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RESEARCH ARTICLE

General obstetrics

Association between high levels of comorbid anxiety and depressive symptoms and decreased likelihood of birth without intervention: A longitudinal prospective cohort study

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Abstract

Objective: To assess the association between trajectories of comorbid anxiety and depressive (CAD) symptoms assessed in each pregnancy trimester and physiological birth.

Design: Large longitudinal prospective cohort study with recruitment between January 2013 and September 2014.

Setting: Primary care, in the Netherlands.

Population: Dutch-speaking pregnant women with gestational age at birth ≥37 weeks, and without multiple pregnancy, severe psychiatric disorder or chronic disease history.

Methods: Pregnancy-specific anxiety and depressive symptoms were measured prospectively in each trimester of pregnancy using the negative affect subscale of the Tilburg Pregnancy Distress Scale and Edinburgh (Postnatal) Depression Scale. Data on physiological birth were obtained from obstetric records. Multivariate growth mixture modelling was performed in MPLUS to determine longitudinal trajectories of CAD symptoms. Multiple logistic regression analysis was used to examine the association between trajectories and physiological birth.

Main outcome measures: Trajectories of CAD symptoms and physiological birth.

Results: Seven trajectories (classes) of CAD symptoms were identified in 1682 women and subsequently merged into three groups: *group 1*—persistently low levels of symptoms (reference class 1; 79.0%), *group 2*—intermittently high levels of symptoms (classes 3, 6 and 7; 11.2%), and *group 3*—persistently high levels of symptoms (classes 2, 4 and 5; 9.8%). Persistently high levels of CAD symptoms (*group 3*) were associated with a lower likelihood of physiological birth (odds ratio 0.67, 95% confidence interval 0.47–0.95, $P = 0.027$) compared with the reference group (persistently low levels of symptoms), after adjusting for confounders.

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Conclusions: This study is the first showing evidence that persistently high CAD levels, assessed in each pregnancy trimester, are associated with a lower likelihood of physiological birth.

KEYWORDS
anxiety, caesarean, comorbid anxiety and depression, depression, forceps, instrumental birth, multivariate growth mixture modelling, physiological birth, pregnancy distress, trajectories, ventouse

1 | INTRODUCTION

Physiological birth involves a spontaneous vaginal birth at term (between 37 and 42 weeks' gestation) with mother and infant being in good condition after birth.[1] Physiological birth improves childbirth experience, as the use of medical interventions during birth, such as augmentation, vacuum- or forceps-assisted vaginal birth and/or unplanned caesarean section, has been related to a more negative childbirth experience.[2–6] A woman's negative childbirth experience is a risk factor for developing postpartum depression[7] and childbirth-related posttraumatic stress symptoms[8–10] which could in turn affect infant development,[11–15] parenting, and the mother–infant interaction.[15,16] Moreover, caesarean section has been associated with prolonged maternal recovery after birth and negative long-term infant outcomes, such as an increased risk of asthma and obesity.[17] Another pregnancy after a caesarean section has been associated with an increased risk of miscarriage, stillbirth and placenta complications.[17]

Physiological birth is less common in nulliparous women,[18] obese women[19,20] and women with advanced maternal age.[21,22] Until now, cross-sectional studies, mostly focusing on anxiety *or* depressive symptoms, showed inconclusive data regarding a possible effect on physiological birth.[23,24] Elevated levels of anxiety and depressive symptoms have been related to lower childbirth self-efficacy.[25] The confidence women have in giving birth seems likely to be an important factor for a physiological birth. It is hypothesised that heightened levels of stress could affect the labour physiology by increasing the output of stress hormones.[26,27] Stress hormones may negatively influence oxytocin levels[28,29] and consequently the initiation of labour, and they are correlated with uncoordinated and decreased uterine activity during labour.[30,31] Indeed, heightened levels of emotional stress and anxiety have been associated with prolonged labour[32–34] (which could interfere with physiological birth).

Comorbidity of anxiety and depression in the general population is common, as up to 50% of individuals with anxiety also suffer from depression and vice versa.[35] Because young women in general are especially at risk for both anxiety and depression, the prevalence is high during the perinatal period, at syndrome and at symptom level.[36–38] Until now, no studies have been published taking *comorbid* symptoms of anxiety and depression (CAD) into account assessed in each pregnancy trimester. Most studies investigate either anxiety *or* depressive symptoms, mostly at one time point during pregnancy. However, symptoms can vary substantially over time both between and within individuals,[39] which emphasises the need to use CAD symptom trajectories during pregnancy instead of single measurements.

