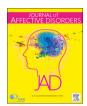
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Research paper

Increase of depressive symptomatology during pregnancy over 25 years' time in four population based cohorts



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ABSTRACT

Background: The use of psychotropic drugs for depression during pregnancy has increased over the past decades, but it is unclear whether women are becoming more depressed over time.

Methods: We investigated the occurrence of depressive symptoms during pregnancy in four cohorts (N 300–2000) in the same area in the Netherlands over a period of 25 years using a similar study design. Depressive symptoms were assessed using the Edinburgh Depression Scale (EDS) at various time points during pregnancy. Demographics, lifestyle factors, obstetric characteristics and EDS scores were compared between the four cohorts

Results: From 1988 to 2014, Mean EDS scores during the first and third trimester of pregnancy increased significantly (P < 0.001). The number of women with elevated EDS scores doubled from 7% in 1988–1989 to 14% in 2012–2014 (P = 0.001). The number of highly educated women increased from 23% to 66% and those with paid employment from 75% to 95%, while smoking and alcohol use decreased significantly (all Ps < 0.001). These trends were similar to those of the National Statistics. A previous history of depression, multi-parity and paid employment were associated with higher EDS scores.

Limitations: Women were highly educated, predominantly Caucasian and had a partner.

Conclusions: Paradoxically, there was a significant increase in depressive symptomatology during pregnancy over a period of 25 years, while protective factors for depression during pregnancy improved. Potential explanations could be greater awareness, high societal expectations, use of social media or the stressful combination of paid work and children at home.

1. Introduction

Pregnancy is a challenging period for women, especially the first time, and mood symptoms are common during this period (Dayan et al., 2010). The prevalence of depression during pregnancy is estimated to be in the range of 5–20% depending on the definition of 'depression' and demographical characteristics of the investigated cohorts (Ashley et al., 2016; Munk-Olsen et al., 2016). Depression during pregnancy can have a profound negative impact on both the health of the mother and child including increased risk of preterm birth and small for gestational age neonates (Jarde et al., 2016).

Multiple previous studies have investigated determinants of depressive symptomatology during pregnancy. Some of these are well known risk factors for mood disorders in general, such as a history of previous depression, being single, lack of partner support, relationship problems, low education, unemployment, or having serious difficulties at work, (Field et al., 2006; Dayan et al., 2010; Fortner et al., 2011; Figueiredo et al., 2018; van Broekhoven et al. 2018; Boekhorst et al., 2019). Other determinants are pregnancy-specific, such as a history of pregnancy/delivery complications, unplanned pregnancy, or stress related to potential adverse fetal outcomes (Dayan et al., 2010; Truijens et al., 2017; Boekhorst et al., 2019).

Abbreviations: BMI, body mass index; EDS, Edinburgh (Postpartum) Depression Scale; HAPPY, Holistic Approach to Pregnancy and the first Postpartum Year (study); M, mean; SD, standard deviation; SPSS, Statistical Package for Social Sciences

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Over the past decades, the use of psychotropic drugs for depression and or anxiety during pregnancy has increased (Cooper et al., 2007; Charlton et al., 2015,), but it is unknown whether pregnant women are getting more depressed over time. Accordingly, we investigated the occurrence of depressive symptoms during pregnancy over a period of 25 years (1988–2014). We used data from four pregnancy cohorts (N between 300–2000) from the same area in the south-east of the Netherlands. Recruitment methods did not change and these cohorts had a similar study design over time, which enabled us to investigate the prevalence of depression during pregnancy over a 25-year period.

2. Methods

All four studies have been published and described in detail elsewhere (Pop et al., 1991; Kuijpens et al., 2001; Pop et al., 2006; Truijens et al., 2017), and here we present a summary of the methodology.

2.1. Participants

Women were all recruited in a similar manner: they were invited to participate during their first appointment (6–8 weeks gestation) with the community midwife. In three cohorts, depressive symptoms were measured at multiple time points during pregnancy. In the first cohort, this was only carried out at 32 weeks' gestation (Table 1).

