Original Investigation

Maternal Depression During Pregnancy and the Postnatal Period

Risks and Possible Mechanisms for Offspring Depression at Age 18 Years

Rebecca M. Pearson, PhD; Jonathan Evans, MD; Daphne Kounali, PhD; Glyn Lewis, PhD; Jon Heron, PhD; Paul G. Ramchandani, DPhil; Tom G. O'Connor, PhD; Alan Stein, FRCPsych

IMPORTANCE Some small studies suggest that maternal postnatal depression is a risk factor for offspring adolescent depression. However, to our knowledge, no large cohort studies have addressed this issue. Furthermore, only 1 small study has examined the association between antenatal depression and later offspring depression. Understanding these associations is important to inform prevention.

OBJECTIVE To investigate the hypothesis that there are independent associations between antenatal and postnatal depression with offspring depression and that the risk pathways are different, such that the risk is moderated by disadvantage (low maternal education) with postnatal depression but not with antenatal depression.

DESIGN, SETTING, AND PARTICIPANTS Prospective investigation of associations between symptoms of antenatal and postnatal parental depression with offspring depression at age 18 years in a UK community-based birth cohort (Avon Longitudinal Study of Parents and Children) with data from more than 4500 parents and their adolescent offspring.

MAIN OUTCOMES AND MEASURES Diagnosis of offspring aged 18 years with major depression using the *International Classification of Diseases, 10th Revision*.

RESULTS Antenatal depression was an independent risk factor. Offspring were 1.28 times (95% CI, 1.08-1.51; $P = .003$) more likely to have depression at age 18 years for each standard deviation increase in maternal depression score antenatally, independent of later maternal depression. Postnatal depression was also a risk factor for mothers with low education, with offspring 1.26 times (95% CI, 1.06-1.50; $P = .01$) more likely to have depression for each standard deviation increase in postnatal depression score. However, for more educated mothers, there was little association (odds ratio, 1.09; 95% CI, 0.88-1.36; $P = .42$). Analyses found that maternal education moderated the effects of postnatal but not antenatal depression. Paternal depression antenatally was not associated with offspring depression, while postnatally, paternal depression showed a similar pattern to maternal depression.

CONCLUSIONS AND RELEVANCE The findings suggest that treating maternal depression antenatally could prevent offspring depression during adulthood and that prioritizing less advantaged mothers postnatally may be most effective.

JAMA Psychiatry. 2013;70(12):1312-1319. doi:10.1001/jamapsychiatry.2013.2163
Published online October 9, 2013.

Supplemental content at jamapsychiatry.com

Author Affiliations: Centre for Mental Health, Addiction and Suicide Research, School of Social and Community Medicine, University of Bristol, England (Pearson, Evans, Kounali, Heron); Mental Health Sciences Unit, University College, London, England (Lewis); Academic Unit of Child and Adolescent Psychiatry, Imperial College, London, England (Ramchandani); School of Medicine and Dentistry, University of Rochester, New York (O'Connor); Department of Psychiatry, Oxford University, England (Stein).

Corresponding Author: Rebecca M. Pearson, PhD, Centre for Mental Health, Addiction and Suicide Research, University of Bristol, Oakfield House, Oakfield Grove, Bristol BS14 8TF, UK (rebecca.pearson@bristol.ac.uk).

Depression in late adolescence is a major public health issue worldwide. It is associated with substantial present and future morbidity and is predictive of depression persisting into adulthood.[1] By late adolescence, the prevalence rates are particularly high,[2] and depression can have a severe and persisting effect on socioemotional functioning, education, and employment. The identification of early-life risk factors is important to guide prevention and intervention.

Evidence shows that maternal postnatal depression (PND) is associated with problems in later child development because of the effect of depression on caregiving.[3,4] It may be a period when suboptimal caregiving confers particularly high risk because of the infant's dependence on parents.[4] To date, the association between PND and offspring depression has been studied up to age 16 years.[5,6] However, findings of an independent association with offspring depression have been inconsistent,[1] and sample sizes have been small. To our knowledge, there have been no large published prospective cohort studies and no reports into late adolescence.

Despite receiving less attention, emerging evidence suggests that antenatal depression (AND) is associated with independent risks for child development.[7,8] The mechanism for this is unclear, but if it is causal rather than being explained by the continuation of AND postnatally, then the mechanisms for the transmission of risk from mother to fetus would differ from those related to maternal depression during the child's life. One explanation is that cortisol, elevated in depression, passes through the placenta and directly alters fetal neural development with long-term consequences.[9] One small study found an association between AND and offspring depression at age 16 years.[6] However, the study did not have the power to distinguish the effects of AND from maternal depression at later time points. To our knowledge, no studies have investigated the effects of AND on depression during late adolescence.