The current study aimed to determine whether trajectories of CAD symptoms were (negatively) associated with physiological birth.

2 | METHODS

2.1 | Participants and procedure

The current research was part of the longitudinal prospective HAPPY cohort study (*H*olistic *A*pproach to *P*regnancy and the first *P*ostpartum *Y*ear).[40] As part of the entire cohort study, data were collected on psychological and physiological factors that may influence maternal perinatal wellbeing (e.g. maternal mood, pregnancy-related somatic symptoms [e.g. nausea and vomiting], thyroid function, human chorionic gonadotropin [HCG], as well as pregnancy and birth outcomes of mother and fetus). Recruitment of Dutch-speaking women took place between January 2013 and September 2014 at the first antenatal appointment. Exclusion criteria were multiple pregnancy, severe psychiatric disorder (e.g. schizophrenia, borderline personality disorder and bipolar disorder) and/or a documented history of chronic disease (e.g. diabetes, thyroid dysfunction, colitis ulcerosa and Crohn's disease). All women provided written informed consent. Of the 2269 women who returned informed consent, 1828 women completed the questionnaires assessing anxiety and depressive symptoms at 12, 22 and 32 weeks of pregnancy within a timeframe of +/− 4 weeks. In addition, women with a preterm birth (n = 71) and women with a primary caesarean section (n = 86) were excluded from the analyses. This resulted in a final study sample of 1682 women, whose characteristics are shown in Table 1 (comparison with remainder HAPPY sample is shown in Table S1). Participating women were not actively involved in the research. The HAPPY study was approved by the ethical committee of Tilburg University (protocol number EV-2012.25) and reviewed by the Medical Ethics Committee of the Máxima Medical Centre Veldhoven.

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TABLE 1 Characteristics of 1682 pregnant women with gestational age ≥37 weeks at birth

	n (%)	M (SD)	Range	Mdn (IQR)
Demographics				
Age		30.4 (3.6)	19–43	30 (28–33)
High level of education	1084 (64.8)			
Living with partner	1660 (98.7)			
Employment	1553 (92.3)			
Lifestyle habits				
BMI pre-pregnancy		23.8 (4.0)	16.0–41.7	23 (21–26)
Smoking in pregnancy	100 (6.0)			
Alcohol use in pregnancy	65 (3.9)			
Obstetrics				
Nulliparous	820 (48.8)			
Multiparous	862 (51.2)			
Previous miscarriage	446 (26.5)			
Unplanned pregnancy	98 (5.8)			
Gestational age at birth		39.9 (1.1)	37.0–41.9	40 (39–41)
Pregnancy complications[a]	185 (11.0)			
Physiological birth[b]	791 (47.0)			
Psychiatric history				
History of anxiety	127 (7.6)			
History of depression	282 (16.8)			
History of both anxiety and depression	64 (3.8)			

Abbreviations: BMI, body mass index; high level of education, Bachelor's or Master's degree; M, mean; SD, standard deviation; Mdn, median; IQR, interquartile range.

[a]Pregnancy complications: one (or more) of the following obstetric complications during pregnancy: antepartum haemorrhage, intrauterine growth restriction, evidence of ultrasound abnormalities on the standardised 20-week ultrasound, pre-eclampsia and diabetes gravidarum.

[b]Physiological birth: a birth that spontaneously started between 37 and 42 weeks of pregnancy without any intervention during labour (augmentation and/or an instrumental birth: vacuum- or forceps-assisted vaginal birth, secondary caesarean section).[1]

2.2 | Measures

2.2.1 | Pregnancy-specific anxiety symptoms

Pregnancy-specific anxiety symptoms during pregnancy were measured at 12, 22 and 32 weeks of pregnancy using the *negative affect* subscale (TPDS-NA) of the Tilburg Pregnancy Distress Scale (TPDS).[41] Total scores of this 11-item measure range from 0 to 33, with higher scores indicating more pregnancy-specific anxiety. The TPDS-NA has been shown to have good psychometric properties in each trimester of pregnancy.[41,42] In a review comparing self-report instruments of anxiety during pregnancy, the structural validity and internal consistency of this measure have been evaluated as excellent.[43] Studies have shown the TPDS-NA to be significantly correlated with other validated anxiety instruments during pregnancy, such as Generalised Anxiety Disorder-7[41] and the Fear of Childbirth Scale.[44] In the current study, Cronbach's alphas in the three trimesters of pregnancy were 0.76, 0.78 and 0.78, respectively.

