Accepted Manuscript

Maternal depression and family adversity: Linked pathways to offspring depression?

Jake M. Najman, M. Plotnikova, G.M. Williams, R. Alati, A.A. Mamun, J. Scott, A.M. Clavarino, N. Wray

Please cite this article as: Najman JM, Plotnikova M, Williams GM, Alati R, Mamun AA, Scott J, Clavarino AM, Wray N, Maternal depression and family adversity: Linked pathways to offspring depression?, *Journal of Psychiatric Research* (2017), doi: 10.1016/j.jpsychires.2017.01.006.

TITLE

Maternal Depression and Family Adversity: Linked Pathways to Offspring Depression?

AUTHORS

.M. Najman, PhD[a]; M. Plotnikova, PhD[b]; G.M. Williams, PhD[b] ; R. Alati, PhD[b] ; A.A. Mamun, PhD[b] ; J. Scott. MD, PhD[c]; A.M. Clavarino, PhD[d]; N. Wray PhD[e]

[a] *Schools of Public Health and Social Science, The University of Queensland, Brisbane, Australia*

[b] *School of Public Health, The University of Queensland, Brisbane, Australia*

[c] *UQCCR, The University of Queensland, Brisbane Australia.*

[d] *School of Pharmacy, The University of Queensland, Brisbane, Australia*

[e] *Queensland Brain Institute, The University of Queensland, Brisbane, Australia*

CORRESPONDING AUTHOR:

Jake M. Najman, PhD FASSA

School of Public Health, The University of Queensland

Herston Road, Herston, QLD 4006, AUSTRALIA

Phone: +61 7 336 55180

Fax: +61 7 336 55509

Email: j.najman@uq.edu.au

Maternal Depression and Family Adversity: Linked Pathways to Offspring Depression?

ABSTRACT

There is conflicting evidence about the contribution of maternal depression and family adversity to depression experienced by offspring. Because maternal depression and family adversity are related, there is a need to determine how they independently contribute to offspring depression. Data are from a long-running prospective birth cohort study (Mater-University of Queensland Study of Pregnancy and its outcomes – MUSP). For this study some 2200 offspring were followed up at 30 years of age. We first examine the association between maternal depression and family adversity over the period from the pregnancy to the child reaching adulthood. Then we consider the extent to which maternal depression and family adversity trajectories over this period predict CIDI/DSM-IV episodes of depression in the offspring of these mothers at 30 years of age. We find a strong bi-directional association between maternal depression and family experiences of adverse life events over the entire period the child is at home. After adjustment, children reared in a family experiencing high levels of adverse life events are more likely to experience a lifetime ever DSM-IV diagnosis of depression, are more likely to have experienced multiple episodes of lifetime ever depression, and are more likely to report their first episode of depression was at a younger age. The findings suggest the association between maternal depression and offspring depression appears to be partly attributable to the higher levels of family adversity characteristic of depressed mothers.

KEY WORDS: depression; child/adolescent; life events/stress; maternal-child

Maternal Depression and Family Adversity: Linked Pathways to Offspring Depression?

INTRODUCTION

In the continuing debate about the causes of depression, particularly depressions affecting

young adults, two related factors have been repeatedly implicated. The first involves the

transmission of maternal depression from parents (particularly mothers) to their offspring

(Goodman et al., 2011). The second involves life adversities or stresses to which children are

exposed in their developmental years (Kessler et al, 2010). While it is likely that maternal

depression and living in an environment characterised by more frequent experiences of life

adversities are connected (Barker et al., 2012; Barker, 2013), the nature of this association,

particularly as it is likely to account for offspring depression, has had little scrutiny. Taking

data from a long-running birth cohort study, we examine maternal depression and adversity

as these are related to each other over more than a 20-year period. We then examine the

extent to which a pattern of early life exposure to maternal depression and early life

experiences of adversity predict episodes of major depression experienced by 30 year old

offspring. We test the hypothesis that child exposure to maternal depression and life

adversities experienced separately and independently contribute to levels of depression when

these children become adults.

Maternal depression as a cause of depression in offspring

There is now ample evidence that parents (particularly mothers) who are depressed have

children at increased risk of mental illness, leading to the proposition that depression runs in

families (Hammen, 1996). A systematic review (Goodman, 2007) and a meta-analysis

(Goodman et al., 2011) of 193 studies provides details of robust associations between

parental and offspring psychopathology. Recent findings using data from the World Health

Survey find that parental psychopathology is a consistent but non-specific predictor of psychopathology in offspring (McLaughlin, 2012).

Even in very young children, rates of depression in offspring of depressed mothers are higher than those found in non-depressed mothers (Goodman, 2007). For those meeting the clinical criteria for depression, psychopathology in offspring has an earlier age of onset, a longer duration of disorder, a greater likelihood of recurrence as well as a higher level of functional impairment (Goodman, 2007). While the evidence supports the intergenerational transmission of depression from mothers to offspring, the factors contributing to this transmission, particularly the contribution of a range of life adversities to the intergenerational transmission of depression, needs to be determined.

Early life course adversity as a cause of depression in offspring

While the association between experiences of adversity and depression has been well documented, this association has rarely been tested in the context of the intergenerational transmission of depression and adversity. Parents who have experienced such traumatic events as the Holocaust (Scharf, 2007), or have had combat experience in a war (Dekel and Goldblatt, 2008), are understandably affected, but these are relatively rare and possibly short-term exposures which may not provide a reliable guide to the more common and potentially chronic adverse life events many may experience. Common adverse early life exposures of families have been found to predict subsequent depression (Brown and Moran, 1994; Green et al., 2010; Kessler et al., 2010; Turner and Butler, 2003). The WHO World Mental Health Surveys involved data gathered from 21 countries, some 51,945 adult respondents using standardised measures of childhood adversity and psychopathology. Childhood adversities were found to account for about 30% of all psychopathology across countries (Kessler et al.,

2010). Importantly, adversities such as marital conflict and breakdown, financial problems and child maltreatment were found to be common and cumulative, and experienced by a majority of families (Green et al., 2010; Kessler, R. C. et al., 1997; Turner and Butler, 2003).