These findings raise 2 important questions: first, is there evidence that both AND and PND are independently associated with an increased risk of offspring depression up to age 18 years, and if so, which period carries the greater risk? However, given that AND often continues and is the strongest predictor of PND,[10] large studies are required to provide sufficient power to assess whether the risks associated with AND and PND are independent. Second, is there evidence that any effects of AND and PND operate through different mechanisms? One way to investigate whether the pathways by which AND and PND influence offspring depression are different is to look at moderation effects. Moderation operates by altering the pathway from exposure (maternal depression) to outcome (adolescent depression); thus, differential moderation would provide indirect evidence for different and independent pathways.

Evidence suggests that associations between PND and negative child outcomes are moderated by socioeconomic status (SES): children whose mothers have the same degree of PND but who are from a higher SES are less likely to be adversely affected than children of mothers from a lower SES.[3,11,12] Of the variables that constitute SES, maternal education is most strongly associated with the quality of the home environment.[13,14] One explanation for the moderating effects of SES is that education diminishes the association between maternal depression and home environmental adversity,[3,13,15,16] therefore mitigating any adverse effects on offspring. This would not apply to the effects of AND if such effects result directly from the biological consequences of AND in utero. In contrast, if any effect of AND on offspring depression occurs only because AND continues postnatally, then maternal education should moderate the antenatal effect.

Investigating paternal depression may also help to understand these pathways. For example, there should be no effect of paternal AND on the child if AND has an effect through biologically mediated pathways in utero, while paternal PND may have more similar effects to maternal PND if they operate through the home environment.

This study uses data from a large UK community-based birth cohort. Several measurements of maternal and paternal depressive symptoms were collected during the antenatal and postnatal periods, and a validated interview measure of offspring depression was completed at age 18 years. Our questions were the following:

1. Are maternal AND and PND associated with offspring depression at age 18 years?
2. Do AND and PND have independent effects on offspring depression? If so, are the risks of different magnitude?
3. Does maternal education moderate the effects of PND but not AND?
4. Are the effects of AND, but not PND, unique to mothers?

Methods

Data Source

The sample comprised participants from the Avon Longitudinal Study of Parents and Children (ALSPAC). All pregnant women resident in the former Avon Health Authority in southwest England, having an estimated date of delivery between April 1991 and December 1992, were invited to take part. The children of 15 247 pregnancies were recruited.[17] Ethical approval for the study was obtained from the ALSPAC Law and Ethics Committee and the Local Research Ethics Committees, and participants gave informed consent. Information on the ALSPAC study is available at www.bristol.ac.uk/alspac/.[17] Detailed information has been collected about the cohort since early pregnancy, including regular self-reported information from mothers and children and face-to-face assessments in research clinics. The current study uses data from the child sample (singletons only) attending the most recent research clinic.

Sample

Our starting sample comprised those with maternal AND and PND data (N = 8937). Outcome data were available for 4566 adolescents at age 18 years. A sample with complete data across all exposure, outcome, and confounding variables (n = 2847) was used to investigate main and independent effects of maternal depression. Data were available on paternal depression and education from a sample of 2475. To maximize power

to examine magnitude of risk and moderation, we used all available data from exposures and outcomes for these analyses. All missing data were imputed, and all analyses were repeated using the same sample (N = 8937).

We imputed for missing data because if those with missing data are ignored, it can result in bias by making the assumption that data are missing completely at random.[18] Full details of the imputation method are given in the eMethod in the Supplement.

Measures

Parental Depression

Symptoms of maternal depression were measured using the Edinburgh Postnatal Depression Scale (EPDS).[19] The EPDS is a 10-item self-report depression questionnaire validated for use in the perinatal period because it avoids physical symptoms.[19] It is validated for use outside of the perinatal period and for men.[20-22] Scores of more than 12 have a high sensitivity and specificity in predicting clinically diagnosed major depressive disorder.[21-23] We primarily used the continuous scores to make full use of the variation in symptoms, although we also applied the threshold of 12 or higher to test for main effects.

Postal questionnaires, including EPDS measures, were administered at approximately 18 and 32 weeks antenatally and 8 weeks and 8 months postnatally. For the current study, the periods of interest were pregnancy (while the mother and fetus were physiologically attached) and the first year postnatally (while the infant was heavily dependent on caregivers and exposed to the home environment). We calculated the mean EPDS scores across the 2 available measures within these a priori selected and theoretically defined periods, providing a more stable and reliable estimate of levels during that period than would be obtained using 1 measure alone,[24] as used previously.[25] We took the mean of the antenatal EPDS scores at 18 and 32 weeks as the AND measure and the mean of the postnatal EPDS scores at 8 weeks and 8 months as the PND measure. Analyses were repeated, examining the effect of each of the 4 EPDS measures separately, with individual EPDS scores having comparable effects to those reported for mean AND or PND scores.