2.2.2 | Depressive symptoms

The 10-item Edinburgh (Postnatal) Depression Scale, E(P)DS, was used to assess depressive symptoms at 12, 22 and 32 weeks of pregnancy.[45,46] Total scores range from 0 to 30 and higher scores indicate more depressive symptoms. The E(P)DS has been shown to be a valid and reliable instrument for measurement of depressive symptoms in each trimester of pregnancy.[45,47] In the current study, Cronbach's alphas were 0.82, 0.83 and 0.82 per trimester, respectively.

2.2.3 | Physiological birth

As described by the World Health Organization (WHO) in 1997,[1] we used the following definition of a physiological birth: a *birth that spontaneously started between 37 and 42 weeks of pregnancy without any intervention during labour (augmentation and/or an instrumental birth: vacuum- or forceps-assisted vaginal birth, secondary caesarean section). After birth, mother and infant should be in good condition*. Women were defined as being in good condition when they gave birth at home or in hospital where they were discharged within 48 hours. Neonates were regarded as being in good condition when the 5-minute APGAR scores were ≥7. The occurrence of physiological birth (and the condition of both mother and neonate) was obtained from the obstetric records by a research-midwife (yes/no).

2.2.4 | Characteristics

Demographic characteristics, lifestyle habits, psychological characteristics and obstetric features were assessed by means of a questionnaire at 12 weeks of pregnancy. Psychological characteristics included *previous diagnosis of anxiety* and/or *depression*. Obstetric features included *parity*, *previous miscarriage, unplanned pregnancy* and *pregnancy complications* (one [or more] of the following obstetric complications during pregnancy: antepartum haemorrhage, intrauterine growth restriction, evidence of ultrasound abnormalities on the standardised 20-week ultrasound, pre-eclampsia and diabetes gravidarum). In addition, obstetric data were extracted from the obstetric records, such as *gestational age at birth*.

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2.3 | Statistical analysis

Multivariate growth mixture modelling was performed in MPLUS version 8.5[48] to estimate trajectories (classes) of CAD symptoms, based on the TPDS-NA and E(P)DS total scores at 12, 22 and 32 weeks of pregnancy. Maximum likelihood estimation with robust standard errors (MLR) was used, as the TPDS-NA and E(P)DS scores were positively skewed with a substantial number of scores being equal to zero. First, a one-class model was fitted and thereafter models with increasing numbers of classes. Several information criterion (IC) values were considered to determine the optimal number of classes: Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC) and Sample-Size Adjusted Bayesian Information Criterion (SABIC).[49,50] Better model fit is indicated by lower IC values.[50,51] We also considered the entropy, in which a value closer to 1 indicates a clearer delineation of classes.[52] Furthermore, when determining the optimal number of classes, we required each class to include >1% of the total sample.[53]

Subsequently, we exported a variable indicating class membership from MPLUS to R (version 3.6.3) for further analyses. We used an alpha level of 0.05 for all statistical tests. At each measurement occasion, one-way analyses of variance (ANOVA) with post-hoc Tukey analyses were used to compare anxiety and depressive symptom scores between classes. Other participant characteristics were compared between classes using one-way ANOVA with post-hoc Tukey analyses for continuous variables and Chi-square tests with Bonferroni corrections for dichotomous variables. The test statistic used in Tukey's test is a modified *t*-statistic that corrects for multiple comparisons. When performing pairwise comparisons for dichotomous variables, a Bonferroni correction for multiple testing was used, dividing the alpha level by the number of pairwise comparisons. The class that was characterised by the lowest anxiety and depressive symptom mean scores was set as the reference class. Effect sizes were calculated with regard to Cohen's *d* (0.20 = small, 0.50 = medium and 0.80 = large) and phi coefficient/Cramer's V (0.10 = small, 0.30 = medium and 0.50 = large).[54]

Finally, a multiple logistic regression analysis was performed to assess a possible association between classes of CAD symptoms (predictor) and physiological birth (outcome variable). We adjusted for several confounders: age, level of education, body mass index (BMI), smoking, parity, gestational age and pregnancy complications.