2.2. Procedure in all four cohorts

In The Netherlands, community midwives are allowed only to be responsible for antenatal care for "low-risk" pregnant women: 'healthy' women without a diagnosis of a (chronic) somatic condition or mental disorder. Accordingly, women with (pre-existing) chronic conditions such as type 1 diabetes, Thyroid disease, bipolar disorder or schizophrenia are followed by obstetricians and were not included in these 4 cohorts. Women treated for depression at the time of conception were also not eligible for inclusion. The criteria for eligibility of antenatal controls by a community midwife has been developed by the national Society of Obstetrics and Gynaecology and and the Royal Dutch Midwifere Association did not change during the period of 25 years. Throughout the four studies, the percentage of women seeing the community midwife during early pregnancy was stable over time: between 80-85% of all pregnant women nationwide. The response rates in all studies of women who gave written informed consent were also stable: between 76-82%. Only women with singleton pregnancies and full understanding of dutch language were included. This led to an absence of ethnic diversity with over 95% of women being white Caucasian. Over the period of 25 years, all women were recruited from the same area in the south-east of the Netherlands. In all studies, blood samples were taken in order to analyze thyroid function. These studies were approved by the Medical Ethical Review Board of the Maxima Medical Centre, Veldhoven. All participants provided written informed consent.

Table 1 Design of four studies involved in the 25-year assessment of depressive symptoms during pregnancy using the EDS, total N = 3376.

Trimester	1	2	3
Study 1: 1988–1989, <i>N</i> = 305	-	_	+
Study 2: 1992–1993, $N = 296$	+	_	+
Study 3: 2002–2004, N = 872	+	+	+
Study 4: 2013–2014, N = 1903	+	+	+

2.3. Assessment of depressive symptoms in all four cohorts

Depressive symptoms were assessed using the ten item Edinburgh (Postpartum) Depression Scale (EPDS) (Cox et al., 1987, Cox et al. 1996). We validated the EPDS in study 1 for use in the Netherlands during the postpartum period (Pop et al., 1992). In 2008, the EDS was validated for use via Internet, and showed similar psychometric properties as the paper and pencil version (Spek et al., 2008). In study 3 we validated the EDS for *use during pregnancy*, with trimester-specific cutoff values of ≥ 11 in the first trimester and ≥ 10 in the second and third trimesters giving the best combination of sensitivity, specificity and positive predictive value for depression during pregnancy (Bergink et al., 2011). Cronbach's alphas of the EDS varied at the various trimesters and in the separate studies between 0.79–0.85. (Table 1)

2.4. Assessments of covariates

Over the 25-year period, a similar set of demographic, psycho-social and obstetric variables was assessed in all the studies. These included age, education level, marital status, employment, smoking habits, alcohol intake, BMI at baseline, previous history of depression, previous history of miscarriage, and parity.

2.5. Statistical analyses

Descriptive statistics were calculated using SPSS (IBM, version 24). Mean, SD, and ranges of EDS scores were calculated as well as reliability (Cronbach's alpha). Differences in prevalence of demographic and obstetric characteristics and in the number of cases with high EDS scores between the studies, were analyzed using X^2 statistics. Mean EDS scores between the various samples were compared using ANOVA.

3. Results

3.1. Demographic and obstetric characteristics, and lifestyle habits (Table 2)

No differences in obstetric characteristics were found, with the exception of a higher number of previous miscarriages reported in study 4.

Moreover, the percentage of women with a history of depression was similar in all cohorts. We observed various changes in demographic and lifestyle characteristics. Age significantly increased over time in both nulliparous and multiparous women (Welch F (3, 821): 25, P < 0.001). The mean age of nulliparous women in study 1 was 27.7 years; 25 years later, in study 4, it was 29.4 years (paired-T (1076) = 4.99, P < 0.001).

Over time, the educational level increased substantially, particularly in the last decade. In 1989, 23% of the women were highly educated, while in 2014 this percentage was 66% (X^2 (6) = 581, P < 0.001). This increase in education level over time was similar to other Dutch national surveys (CBS) as shown in the supplementary table. Nationally, the percentage of less educated women dropped three times (from 40% to 14%) compared to five times in the study population (from 26% to 5%). The percentage of highly educated women increased three times in both the national as well as the study population (supplementary table).

Moreover, the number of women in paid employment increased from 74% in 1989 to 93% in 2014 (X^2 (3) = 160, P < 0.001). This increase was mainly due to the increase of paid employment in the multiparous group: 58% of multiparous women were in paid employment in 1998, while in 2014, this amounted to 92% (X^2 (3) = 184, P < 0.001). In study 1, 28% of nulliparous women in paid employment during pregnancy stated that they intended to stop working after birth, a figure that dropped to 21% in study 2, 11% in study 3, and to 5% in study 4 (2014).