Because the EPDS is validated beyond the postnatal period, this same measure of maternal depression was used repeatedly during the child's life, allowing us to consider later maternal depression. We applied the latest available measure of maternal depression when the children were aged 12 years (closest to the 18-year outcome) to account for later maternal depression. To account for repeated exposure to maternal depression, we derived a count of subsequent depression episodes in the child's life (number of times the mother scored >12 on any of 6 EPDS measures from ages 1-12 years). This measure is only valid if all time points are included. However, because most women missed only 1 or 2 of the EPDS questionnaires, we were able to impute this variable using data from EPDS scores at other time points. Fathers also completed the EPDS at 18 weeks of pregnancy (paternal AND) and 8 months postnatally (paternal PND).

Parent Education

Mothers completed questionnaires concerning their education and their partner's education at 32 weeks of pregnancy. Response categories were minimal education or none, compulsory secondary level (up to age 16 years), noncompulsory secondary level (up to age 18 years), or post-school university-level education. Education up to age 16 years (compulsory education only) was categorized as low education and post 16 as high education. Low education was relatively common (>50%). This socioeconomic indicator was chosen a priori for theoretical reasons, as explained earlier.

Adolescent Depression

Depression in the offspring was measured using the computerized version of the Clinical Interview Schedule-Revised (CIS-R),[26] which derives a diagnosis of depression according to *International Classification of Diseases, 10th Revision* criteria. The interview is fully standardized and equally reliable whether conducted by a clinically trained interviewer or self-administered on the computerized version.[26-28] The CIS-R is designed for, and has been widely used within, community samples, including the National Surveys of Psychiatric Morbidity and the 1958 birth cohort.[28-31] A binary variable indicating a primary diagnosis of major depression on the CIS-R or no such diagnosis was the outcome measure.

Confounding Variables

Maternal characteristics identified in previous studies as being associated with maternal depression[7] or education were obtained from maternal questionnaires administered antenatally and during the child's life. These included maternal age (in years), social class (categorized 1 [highest] to 5 [lowest on the basis of occupation status), parity, history of depression before pregnancy (self-report yes or no), smoking during pregnancy, breastfeeding in the first year (none, <3 months, 3-6 months, or >6 months), and use of nonparental child care within the first 6 months (yes or no). Smoking is important because the association between prenatal smoking and child psychiatric outcomes may reflect genetic confounding.[32]

Statistical Analyses

Main Effects

To test main effects of both AND and PND, we investigated associations of AND and PND symptoms with offspring depression in separate logistic regression models. Later maternal depression and potentially confounding variables were then included in these models.

Independent Effects

To assess independent effects, both AND and PND were included in the same regression model. The reported effects reflect the association between AND and offspring depression, adjusted for PND, and the association between PND and offspring depression, adjusted for AND. We also investigated independent effects by repeating each main effect analysis, excluding women reaching above thresholds for depression (>12) at the other timing (ie, women with PND were removed from

Table 1. Odds Ratio for Offspring Depression According to Each 5-Point (1-SD) Increase in Antenatal and Postnatal Depression Scores in 2847 Complete Cases (All Variables)

Timing of Maternal Depression	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]		Model 5[e]	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
Antenatal	1.28 (1.08-1.51)	.003	1.27 (1.08-1.51)	.003	1.23 (1.03-1.44)	.03	1.27 (1.02-1.59)[f]	.04	1.29 (1.08-1.55)[g]	.01
Postnatal	1.24 (1.03-1.49)	.02	1.21 (1.01-1.44)	.03	1.13 (0.94-1.34)	.19	0.98 (0.77-1.23)[h]	.86	1.20 (0.98-1.48)[i]	.08

Abbreviation: OR, odds ratio.

[a] Univariable associations between each timing of maternal depression and caseness of depression at age 18 years.

[b] Model 1 with adjustments for exceeding thresholds (>12) on the most recent maternal depression measure available (age 12 years).

[c] Model 1 including confounding variables (maternal age, parity, social class, maternal education, maternal history of depression, smoking during pregnancy, child sex, breastfeeding in the first year, and child care).

[d] Model 1 with adjustments for the other timing of maternal depression.

[e] Model 1 excluding women exceeding thresholds for depression at the other timing.

[f] Adjusted for postnatal depression.

[g] Excluding women with postnatal depression (n = 2778).

[h] Adjusted for antenatal depression.

[i] Excluding women with antenatal depression (n = 2272).

the AND analyses). The interaction between AND and PND was also examined.

Heightened Risk

To investigate whether the antenatal or postnatal period represents a time of heightened risk to the child, we conducted analyses to disentangle the correlated aspects of AND and PND from separable timing effects. A joint multilevel model of the outcome and maternal depression trajectories across the antenatal and postnatal periods was used.[33] The 4 antenatal and postnatal EPDS scores were included, modeling repeated measures within theoretically relevant periods (period 1, pregnancy; period 2, first year postnatally) as within-period variation, which was accounted for in the model. Latent depression trajectories were summarized by 2 parameters: (1) initial levels of maternal depression in period 1 (the intercept) and (2) the change in maternal depression levels across periods (the slope) using a longitudinal random-effects model. Parameters were allowed to vary across individuals (random effects) and their dependence on the outcome estimated with the Bayesian approach.[33] If either the antenatal or postnatal period were one of greater risk, then an effect of the change in depression across periods would be expected.