3 | RESULTS

3.1 | Comorbid anxiety and depressive symptoms

A seven-class model was chosen to represent different trajectories of CAD symptoms, based on the prespecified criteria to determine the optimal number of trajectory classes (AIC, BIC, SABIC, entropy and class size >1%; see Table S2). Figure S1 shows a graphical overview of the mean anxiety and depressive symptom scores throughout pregnancy in the seven classes. Women in class 1 ($n = 1329$, 79.0%) showed persistently low levels of CAD symptoms throughout pregnancy and this class was therefore set as the reference class and categorised as *group 1*: 'Persistently low levels of CAD symptoms'. Women in the remaining six classes were categorised into two groups based on their TPDS-NA and E(P)DS scores (Table S2). Women in classes 3, 6 and 7 were categorised as *group 2*. They showed 'Intermittently high CAD symptoms' throughout pregnancy because their anxiety and depressive symptom mean scores were *intermittently* (*not* in each trimester) higher than those in the reference class (classes 3, 6 and 7, $n = 188$ [11.2%], post-hoc Tukey: $P = 0.634$ to $P < 0.001$). Women in classes 2, 4 and 5 were categorised as *Group 3*. They showed 'Persistently high CAD symptoms' throughout pregnancy, because their anxiety and depressive symptom mean scores were *in each trimester higher* than those in the reference class (classes 2, 4 and 5, $n = 165$ [9.8%], post-hoc Tukey: all $P < 0.001$, Cohen's $d = 0.79–3.61$, large effect sizes). The characteristics of the three groups are shown in Table 2.

Compared with *group 1* (persistently low levels), women in *group 2* (intermittently high levels) more often had a history of anxiety and/or depression ($\chi^2[1] = 8.8–18.1$, $P = 0.003$ to $P < 0.001$, Bonferroni correction: alpha = 0.05/3 = 0.016, phi coefficient = 0.08–0.11, small effect sizes). Compared with *group 1* (persistently low levels), women in *group 3* (persistently high levels) were younger (post-hoc Tukey: $P = 0.002$, Cohen's $d = 0.27$, small effect size), less often highly educated, more often unemployed, more often had an unplanned pregnancy, and more often a history of anxiety and/or depression ($\chi^2[1] = 6.4–49.0$, $P = 0.011$ to $P < 0.001$, alpha = 0.016, phi coefficient = 0.07–0.18, small effect sizes). There were no differences between the three groups with regard to parity ($P = 0.277$).

3.2 | Physiological birth

In total, 791 women (47.0%) had a physiological birth using the WHO criteria: 256 nulliparous (32.4%) and 535 multiparous women (67.6%, $\chi^2[1] = 159.3$, $P < 0.001$, phi coefficient = 0.31, medium effect size). Figure 1 shows that the percentage of women with a physiological birth for the three groups of CAD symptoms differed ($\chi^2[2] = 7.9$, $P = 0.019$, Cramer's V = 0.07, small effect size). In particular, women belonging to *group 3* (persistently high) had fewer physiological births compared with those in *group 1* (persistently low levels, 37.0% versus 47.8%, $\chi^2[1] = 6.5$, $P = 0.011$, alpha = 0.016, phi coefficient = 0.07, small effect size). No difference was found between women belonging to *group 2* (intermittently high) and *group 1* (persistently low levels) ($P = 0.530$).

We performed a multiple logistic regression analysis to assess a possible independent association of belonging to a class with intermittently high (*group 2*) or persistently

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TABLE 2 Characteristics of three groups of CAD symptoms (n = 1682)