3.2. Lifestyle habits

The number of women reporting smoking during pregnancy significantly decreased from 16% in the first study to 7% in the final study (X^2 (3) = 127, P < 0.001). Similarly, the number of women who reported consuming alcohol during pregnancy decreased from 20% in 1989 to 4% in 2014 (X^2 (3) = 278, P < 0.001). Mean BMI did not alter substantially over time.

3.3. Depressive symptomatology

The mean EDS scores in the four studies at different trimesters are shown in Table 3.

When we compared mean the EDS scores over time assessed at different trimesters, the ANOVA results showed a violation of the homogeneity of variances: the variance in scores was not the same in each group (P of Levene test < 0.05). Therefore, the Welch F is reported. Mean EDS scores in first trimester assessments (studies 2, 3 and 4) increased significantly during the 25-year period (ANOVA: Welch F (2, 836) = 10.0, P < 0.001) as well as third trimester assessments (ANOVA: Welch F (3, 830) = 14.0, P < 0.001).

Fig. 1 shows that the number of depressive cases above the EDS cutoff increased significantly (X^2 (3) = 18, P, 0.001) during the 25-year period. When we compared the prevalence of elevated EDS scores in study 1 with that in study 4 at 32 weeks' gestation, the number doubled from 7% in 1988–1989 to 14% in 2012–2014 (chi² (1): 11.01, P = 0.001). Similar figures were found for EDS scores > 13, which are generally considered to reflect major depressive symptoms (Fig. 1). The percentage of women with EDS scores > 13 increased fourfold from 1% in study 1 to 4% in study 4 (chi² (1): 11.1, P = 0.001). Of all women included in the four studies (N = 3376), 465 (13.7%) women reported a history of depression (Table 2). Of these 465 women, 250 (53.7%) had an EDS > cut-off at least once during pregnancy, compared to 1013 (34.8%) of the 2911 women without a previous history of depression (chi² (1): 61, P < 0.001).

3.4. Correlates of depressive symptomatology

In order to examine the significant correlates of depressive symptoms, we performed a multiple linear regression analysis (Table 4) with the EDS scores at 32 weeks as the dependent variable. Preliminary analyses were conducted to ensure that no violation of the assumption of normality, multicollinearity or homoscedasticity occurred. We created dummy variables of each study, using study 1 as the reference

Table 2 Characteristics of four different samples of pregnant women assessed during a 25-year period, total N = 3376.

	Study 1, <i>N</i> = 305 1988–1989	Study 2, <i>N</i> = 296, 1991–1993	Study 3, <i>N</i> = 872 2002–2004	Study 4, <i>N</i> = 1903 2013–2014
Demographic				
features				
Age				
M, SD	29.3 (3.3)	29.6 (3.2)	31.0 (3.7)	30.4 (3.7)
Range	19–39	19–39	18-43	19-43
Median	29	30	31	30
Age nulliparous (M, SD)	27.7 (3.2)	28 (3.3)	29.7 (3.6)	29.4 (3.5)
With partner (%)	302 (99)	290 (98)	846 (97)	1884 (99)
Education level N (%)				
Low	79 (26)	71 (24)	70 (8)	95 (5)
Medium	156 (51)	154 (52)	480 (55)	552 (29)
High	70 (23)	71 (24)	322 (37)	1256 (66)
Paid employment N (%)	226 (74)	225(76)	756 (87)	1770 (93)
nulliparous	127 (95)	117 (94)	381 (93)	895 (96)
multiparous	99 (58)	110 (64)	379 (82)	893 (92)
Lifestyle habits				
BMI at baseline				
M, SD	24.2 (3.7)	24.5 (3.6)	25.5 (4.5)	23.8 (3.9)
Range	17 – 40	19 – 39	17 – 45	16 – 42
BMI > 30 N (%)	21 (7)	24 (8)	78 (9)	133 (7)
Smoking N (%)	49 (16)	44 (15)	113 (13)	133 (7)
Alcohol intake N (%)	61 (20)	50 (17)	114 (13)	76 (4)
Obstetric features N (%)				
previous miscarriage	55 (18)	56 (19)	157 (18)	514 (27)
nulliparous	134 (44)	124 (42)	410 (47)	932 (49)
multiparous	171 (56)	172 (58)	462 (53)	971 (51)
term at delivery (M, SD)	39.6 (1.5)	39.9 (1.9)	39.9 (1.3)	39.7 (1.5)
birth weight (grams, M, SD)	3462 (510)	3440 (574)	3519 (481)	3475 (498)
Previous episode of depression N (%)	37 (12)	38 (13)	105 (12)	285 (15)

Note: BMI, Body Mass Index; M, Mean; SD, Standard Deviation.