Moderating Effects and Paternal Depression

Analyses were conducted to investigate whether maternal education moderated the associations between both AND and PND and offspring depression. Analyses used continuous exposure variables and compared models with and without interaction terms, testing moderation effects of maternal education using likelihood ratio tests.

We also investigated the association between paternal AND and PND with offspring depression at age 18 years and whether any effects were moderated by paternal education.

Results

For the sample with complete exposure measures (N = 8937), the mean (SD) maternal depression score was 6.7 (4.7; range, 0-29) antenatally and 5.5 (4.4; range, 0-27) postnatally. Measures of maternal depression were highly correlated with each other (correlations ranging from 0.6-0.7). The number of women who exceeded thresholds for depression (mean scores of >12 across the 2 antenatal time points) was 1034 (11.6%) antenatally and 664 (7.4%) postnatally. Associations between AND and PND with sociodemographic confounding variables are given in eResults 1 in the Supplement.

At age 18 years, 4566 adolescents completed the CIS-R. A primary diagnosis of depression according to the *International Classification of Diseases, 10th Revision* was given for 360 (7.9%): 3374 mothers of these adolescents had provided data on all measures of depression during the antenatal and postnatal periods, and 3335 also had maternal education data. Characteristics for the sample with complete CIS-R outcome and maternal depression data compared with the rest of the ALSPAC sample are given in eTable 1 in the Supplement.

Main and Independent Effects

The univariable results provide evidence for main effects of both AND and PND scores on offspring depression (**Table 1**, model 1). These results were replicated with binary EPDS variables, derived using the clinical threshold of 12 or higher, with an odds ratio (OR) of 1.47 (95% CI, 1.0-2.2; $P = .047$) for AND and an OR of 1.67 (95% CI, 1.1-2.6; $P = .03$) for PND. Both associations were independent of later depression (model 2). There was little evidence that the association with AND was subject to confounding by sociodemographic variables. However, the association with PND was reduced once these variables were included (model 3). The association between AND and offspring depression remained after including PND in the same model. In contrast, the association with PND was substantially reduced once AND was included (model 4). It is difficult to draw firm conclusions from these results because the correlation between AND and PND could result in overadjustment.[34] Considering AND by excluding women with antenatal depression diminished the association to a lesser extent (model 5). There was no evidence for an interaction between AND and PND on adolescent depression ($P = .32$).

Results were comparable when using imputed data sets for the main effect (model 1) of AND (OR, 1.36; 95% CI, 1.18-1.56; $P < .001$) and PND (OR, 1.29; 95% CI, 1.12-1.49; $P = .001$). Imputed data sets were used to investigate the impact of future

Table 2. Odds Ratio for Offspring Depression According to Antenatal or Postnatal Depression and Stratified by Maternal Education Using Continuous Measures of Antenatal and Postnatal Depression as Exposure Variables[a]

Timing of Maternal Depression	Exposure Measure[b]	Entire Sample (N = 3335)		High Maternal Education (n = 1644)		Low Maternal Education (n = 1691)		Interaction Term		Test for Interaction[c]	
		OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	χ^2	P Value
Antenatal	5	1.28 (1.08-1.51)	.003	1.27 (1.02-1.57)	.03	1.34 (1.12-1.60)	.001	0.96 (0.90-1.11)	.18	0.62	.43
Postnatal	5	1.24 (1.03-1.49)	.02	1.09 (0.88-1.36)	.42	1.26 (1.06-1.50)	.01	0.93 (0.88-0.99)	.04	4.52	.03

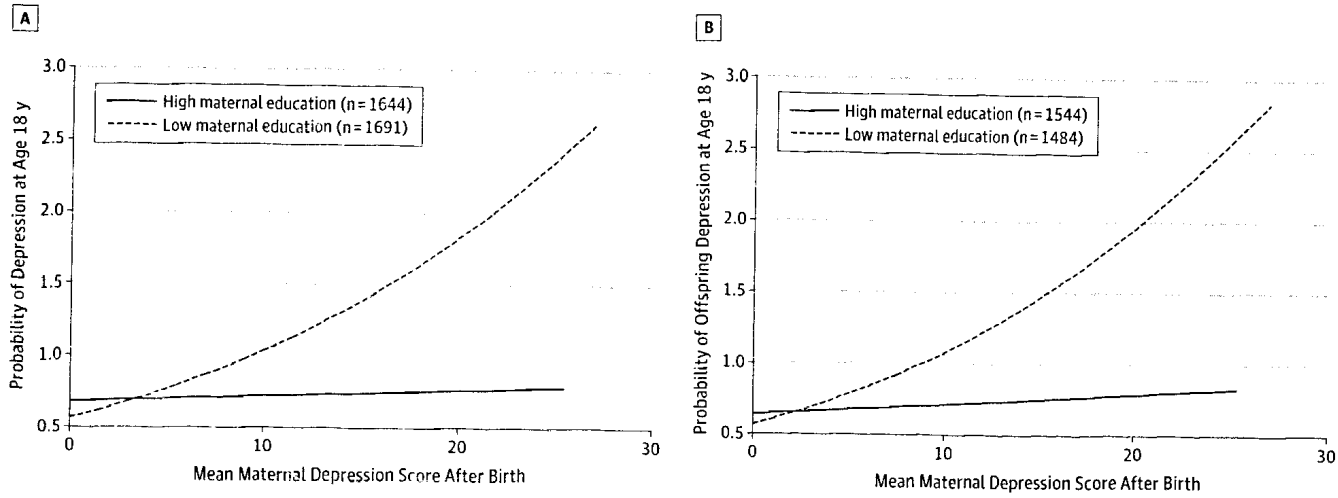
Abbreviation: OR, odds ratio.