	Group 1 n = 1329 (79.0%)				Group 2 n = 188 (11.2%)				Group 3 n = 165 (9.8%)				
	n (%)	M (SD)	Range	Mdn (IQR)	n (%)	M (SD)	Range	Mdn (IQR)	n (%)	M (SD)	Range	Mdn (IQR)	p Value[a]
Demographics													
Age		30.5 (3.5)	19–43	30 (28–33)		30.5 (3.7)	21–42	31 (28–33)		29.5 (4.0)	19–39	29 (27–32)	0.003
High level of education	877 (66.2)				116 (62.4)				91 (55.8)				0.025
Living with partner	1314 (98.9)				186 (98.9)				160 (97.0)				0.122
Employment	1214 (93.4)				170 (90.4)				142 (86.1)				0.002
Lifestyle habits													
BMI pre-pregnancy		23.8 (3.9)	16.8–41.7	23 (21–26)		23.6 (4.3)	16.0–41.4	23 (21–25)		24.5 (4.4)	16.0–41.0	24 (21–27)	0.050
Smoking in pregnancy	73 (5.5)				12 (6.4)				15 (9.1)				0.176
Alcohol use in pregnancy	48 (3.6)				10 (5.3)				7 (4.2)				0.506
Obstetrics													
Nulliparous	653 (49.1)				82 (43.6)				85 (51.5)				0.277
Multiparous	676 (50.9)				106 (56.4)				80 (48.5)				0.277
Previous miscarriage	357 (26.9)				51 (27.1)				38 (23.0)				0.564
Unplanned pregnancy	62 (4.7)				12 (6.4)				24 (14.5)				<0.001
Gestational age at birth		39.9 (1.1)	37.0–41.9	40 (39–41)		39.9 (1.0)	37.0–41.7	40 (39–41)		39.8 (1.2)	37.0–41.9	40 (39–41)	0.430
Pregnancy complications[b]	141 (10.6)				22 (11.7)				22 (13.3)				0.544
Psychiatric history													
History of anxiety	81 (6.1)				23 (12.2)				23 (13.9)				<0.001
History of depression	181 (13.6)				43 (22.9)				58 (35.2)				<0.001
History of both anxiety and depression	32 (2.4)				16 (8.5)				16 (9.7)				<0.001

Note: Group 1 = Persistently low levels of CAD symptoms (reference class 1). *Group 2* = Intermittently high levels of CAD symptoms (classes 3, 6 and 7). *Group 3* = Persistently high levels of CAD symptoms (classes 2, 4 and 5).

Abbreviations: BMI, body mass index; CAD, comorbid anxiety and depression; High level of education, Bachelor's or Master's degree; M, mean; SD, standard deviation; Mdn, median; IQR, interquartile range.

[a]One-way ANOVA for continuous variables and chi-square tests for dichotomous variables.

[b]Pregnancy complications: one (or more) of the following obstetric complications during pregnancy: antepartum haemorrhage, intrauterine growth restriction, evidence of ultrasound abnormalities on the standardised 20-week ultrasound, pre-eclampsia and diabetes gravidarum.

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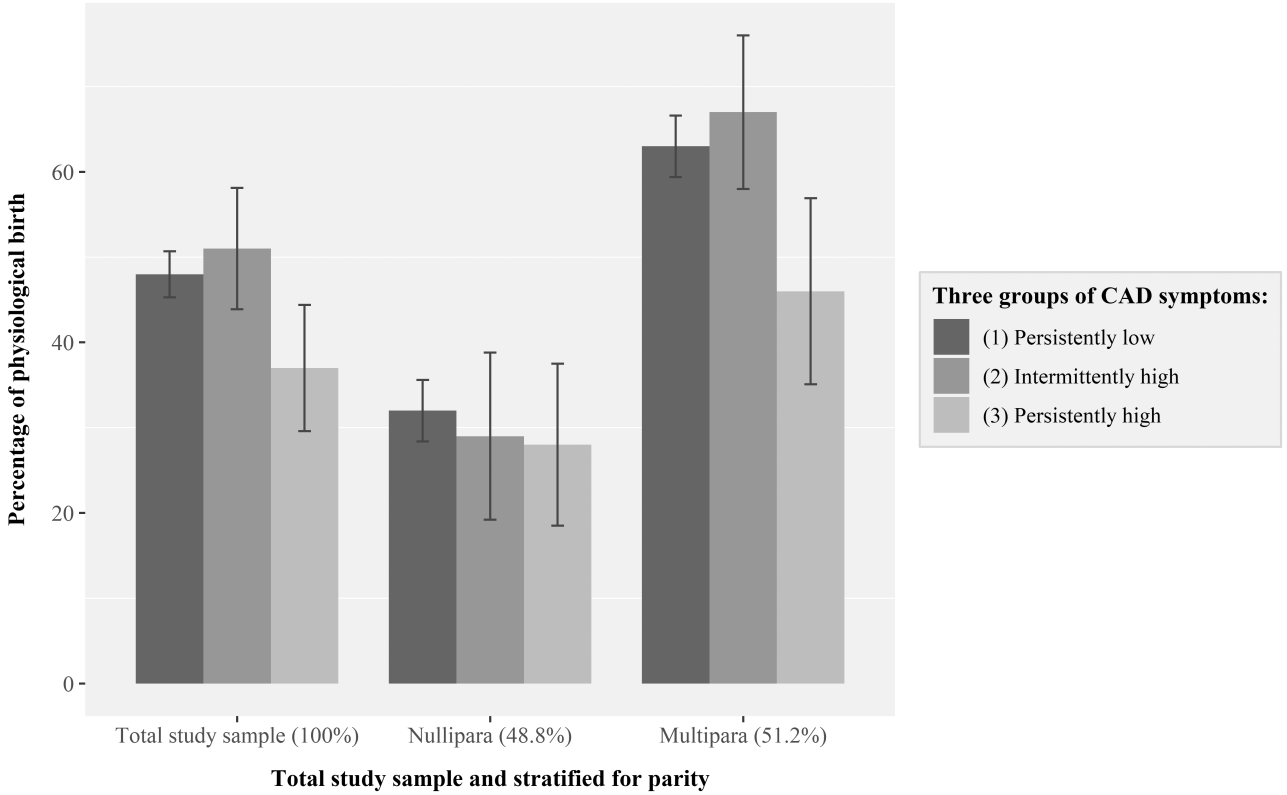