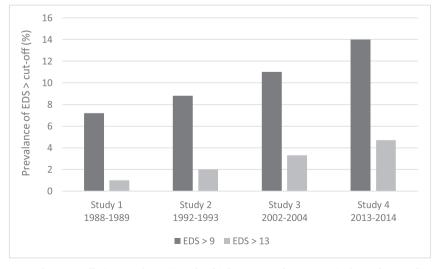


Fig. 1. Prevalence (%) of EDS scores above cut-offs (> 9 and > 13) at the third trimester of pregnancy in four cohort studies assessed over a 25-year period (EDS > 9: chi^2 (3): 18.01, P < 0.001 and EDS > 13: chi^2 (3): 14.2, P = 0.003).

Table 3 Mean EDS scores in four consecutive studies at different trimesters between 1989 and 2014. Total N = 3376.

	Study 1, n = 305 1988–1989	Study 2, n = 291 1992–1993	Study 3, n = 872 2002–2004	Study 4, n = 1903 2013–2014
Trimester 1	_			
Mean EDS (SD)		3.9 (3.4)	4.8 (4.0)	4.4 (4.2)
Range		0–16	0-25	0-25
Trimester 2	-	-		
Mean EDS (SD)			4.3 (3.9)	5.1 (4.2)
Range			0-26	0-25
Trimester 3				
Mean EDS (SD)	3.9 (3.5)	4.0 (3.6)	4.3 (4.0)	5.0 (4.3)
Range	0–18	0–20	0–22	0–24

Note: EDS, Edinburgh Depression Scale; SD, Standard Deviation.

Table 4 Multiple linear regression, dependent variable: EDS scores at 32 weeks' gestation, total N=3376.

	Standardized Beta	T	p
Study 2, 1988–1989	0.098	5.50	< 0.001
Study 3, 2002-2003	0.087	4.94	< 0.001
Study 4, 2013-2014	0.071	4.04	< 0.001
History of depression	0.202	12.06	< 0.001
Multi-parity	0.080	4.42	< 0.001
Lower education	0.049	2.39	0.017
Younger age	0.043	2.37	0.018
Paid employment	0.049	2.79	0.005

Note. Study 1 (1988–1989) was used as a reference. F (8, 3367) = 36.2, P < 0.001.

study, and adjusting for age, previous episodes of depression, parity, and paid employment as important covariates. The total N was 3376.

History of depression was the most important correlate of the EDS scores at 32 weeks' gestation (standardized beta: 0.20). Compared to study 1, the more recent studies were positively associated with higher EDS scores. Younger age, lower education, multi-parity, and paid employment were also associated with higher EDS scores. The total variance explained in this model was 11%, F (8, 3367) = 36.2, P < 0.001.

3.5. Mental health referrals

Information on mental health referrals was available for study 3 and 4 only. In study 3, 182 (21%) women had at least once an EDS above the trimester specific cut-off. Of these, 12 women (1.4%) visited their GP or psychiatrist because of mental health problems. In study 4, there were 462 women (24.3%) with an EDS score at least once above the trimester specific cut-off of whom 31 women (1.6%) visited their GP or gynecologist because of mental health problems.

4. Discussion

This large multi-cohort study shows a significant increase in self-reported depressive symptoms in pregnant women over a 25-year period. This increase in depressive symptomatology is remarkable given our findings that education as a protective factor against depression during pregnancy increased over time, and poor life style habits (smoking and alcohol use) improved over time.

The mean age of nulliparous women increased significantly over the 25-year period, which is in line with national obstetric data (Gissler et al., 2010); *i.e.*, nowadays, women are significantly older when they have their first child. The number of lower educated women

dropped fivefold, while that of highly educated women increased threefold. Indeed, this area of south-east Netherlands was nominated as being the smartest in the world in 2011 by the international think-tank Intelligent Community Forum (ICF) in New York. There is significant evidence that a lower educational level is associated with a higher incidence of (gestational) depression (Field et al., 2006; Dayan et al., 2010; Fortner et al., 2011). Poor lifestyle habits (such as smoking) are associated with lower education and, as expected, the percentage smokers decreased over time: in 1988, 16% of pregnant women were smoking, but this was only 7% in 2014.