[a] Results are for those with complete data for both timings of depression and maternal education.

[b] Mean Edinburgh Postnatal Depression Scale continuous score.

[c] Using the likelihood ratio test for the model with and without interaction.

Figure 1. Association Between Maternal Postnatal Depression and Offspring at 18 Years According to Maternal Education Level



Predicted probability of offspring depression at age 18 years according to the maternal depression score during the first year after birth, stratified by (A) maternal education for the sample with exposures and outcomes (n = 3335) and (B) with the exclusion of women who exceeded thresholds for depression during pregnancy (n = 3028).

episodes of maternal depression. The number of episodes was associated with an increased risk of offspring depression (OR, 1.12; 95% CI, 1.02-1.22; $P = .01$). However, adjusting for this imputation did not diminish the effects of either AND (adjusted OR, 1.30; 95% CI, 1.12-1.55; $P = .001$) or PND (adjusted OR, 1.23; 95% CI, 1.04-1.45; $P = .01$).

Heightened Risk

The intercepts of mothers' depression trajectories from the antenatal to postnatal period were positively associated with risk of offspring depression at age 18 years; the OR for offspring depression for a 5-point increase in initial depression scores was 1.58 (95% CI, 1.2-2.1). However, the model did not provide evidence for an effect of change in maternal depression from the antenatal to postnatal period, suggesting no difference in the magnitude of risk associated with AND and PND. The OR for offspring depression for each 5-point reduction in EPDS scores across periods was 0.77 (95% CI, 0.25-1.8). Results were comparable after accounting for missing data.

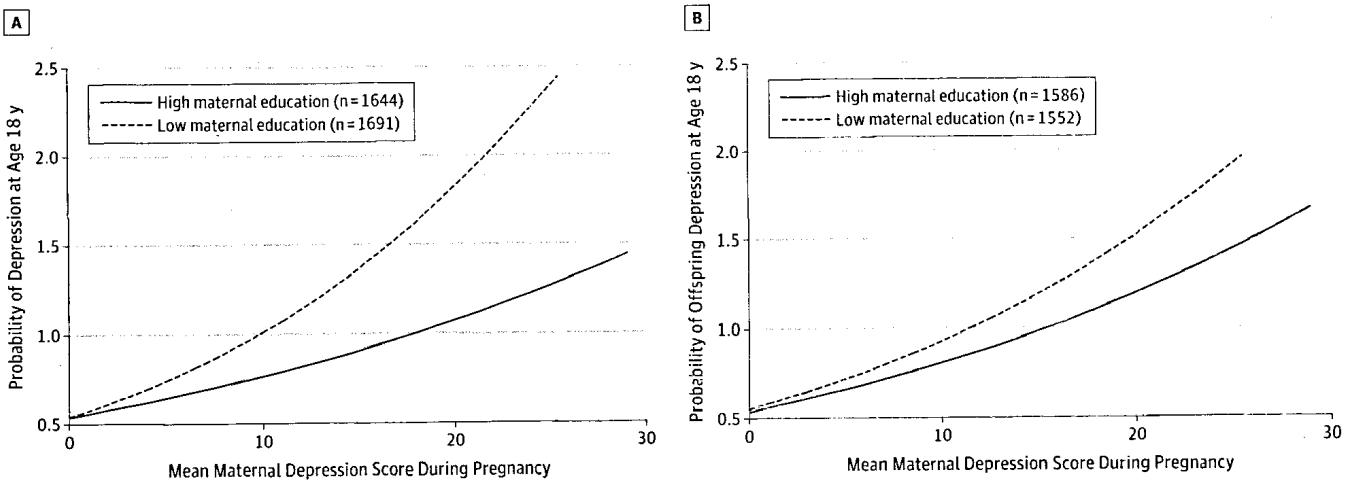
Moderating Effects

There was evidence for an interaction between PND and maternal education but no evidence for an interaction between AND and maternal education (**Table 2**). Stratified analyses provided evidence that the effect of PND was limited to mothers with lower education (**Figure 1**). In contrast, the effects of AND were present in mothers with both higher and lower education (**Figure 2**). Sensitivity analyses using another SES indicator (income) found similar patterns of moderation (results available on request). Results were comparable after imputing for missing data. This pattern of moderation was replicated using a different approach, investigating moderation of AND and PND in a combined model (see eResults 2 and eTable 2 in the Supplement).