FIGURE 1 Physiological birth for three groups of comorbid anxiety and depressive (CAD) symptoms: total study sample and stratified for parity (n = 1682). The error bars represent the 95% confidence intervals of the estimated percentages.

high (*group 3*) CAD symptoms (predictor) with physiological birth (outcome variable). The groups (*group 1–3*) were dummy-coded, with *group 1* (persistently low levels) as reference. Unadjusted estimates were an odds ratio [OR] of 1.12 (95% confidence interval [CI] 0.82–1.51, P = 0.480) for belonging to *group 2* (intermittently high levels) and an OR of 0.64 (95% CI 0.46–0.89, P = 0.009) for belonging to *group 3* (persistently high levels), compared with belonging to *group 1* (persistently low levels). Adjusted for confounders (age, level of education, BMI, smoking, parity, gestational age and pregnancy complications), belonging to *group 3* (persistently high levels) was negatively associated with physiological birth (OR = 0.67, 95% CI 0.47–0.95, P = 0.027), whereas belonging to *group 2* (intermittently high levels) did not show an association with physiological birth (OR = 1.03, 95% CI 0.74–1.44, P = 0.849). The odds ratio of 0.67 can be interpreted as follows: a woman belonging to *group 3* (persistently high levels) was 33% less likely to have a physiological birth compared with a woman belonging to *group 1* (persistently low levels), after adjustment for all other variables in the logistic regression model.

We finally defined a risk profile enabling us to detect the group of women at 12 weeks' gestation who subsequently developed a trajectory of persistently high comorbid depressive and anxiety symptoms (n = 165), defined as the 'vulnerable' group with regard to high distress symptom levels. We used different cut-offs of the TPDS-NA and E(P)DS to evaluate the most optimal combination of positive predictive value (PPV), sensitivity and specificity of predicting women belonging to this vulnerable group (Table S4). The most optimal combination was found for TPDS-NA ≥15 *or* E(P)DS ≥10, with a PPV of 0.51, sensitivity of 0.82 and specificity of 0.91 (of which there were 28 [2%] false positives in the group of women with persistently low levels of comorbid depressive and anxiety symptoms). The accuracy (i.e. *the proportion of true results, both true positive and true negative, measuring the degree of veracity of a test*) of this risk profile was 0.91.

4 | DISCUSSION

4.1 | Main findings

Assessing CAD symptoms in each trimester during pregnancy, we identified seven different CAD trajectories (classes) by means of multivariate growth mixture modelling. Apart from the reference class (79.0%) with persistently low levels of CAD symptoms (*group 1*), three classes showed intermittently high levels of CAD symptoms (classes 3, 6 and 7; 11.2%, *group 2*) and three classes showed persistently high levels of CAD symptoms (classes 2, 4 and 5; 9.8%, *group 3*). Having persistently high levels

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of CAD symptoms, was associated with a lower likelihood of physiological birth after adjustment for age, level of education, BMI, smoking, parity, gestational age and pregnancy complications.