Another trend in western society is the increase in the number of women in paid employment, which was also seen in our cohorts. In particular, the number of multiparous women in paid employment almost doubled. Historically, the labor participation of women after World War II in the Netherlands was among the lowest in Europe. The steep increase in paid labor for women in the Netherlands took place at the end of 20th century and the increase of labor participation over time reflects the national societal changes for women. Interestingly, both multi-parity and being in paid employment were independently and positively associated with higher EDS scores in the multivariable analysis. This suggests that multiparous women in paid employment are especially at risk for higher depression levels. The combination of children at home and paid employment could be perceived as being stressful, both for employment outside or inside the home. Working from home, might not alleviate stress because boundaries between work and private life easily disappear. Notably, the number of women with a history of depression did not change substantially over the 25year period. As expected, a history of depression was a major correlate of high EDS scores.

It is challenging to find an explanation for our main finding that EDS scores increased during the 25-year period, while most determinants of depression remained stable, and the occurrence of risk markers such as lower education, unemployment or smoking/alcohol intake actually decreased over time. Potential explanations for this paradox include greater awareness of depressive symptoms, less societal stigma toward mental health issues, or an absolute increase in the prevalence of depression over time. Nowadays, women might be more open to reporting depressive symptoms compared to 25 years ago, especially when they are highly educated. As a consequence, they may rate their mood as being 'depressed' more frequently, resulting in more 'false positive' high EDS scores compared to previous studies. In agreement with this hypothesis, consultations with health professionals because of mental health problems did not increase over the last 10 years (study 3 and 4: 1.4–1.6%).

Although greater awareness of symptoms and less stigma may have played a role in higher EDS scores over time, an absolute increase in the prevalence of depressive symptomatology cannot be ruled out. For example, this could be due to profound changes in society, including the extensive use of social media. Research has shown that the use of social media is associated with symptoms of depression (Lin et al., 2016; Primack et al., 2017; Hardy and Castonguay, 2018). All the women in study 4 were internet users since they had to complete the questionnaire online. Pregnancy is a challenging period for most women, and it may well be harder to cope with these challenges when they are faced with the 'exciting life' of peer groups of a similar age on social media who are not involved in the process of the transition to parenthood.

In addition to the sample size, the current study has several other strengths. Firstly, during a 25-year period, all the women were recruited from the same area and, in a similar way, during their first consultation with the community midwife. In all studies, recruitment biases was very limited because we did not recruit via advertisement or media and there was no financial incent to participate. Secondly, during this period, the same instrument for assessing depressive symptoms was used: the Edinburgh (Postnatal) Depression scale. Thirdly, the same correlates associated with depression were recorded in all cohorts. And

finally, in three of the four cohorts, depression was assessed during more than one trimester. Several limitations should also be mentioned: firstly, we assessed depressive symptoms rather than depression as a syndrome. Moreover, the women in our study were highly educated, Caucasian, had a partner, and the majority were in paid employment. Therefore, our findings cannot be generalized to include socially disadvantaged populations or women of other ethnic origins. In addition, we do not know whether our findings are culture-specific, since we are not aware of any similar studies in other countries. Recently, the British Alspac study published an interesting report on depression during pregnancy in 180 mothers and the pregnancies of their daughters 20-25 years later (Pearson et al., 2018). Unfortunately, their findings cannot be compared to ours, due to the inter-generational design and the higher familial risk of depression of the daughter. Finally, although in all cohorts data on partner support were collected, different instruments were used and therefore we were unable to make systematic comparisons between the cohorts.

In conclusion, we report an increase in depressive symptomatology during pregnancy over a 25-year period. This was investigated in four large cohorts covering the entire period. Our findings are intriguing because well-known protective factors, such as higher education, less financial distress due to paid employment, and a healthy lifestyle, improved over time, while the most important predictor of depressive symptoms (a previous episode of depression) remained stable. There is no simple explanation for this, but greater awareness may play a role in addition to high societal expectations and the use of social media.

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CRediT authorship contribution statement

Victor Pop: Conceptualization, Writing - original draft, Methodology. Maarten van Son: Methodology. Hennie Wijnen: Writing - review & editing. Viola Spek: Methodology. Johan Denollet: Writing - review & editing. Veerle Bergink: Conceptualization, Writing - original draft.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2019.08.062.

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