Paternal Depression

There was no evidence for an association between paternal AND and offspring depression (OR for a 5-point increase in EPDS score, 0.9; 95% CI, 0.7-1.1; $P = .19$) or that this effect was moderated by paternal education (depression × education interaction, $P = .74$). In contrast, there was evidence for an association between paternal PND and offspring depression, but this was limited to offspring of fathers with low education, with an OR of 1.5 (95% CI, 1.1-2.0) for low education vs an OR of 1.0 (95% CI, 0.7-1.3) for high education (depression × education interaction, $P = .048$). Effects were comparable using imputed data.

Figure 2. Association Between Maternal Antenatal Depression and Offspring Depression at 18 Years, According to Maternal Education Level



Predicted probability of offspring depression at age 18 years according to maternal depression score during pregnancy, stratified by (A) maternal education for the sample with exposures and outcomes (n = 3335) and (B) with the exclusion of women who exceeded thresholds for depression after birth (n = 3138). Antenatal depression is strongly correlated with postnatal depression. Therefore, some of the effect of antenatal depression on child depression will be mediated through a postnatal depression pathway. This indirect pathway from antenatal depression would be moderated by education. As can be seen in B, exclusion of women with postnatal depression reduced any residual moderating effects on the association between antenatal depression and child depression.

Discussion

To our knowledge, this is the first study to test the relative effects of depressive symptoms antenatally and postnatally on offspring depression at age 18 years. Initial analyses provided evidence for associations between both AND and PND and adolescent depression, and these associations remained after adjusting for later maternal depression. The unadjusted effects of AND and PND did not suggest differences in the magnitude of risk to the offspring. However, after considering PND and adjusting for other confounders, AND remained an independent predictor of outcome, while the effect of PND (considering confounding variables and AND) was considerably weakened. Moderation analyses indicated that the effects of PND were moderated by maternal education, with only the offspring of mothers with lower education showing an increased risk of adolescent depression, while adolescents whose mothers had higher education appeared unaffected. This moderation by maternal education helps to explain the diminished overall postnatal effect once we adjusted for maternal education. There was no evidence that antenatal effects were moderated in this way. Paternal AND was not associated with offspring depression. In contrast, paternal PND was associated with offspring depression, but this was limited to those whose fathers had lower education.

Mechanisms

This study does not directly test the mechanisms of the transmission of depression from mother to adolescent. However, the findings of the moderation analyses and comparison of the effects of paternal depression with maternal depression provide indirect evidence that the pathways from AND and PND are different. Differential moderation of the effects of AND and PND indicates that an important part of the pathway from maternal AND to adolescent depression does *not* operate through AND continuing into the postnatal period. Rather, it indicates the operation of a separate pathway. Furthermore, evidence that the antenatal, but not the postnatal, effect was unique to mothers further suggests different pathways.

Given that education is associated with several key environmental factors[13] and moderates the effects of PND, this is consistent with an environmental mechanism. Maternal education indicates multiple sources of psychosocial support (eg, mothers with more education were more likely to use nonmaternal child care) and positive home environments, particularly more positive and sensitive parenting,[3,12] which, in turn, are likely to be protective in the context of depression.[35,36]

In contrast, the absence of any moderation by education antenatally is consistent with the effects of AND operating through the biological consequences of depression in utero, which are unlikely to be mitigated by education and associated environmental advantages. This is further supported by the absence of any effect of paternal AND on offspring outcome. To directly test this hypothesis, future studies could measure indices of the dysregulation of the hypothalamic-pituitary-adrenocorticol axis, such as cortisol or catecholamine levels, as well as other physiologic parameters antenatally.[37] Due to the high correlation between AND and PND, the overall effects of AND include both timing-specific effects and the impact of AND continuing postnatally.

It also remains possible that part of the intergenerational transmission of depression, both in the antenatal and postnatal periods, reflects shared genetic risk.[32,35] The current findings suggest that any shared genetic risk associated with PND, but not AND, may be related to maternal education.

Strengths and Limitations

The strengths of this study include the large sample, the long-term follow-up, the repeated measures of maternal depression, and the availability of confounding and moderating variables. Because maternal depression was first measured 18 years earlier than the measure of child depression, reverse causality is implausible.

There were several limitations of the study. Adolescents who attended the 18-year assessment were more likely to come from families of a higher SES than those in the original sample. Although we cannot fully explain the role of selective attrition, the pattern of missing data and analyses after imputation suggests that, if anything, attrition has led to an underestimation of the size of the associations between maternal and offspring depression.

