9.7	10.5	0.98 (0.42-2.29)	1.02 (0.43-2.43)
Black	11.7	14.5	1.28 (0.54-3.01)	1.44 (0.58-3.61)	10.4	9.8	0.73 (0.22-2.46)	0.85 (0.24-2.30)
Referral during labour[3]								
Dutch	49.9	62.0	**1.78 (1.13-2.80)**	**1.94 (1.22-3.10)**	36.3	42.0	1.27 (0.91-1.76)	1.17 (0.82-1.68)
Turkish	47.7	59.4	1.58 (0.61-4.10)	1.45 (0.53-3.99)	39.4	32.4	0.86 (0.38-1.96)	0.67 (0.27-1.65)
Moroccan	57.3	67.7	1.52 (0.76-3.04)	1.63 (0.80-3.32)	45.2	43.5	0.95 (0.50-1.82)	1.00 (0.49-2.02)
Black	52.8	35.0	0.49 (0.23-1.07)	0.54 (0.23-1.27)	38.8	41.4	1.17 (0.53-2.59)	1.14 (0.48-2.68)
Augmentation[2]								

Dutch	32.3	37.9	1.35 (0.95-1.92)	1.42 (0.99-2.04)	23.4	27.8	1.25 (0.95-1.64)	1.17 (0.88-1.56)
Turkish	30.7	32.1	1.01 (0.47-2.15)	0.90 (0.41-2.00)	23.0	17.9	0.64 (0.28-1.46)	0.58 (0.25-1.37)
Moroccan	37.3	33.3	0.81 (0.46-1.44)	0.87 (0.48-1.57)	24.7	19.7	0.79 (0.43-1.47)	0.78 (0.41-1.49)
Black	28.9	30.9	1.10 (0.58-2.06)	1.10 (0.56-2.14)	22.5	15.0	0.63 (0.26-1.54)	0.58 (0.23-1.48)
Pain relief/ sedation[2]								
Dutch	19.4	34.5	**2.29 (1.59-3.30)**	**2.17 (1.49-3.15)**[6]	14.2	19.1	**1.42 (1.04-1.94)**	1.36 (0.99-1.87)
Turkish	32.0	23.2	0.69 (0.31-1.54)	0.71 (0.30-1.66)[6]	15.5	16.1	1.10 (0.47-2.56)	1.15 (0.48-2.76)
Moroccan	23.0	24.4	1.01 (0.53-1.91)	1.03 (0.53-2.00)[6]	13.9	14.5	1.07 (0.53-2.17)	1.00 (0.49-2.06)
Black	23.3	32.4	1.58 (0.84-3.00)	1.86 (0.94-3.69)[6]	15.0	10.0	0.65 (0.22-1.89)	0.50 (0.17-1.50)
Secondary caesarean[2]								
Dutch	11.0	13.1	1.19 (0.71-2.00)	1.15 (0.67-1.96)	8.6	12.2	**1.47 (1.01-2.14)**	1.38 (0.94-2.03)
Turkish	10.7	10.7	0.97 (0.32-1.98)	0.91 (0.28-2.98)	7.1	8.9	1.55 (0.53-4.48)	1.63 (0.53-5.04)
Moroccan	15.9	10.0	0.58 (0.25-1.35)	0.59 (0.25-1.42)	8.9	9.2	1.11 (0.47-2.62)	1.22 (0.50-2.99)
Black	20.1	14.7	0.72 (0.33-1.58)	0.84 (0.37-1.91)	12.8	7.5	0.58 (0.17-2.00)	0.65 (0.19-2.28)
First stage >12 hr[4]								
Dutch	27.8	37.8	**1.64 (1.03-2.62)**	**1.64 (1.02-2.64)**	17.8	21.9	1.30 (0.88-1.92)	1.25 (0.82-1.90)
Turkish	34.9	29.0	0.80 (0.29-2.20)	0.55 (0.17-1.77)	19.1	9.4	0.49 (0.14-1.76)	**0.24 (0.06-0.996)**
Moroccan	35.2	35.0	0.96 (0.48-1.92)	0.96 (0.46-1.99)	20.3	20.0	1.02 (0.46-2.26)	1.00 (0.41-2.43)
Black	30.5	32.3	1.07 (0.44-2.59)	1.11 (0.43-2.89)	21.0	19.2	0.94 (0.33-2.67)	1.04 (0.32-3.42)
Second stage >=90 min[5]								
Dutch	18.5	24.2	1.42 (0.91-2.19)	**1.64 (1.05-2.57)**	12.0	10.0	0.82 (0.53-1.25)	0.80 (0.51-1.25)