4.2 | Strengths and limitations

The current study has several strengths and limitations. Strengths include the relatively large sample size (n = 1682) and the assessment of anxiety and depressive symptoms in each trimester of pregnancy, enabling us to determine longitudinal trajectories by means of multivariate growth mixture modelling. Limitations were that we did not include all outcomes of the core outcome set for perinatal depression (e.g. clinician's diagnosis of depression, quality of life), as recently reported by Hellberg et al.[55] For instance, anxiety and depressive symptoms were measured by self-report only,[41,46] instead of performing a diagnostic interview to assess syndromal anxiety and depression. However, the DSM-5 increasingly advocates assessments of intensity of symptoms rather than using dichotomous definitions of mental disorders such as anxiety and depression.[56] Moreover, we did not use a Bonferroni correction in the multiple logistic regression analysis to adjust the significance level of each tested predictor, which may have increased the risk of a type I error and should be taken into account when interpreting the results. However, this analysis did not meet one of the scenarios described by Armstrong[57] in which adaptation for multiple testing should be considered. Applying a Bonferroni correction nonetheless may unnecessarily increase the risk of a type II error.[57–59] In addition, generalisation of our results is restricted to Dutch, mainly white women with a slightly higher education level compared with the national figures.[60] Future research should examine to what extent our results can be replicated in other high-income countries and in low- and middle-income countries, considering the substantial variability in use of medical interventions during childbirth between high-income countries[18] and the major difference in availability of emergency obstetric care in low-, middle- and high-income countries.[61] Furthermore, data were collected between 2013 and 2014. The current study therefore does not consider the possible influence of the COVID-19 pandemic on women's prenatal mental wellbeing. Earlier studies have shown that the pandemic can have a negative impact on pregnant women, specifically regarding the Quality of Life,[62] anxiety as measured by the TPDS-NA[63] and depressive symptoms.[64]

4.3 | Interpretation

Interestingly, the negative association with physiological birth was only found for the group of women with *persistently* high levels of CAD symptoms in the current study, while belonging to the group with *intermittently* high levels of CAD symptoms failed to show an association. As heightened levels of anxiety and depressive symptoms have been associated with lower childbirth self-efficacy,[25] our findings may suggest that women with persistently high levels of CAD symptoms may have so little confidence in giving birth that it may complicate childbearing. In addition, only persistently high stress levels during pregnancy may result in continuous output of stress hormones, which subsequently may affect the occurrence of a physiological birth. Varying stress levels during pregnancy, on the other hand, may result in more fluctuation of stress hormone output, which may have less impact on the physiological processes during labour. Thus, the interesting finding that intermittently high levels of CAD symptoms were not associated with physiological birth, highlights the relevance of timing and severity of these symptoms during pregnancy, which categorises the persistently high symptom level group. These findings emphasise the clinical importance of examining these symptoms prospectively during pregnancy. Future studies should further investigate this severity and chronicity of CAD by also considering the clinical diagnosis (anxiety and depression) of pregnant women. Moreover, future studies should examine whether physiological birth may be included in the core outcome set for perinatal depression, as recently described by Hellberg et al.[55]

Some previous studies have investigated the association of maternal anxiety or depression with obstetric interventions during birth. A large population-based cohort study examined almost 1 million pregnancies in Sweden between 2001 and 2013 and reported an association between maternal anxiety or depression (i.e. a diagnosis recorded between 1 year prior to pregnancy until childbirth) and assisted vaginal birth or unplanned caesarean section.[24] Another large community-based cohort study among 2825 pregnant women in Canada studied anxiety and depressive symptoms in the second and third trimester of pregnancy in relation to several obstetric interventions and only found an association of depressive symptoms in the third trimester with unplanned caesarean section.[23] However, none of these studies assessed both anxiety and depression in each trimester of pregnancy to account for the high variability in (individual) symptoms over time.