A further limitation was the lack of a measure of maternal depression when the child was age 18 years. However, we adjusted for maternal depression in early adolescence, which had little effect on the impact of AND or PND. Furthermore, any effect would be common to both AND and PND. There is no reason to believe later maternal depression would explain the differential effects observed. The maternal depression measure was a self-report rather than a diagnostic interview. However, a clinical interview was used for the offspring outcome.

In summary, this study provides evidence that the risks associated with AND and PND are different: AND is an independent risk factor for offspring depression, while PND may be a risk factor only in disadvantaged families. The findings have important implications for the nature and timing of interventions aimed at preventing depression in the offspring of depressed mothers. In particular, the findings suggest that treating depression in pregnancy, irrespective of background, may be most effective. However, the association between PND and risk of offspring depression appears to be greatest for children whose mothers have lower education. Hence, there may be benefit in prioritizing support of more disadvantaged mothers. Further work is needed to understand why offspring of postnatally depressed mothers with low education are particularly at risk.

ARTICLE INFORMATION

Submitted for Publication: October 19, 2012; final revision received February 4, 2013; accepted March 19, 2013.

Published Online: October 9, 2013. doi:10.1001/jamapsychiatry.2013.2163.

Author Contributions: Dr Pearson had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Pearson, Evans, Lewis, Stein.
Acquisition of data: Pearson.
Analysis and interpretation of data: All authors.
Drafting of the manuscript: Pearson, Evans, Stein.
Critical revision of the manuscript for important intellectual content: Evans, Kounali, Lewis, Heron, Ramchandani, O'Connor, Stein.
Statistical analysis: Pearson, Evans, Kounali, Lewis, Heron, O'Connor.
Obtained funding: Lewis.
Study supervision: Heron, Stein.

Conflict of Interest Disclosures: None reported.

Funding/Support: This study was supported by grants 084268/Z/07/Z (G.L.) and 090139 from the Wellcome Trust (A.S.), R01 MH073842 from the National Institutes of Health (T.O.), 74882 from the United Kingdom Medical Research Council, and 076467 from the Wellcome Trust, provided core support for the Avon Longitudinal Study of Parents and Children (ALSPAC) from the University of Bristol; and a Wellcome Trust Strategic Award (R.M.P.).

Role of the Sponsors: The Medical Research Council, Wellcome Trust, and National Institutes of Health had no influence on the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Additional Contributions: We thank all the families who took part, the midwives for help in recruiting them, and the entire ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, and nurses.

REFERENCES

1. Thapar A, Collishaw S, Pine DS, Thapar AK. Depression in adolescence. *Lancet*. 2012;379(9820):1056-1067.

2. Brent DA, Weersing VR. Depressive disorders in childhood and adolescence. In: Rutter M, ed. Rutter's Child and Adolescent Psychiatry. *Oxford, England: Blackwell Publishing Ltd; 2008.*

3. Lovejoy MC, Graczyk PA, O'Hare E, Neuman G. Maternal depression and parenting behavior: a meta-analytic review. *Clin Psychol Rev*. 2000;20(5):561-592.

4. Murray L, Halligan SL, Cooper PJ. Effects of postnatal depression on mother-infant interactions, and child development. In: Wachs T, Bremner G, eds. *Handbook of Infant Development*. Malden, MA: Wiley-Blackwell; 2010.

5. Murray L, Arteche A, Fearon P, Halligan S, Goodyer I, Cooper P. Maternal postnatal depression and the development of depression in offspring up to 16 years of age. *J Am Acad Child Adolesc Psychiatry*. 2011;50(5):460-470.

6. Pawlby S, Hay DF, Sharp D, Waters CS, O'Keane V. Antenatal depression predicts depression in adolescent offspring: prospective longitudinal community-based study. *J Affect Disord*. 2009;113(3):236-243.

7. Evans J, Melotti R, Heron J, et al. The timing of maternal depressive symptoms and child cognitive development: a longitudinal study. *J Child Psychol Psychiatry*. 2012;53(6):632-640.

8. O'Connor TG, Heron J, Glover V; Alspac Study Team. Antenatal anxiety predicts child behavioral/emotional problems independently of postnatal depression. *J Am Acad Child Adolesc Psychiatry*. 2002;41(12):1470-1477.

9. Talge NM, Neal C, Glover V; Early Stress, Translational Research and Prevention Science Network: Fetal and Neonatal Experience on Child and Adolescent Mental Health. Antenatal maternal stress and long-term effects on child neurodevelopment: how and why? *J Child Psychol Psychiatry*. 2007;48(3-4):245-261.

10. Heron J, O'Connor TG, Evans J, Golding J, Glover V; ALSPAC Study Team. The course of anxiety and depression through pregnancy and the postpartum in a community sample. *J Affect Disord*. 2004;80(1):65-73.