Turkish	9.1	12.8	1.75 (0.50-6.15)	1.93 (0.51-7.30)	5.3	6.1	1.43 (0.38-5.44)	1.13 (0.28-4.59)
Moroccan	16.2	8.8	0.41 (0.15-1.08)	0.43 (0.16-1.17)	7.1	2.9	0.41 (0.10-1.80)	0.43 (0.10-1.93)
Black	4.9	5.9	1.24 (0.30-5.17)	0.88 (0.18-4.29)	3.0	5.6	1.96 (0.42-9.21)	1.40 (0.27-7.19)
Instrumental delivery[5]								
Dutch	20.4	19.0	0.95 (0.60-1.50)	1.03 (0.64-1.65)	13.6	9.5	0.66 (0.43-1.02)	**0.61 (0.39-0.96)**
Turkish	9.0	18.0	1.87 (0.60-5.80)	2.37 (0.69-8.12)	5.7	7.8	1.17 (0.32-4.34)	1.17 (0.29-4.71)
Moroccan	13.2	11.1	0.81 (0.33-1.98)	0.84 (0.34-2.09)	7.2	5.8	0.80 (0.27-2.37)	0.85 (0.28-2.61)
Black	5.5	13.8	**2.93 (1.01-8.55)**	**3.22 (1.03-10.1)**	4.6	5.4	1.20 (0.27-5.41)	0.96 (0.20-4.65)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol, parity (only in fear of handicapped child) [2]Excluded women with primary caesarean section. [3]Only women under primary care at start of labour [4]Excluded women with caesarean section; data available for 3530 women (only recorded in perinatal registry of midwives) [5]Excluded women with caesarean section (primary/ secondary) [6] interaction ethnicity and fear of labour p=0.03
*Including four respondents how did not complete the total PRAQ, but who completed the subscale 'fear of child'.

Supplemental table 4. Univariable and multivariable associations between PRAQ fear of labour and PRAQ fear of child in the first half of pregnancy and (interventions in) the birth process, according to care at start of labour

Outcome	Pregnancy Related Anxiety, according to Pregnancy Related Anxiety Questionnaire (PRAQ)							
	Fear of labour, only in nulliparae				Fear of handicapped child			
	Low (3-9) n=2851 %	High (10-12) n=542 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)	Low (4-11) n=5384 %	High (12-16) n=630 %	Crude model OR (95% CI)	Adjusted model[1] OR (95% CI)
Augmentation[2]								
primary care	28.5	31.4	1.19 (0.92-1.54)	1.11 (0.84-1.48)	19.6	19.9	1.02 (0.78-1.35)	0.95 (0.71-1.27)
secondary care	42.0	43.9	1.08 (0.80-1.47)	1.16 (0.83-1.62)	32.8	28.8	0.84 (0.63-1.11)	0.80 (0.60-1.08)
Pain relief/sedation[2]								
primary care	16.3	22.5	**1.56 (1.17-2.08)**	1.33 (0.96-1.84)	10.5	12.6	1.26 (0.90-1.75)	1.13 (0.79-1.61)
secondary care	30.0	44.4	**1.89 (1.39-2.58)**	**1.84 (1.31-2.58)**	23.1	24.3	1.05 (0.78-1.43)	0.99 (0.72-1.37)
Secondary caesarean[2]								
primary care	7.6	7.5	1.00 (0.64-1.57)	0.82 (0.50-1.34)	4.7	5.9	1.30 (0.81-2.08)	1.19 (0.73-1.94)
secondary care	20.8	22.9	1.18 (0.82-1.68)	1.01 (0.68-1.50)	17.5	18.0	1.06 (0.76-1.48)	1.07 (0.76-1.52)
First stage >12 hr[3]								
primary care	30.1	36.7	**1.38 (1.05-1.80)**	1.19 (0.88-1.60)	19.5	19.9	1.07 (0.80-1.42)	0.95 (0.70-1.29)
secondary care	32.5	26.7	0.75 (0.22-2.59)	0.64 (0.14-2.91)	23.7	17.6	0.71 (0.19-2.65)	0.87 (0.17-4.54)
Second stage >=90 min[4]								
primary care	18.2	16.1	0.87 (0.61-1.23)	1.17 (0.80-1.72)	10.6	8.6	0.79 (0.52-1.19)	0.86 (0.57-1.31)
secondary care	15.5	11.5	0.74 (0.44-1.26)	1.18 (0.66-2.10)	9.3	6.0	0.64 (0.36-1.15)	0.68 (0.38-1.23)
Instrumental delivery[4]								
primary care	15.9	14.9	0.95 (0.67-1.34)	1.10 (0.75-1.62)	9.4	8.0	0.83 (0.55-1.26)	0.83 (0.53-1.28)

secondary care	25.6	22.2	0.83 (0.55-1.25)	1.22 (0.77-1.94)	16.9	11.9	0.65 (0.42-1.01)	0.65 (0.41-1.03)

[1]Adjusted for BMI, maternal age, years of education, ethnicity, smoking, alcohol [2]Excluded women with primary caesarean section. [3]Excluded women with caesarean section; data available for 3535 women (only recorded in perinatal registry of midwives) [4]Excluded women with caesarean section (primary/ secondary)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

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

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	Suppl file
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, p 11
		(b) Indicate number of participants with missing data for each variable of interest	All tables
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	Table 2 and 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2 and 3
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	19
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-23
Generalisability	21	Discuss the generalisability (external validity) of the study results	23
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.