The current study therefore supports previous findings showing an association between prenatal symptoms of anxiety and depression, and mode of delivery. In turn, previous studies have also demonstrated that mode of delivery can be a risk factor for postpartum depression, more specifically in women with preterm caesarean delivery before 26 weeks[65] and caesarean delivery,[66] but also in women who gave birth prematurely or had a low birthweight baby.[67] This could indicate that women who gave birth with an intervention are also at a higher risk for postpartum depression, especially considering that women with prenatal depression and anxiety have a higher risk of also experiencing these symptoms postpartum.[68,69] It is therefore plausible that the association between prenatal and postnatal anxiety and depression is partly mediated by birth interventions, and this possible mediating effect should be investigated in future research.

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Our sample was similar to the national birth cohorts of 2014–2017 in the Netherlands with regard to obstetric characteristics such as the distribution of nulliparous and multiparous women, and the number of previous miscarriages.[70] Also, the lower occurrence of physiological birth in nulliparous women was similar to the national figures.[70] As expected, women belonging to the groups with intermittently and persistently high levels of CAD symptoms more often showed a history of anxiety and/or depression, which are well-known risk factors for heightened anxiety and depressive symptomatology in general[71,72] as well as during pregnancy.[73,74] Notably, only the group with *persistently* high levels of CAD symptoms showed differences in other characteristics, such as age (lower), education level (lower), employment (less) and unplanned pregnancy (more). These characteristics have all been reported to be potential risk factors for heightened anxiety and depressive symptomatology during pregnancy,[73] which suggests that the women belonging to this group may be the most vulnerable to develop and maintain high levels of CAD symptoms during pregnancy.

The current findings are clinically important, as physiological birth leads to many health benefits for mother and infant. Identifying pregnant women with persistently high levels of CAD symptoms and offering them proper support may enhance the occurrence of a physiological birth. In practice, this could involve early screening of pregnant women for symptoms of anxiety and depression. We encourage the use of the TPDS-NA (which has now been translated into eight different languages) to measure pregnancy-specific anxiety symptoms and the use of the E(P)DS, which already is a widely used screening instrument to measure depressive symptoms during pregnancy.[47] We defined a risk profile at 12 weeks' gestation of TPDS-NA ≥15 (corresponding to the 94 percentile TPDS-NA scores at 12 weeks' gestation) *or* E(P)DS ≥10 (corresponding to the 88 percentile E(P)DS scores at 12 weeks' gestation) with acceptable sensitivity, specificity and PPV figures to detect vulnerable women. Suitable support targeting pregnancy distress could be provided during the remainder of the pregnancy to these women. A very recent meta-analysis showed that psychological interventions are most likely effective in the treatment of perinatal depression, with effects that last at least up to 6–12 months, and possibly with effects on social support, anxiety, functional impairment, parental stress and marital stress as well.[75] In particular, support could focus on enhancing childbirth self-efficacy, as this is negatively related to heightened levels of anxiety and depressive symptoms during pregnancy[25] and may have a beneficial impact on physiological birth. Support could be provided in the form of a childbirth education course, cognitive behavioural therapy-based programme, or mindfulness-based programme, which are programmes with proven effectiveness.[76–85] Moreover, future research could address the development of suitable smartphone applications for pregnant women. Smartphone applications have the ability to incorporate surveys for assessment of distress symptoms, perinatal-specific and psycho-educational information, and therapeutic elements (e.g. cognitive behavioural therapy-based activities).[86]

5 | CONCLUSION

The current study is the first to show an association between persistently high levels of CAD symptoms throughout pregnancy and a decreased likelihood of physiological birth and also that women with persistently high levels of CAD symptoms can easily be detected in the first trimester.

AUTHOR CONTRIBUTIONS

LH contributed to the conceptualisation of the study, data analysis, interpretation of the data and drafting of the manuscript. MB contributed to the interpretation of the data and reviewing and editing of the manuscript. PL contributed to the data analysis and reviewing and editing of the manuscript. EP, IN, VB, GO and CV critically reviewed the analyses and contributed to reviewing and editing of the manuscript. VP contributed to the conceptualisation of the study, design, interpretation of the data and reviewing and editing of the manuscript.

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None.

CONFLICT OF INTERESTS

None declared. Completed disclosure of interest forms are available to view online as supporting information.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS APPROVAL

The HAPPY study was approved by the ethical committee of Tilburg University on 11 November 2012 (protocol number EV-2012.25) and reviewed by the Medical Ethics Committee of the Máxima Medical Centre Veldhoven.

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SUPPORTING INFORMATION

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