11. Goodman SH, Rouse MH, Connell AM, Broth MR, Hall CM, Heyward D. Maternal depression and child psychopathology: a meta-analytic review. *Clin Child Fam Psychol Rev*. 2011;14(1):1-27.

12. Stein A, Malmberg LE, Sylva K, Barnes J, Leach P; FCCC Team. The influence of maternal depression, caregiving, and socioeconomic status in the post-natal year on children's language development. *Child Care Health Dev*. 2008;34(5):603-612.

13. Raviv T, Kessenich M, Morrison FJ. A mediational model of the association between socioeconomic status and three-year-old language abilities: the role of parenting factors. *Early Child Res Q*. 2004;19:528-547.

14. Pearson RM, Heron J, Melotti R, et al. The association between observed non-verbal maternal responses at 12 months and later infant development at 18 months and IQ at 4 years: a longitudinal study. *Infant Behav Dev*. 2011;34(4):525-533.

15. Sohr-Preston SL, Scaramella LV. Implications of timing of maternal depressive symptoms for early cognitive and language development. *Clin Child Fam Psychol Rev*. 2006;9(1):65-83.

16. Parks PL, Smeriglio VL. Parenting knowledge among adolescent mothers. *J Adolesc Health Care*. 1983;4(3):163-167.

17. Fraser A, Macdonald-Wallis C, Tilling K, et al. Cohort Profile: the Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. *Int J Epidemiol*. 2013;42(1):97-110.

18. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med*. 2011;30(4):377-399.

19. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry*. 1987;150:782-786.

20. Edmondson OJ, Psychogiou L, Vlachos H, Netsi E, Ramchandani PG. Depression in fathers in the postnatal period: assessment of the Edinburgh Postnatal Depression Scale as a screening measure. *J Affect Disord*. 2010;125(1-3):365-368.

21. Shakespeare J. *Evaluation of Screening for Postnatal Depression Against the NSC Handbook Criteria*. London, England: National Screening Committee; 2001.

22. Hewitt C, Gilbody S, Brealey S, et al. Methods to identify postnatal depression in primary care: an integrated evidence synthesis and value of information analysis. *Health Technol Assess*. 2009;13(36):1-145; 147-230.

23. Gaynes BN, Gavin N, Meltzer-Brody S, et al. Perinatal depression: prevalence, screening accuracy, and screening outcomes. *Evid Rep Technol Assess (Summ)*. 2005;(119):1-8.

24. Bland JM, Altman DG. Regression towards the mean. *BMJ*. 1994;308(6942):1499.

25. Bowes L, Maughan B, Caspi A, Moffitt TE, Arseneault L. Families promote emotional and behavioural resilience to bullying: evidence of an environmental effect. *J Child Psychol Psychiatry*. 2010;51(7):809-817.

26. Lewis G, Pelosi AJ, Araya R, Dunn G. Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers. *Psychol Med*. 1992;22(2):465-486.

27. Patton GC, Coffey C, Posterino M, Carlin JB, Wolfe R, Bowes G. A computerised screening instrument for adolescent depression: population-based validation and application to a two-phase case-control study. *Soc Psychiatry Psychiatr Epidemiol*. 1999;34(3):166-172.

28. Bell T, Watson M, Sharp D, Lyons I, Lewis G. Factors associated with being a false positive on the General Health Questionnaire. *Soc Psychiatry Psychiatr Epidemiol*. 2005;40(5):402-407.

29. Brugha TS, Morgan Z, Bebbington P, et al. Social support networks and type of neurotic symptom among adults in British households. *Psychol Med*. 2003;33(2):307-318.

30. Brugha TS, Meltzer H, Jenkins R, Bebbington PE, Taub NA. Comparison of the CIS-R and CIDI lay diagnostic interviews for anxiety and depressive disorders. *Psychol Med*. 2005;35(7):1089-1091.

31. Bebbington P, Dunn G, Jenkins R, et al. The influence of age and sex on the prevalence of depressive conditions: report from the National Survey of Psychiatric Morbidity. *Int Rev Psychiatry*. 2003;15(1-2):74-83.

32. Thapar A, Rutter M. Do prenatal risk factors cause psychiatric disorder? be wary of causal claims. *Br J Psychiatry*. 2009;195(2):100-101.

33. Guo X, Carlin BP. Separate and joint modeling of longitudinal and event time data using standard computer packages. *Am Stat*. 2004;58(1):16-24.

34. Weinberg CR. Toward a clearer definition of confounding. *Am J Epidemiol*. 1993;137(1):1-8.

35. Goodman SH, Gotlib IH. Risk for psychopathology in the children of depressed mothers: a developmental model for understanding mechanisms of transmission. *Psychol Rev*. 1999;106(3):458-490.

36. Field T. Postpartum depression effects on early interactions, parenting, and safety practices: a review. *Infant Behav Dev*. 2010;33(1):1-6.

37. Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. *Arch Gen Psychiatry*. 2010;67(10):1012-1024.