There are a number of aspects of family experiences of adversity that have significant implications for research and policy. The first is that some social groups experience "clusters" or multiple adversities (Green et al., 2010; Kessler, R. C. et al., 1997; Raposa et al., 2014). Adversity experiences may persist over time so that earlier life adverse experiences not only predict subsequent adverse experiences, but are plausibly causally implicated in their initiation. It may be the case that previous experiences of adversity and stress may be the best predictor of subsequent experiences of adversity and stress.

Maternal Depression and Family Adversity: Cause and Effect?

In contrast to the conventional view that stressful life events lead to and cause depression, Hammen (1991) and others have argued for the existence of the reverse causal pathway, namely that persons who are depressed may contribute to the stressful contexts in which they live. Depression, it is argued, may lead to dysfunctional responses (a pattern of poor decision making), which then leads to additional life stresses. From this perspective depressed persons can be seen to shape the stressful environments in which they live.

Recent reviews involving clinical samples, studies of children and adolescents and adult samples confirm that depression can lead to a wide range of changes in life circumstances (Hammen and Shahar, 2006). Depressed persons are characterised by negative perceptions of the world around them (Flynn et al., 2009) and negative responses to others (Swann et al.,

1992). This may contribute to depressed persons "provoking" a series of life events which then may contribute to further depression (Hammen, 1991).

Depression appears to impact on a wide range of day-to-day activities including family life (Davila et al., 1997; Shih and Eberhart, 2008). Depressed persons more often experience fatigue and a lack of interest in social activities (Chun et al., 2004), all of which appear to contribute to less positive social interactions including conflict and hostility (Davila et al., 1997). Early age of onset of a mental disorder is associated with teenage parenthood, premarital parenthood and earlier age of first sexual intercourse (Kessler, et al., 1997). Depressed persons disproportionately select partners who also have a mental illness (Wade and Cairney, 2000), and who tend to lack a range of useful interpersonal skills (Chun et al., 2004). A few studies now suggest that depression predicts a decline in marital quality (Najman et al., 2014) and an increase in rates of marital breakdown (Matthews and Reus, 2001) with increased levels of subsequent divorce for male and female respondents (Kessler et al., 1998).

The presence of a mental illness has also been found to be associated with poorer educational outcomes. Data from the US National Comorbidity Survey found that a number of indicators of poor mental health (conduct disorder, anxiety and depressive disorders) were associated with the failure to complete college for those who entered college (AIHW, 2010). Consistent with the findings of poorer educational outcomes (Kessler et al., 1995), depressed persons exhibit poorer work performance (Baune, 2015). A review of recent findings suggests that depressed persons have high absenteeism rates, lost productivity and low levels of overall work performance (Baune, 2015). Partly as a consequence of their lower levels of school and

work performance depressed persons report substantially lower incomes (Davila et al., 1997; Kessler et al., 2008).

Finally, there are persistent findings that those with a previous mental illness experience poor physical health (Goff et al., 2005; Latoo et al., 2015) and have a lower life expectancy (Robson and Gray, 2007). High rates of cardiovascular disease are commonly associated with a serious mental illness (Robson and Gray, 2007). One explanation of these findings is that mental illness leads to smoking, a poor diet and less physical activity, and possibly reduced service use. Depressed persons have also been found to more frequently use illicit drugs (Paton et al., 1977).

Some limitations of previous studies need to be addressed. These limitations include the need for a prospective study design (the majority of previous studies involve the retrospective recall of both life adversities and subsequent depression (Brown and Moran, 1994; Green et al., 2010; Kessler, R. C. et al., 1997; Kessler and Magee, 1993). There is also a need to determine whether exposures to adversity either at a particular stage of the life course, for example in early childhood, differentially predict subsequent depression. Finally, in light of the strong and potentially bidirectional association between depression and adversity there is a need for a research design that is able to simultaneously address the potentially independent effects of offspring early life course exposure to both maternal depression and family adversity as these may predict offspring depression.

MATERIAL AND METHODS

The Mater-University of Queensland Study of Pregnancy (MUSP) and its outcomes is a pre-birth cohort study that commenced in 1981 with 8458 consecutive pregnant women recruited

early in pregnancy. These women gave birth to 7223 live singleton children who comprise the cohort. Women and their children were followed-up shortly after the birth, and then at 5, 14 and 21 years after the birth of the child. Mothers were then followed-up at 27 years, and their children at 30 years. Details of sampling, response rates and study rationale have appeared elsewhere (Najman et al., 2015).

Data Preparation and Data Analysis

Measurement of Adverse life events (ALE)

Mothers, at their first clinic visit, were invited to answer nine questions about their experience of recent adverse life events. (We would like to know if any of the following happened to you IN THE LAST 6 MONTHS). These events are broadly modelled on the life events scale of Holmes and Rahe (1967) (Holmes and Rahe, 1967). At the first clinic visit (FCV) the most common adverse life event was a partner having a major change in job situation (24.5%) and the least common the participant or their partner having a problem with the law (4.4%). Similar adverse life events scales were also created for the 5, 14 and 21-year follow-ups (see Appendix A for the complete list). At the 21-year follow-up reports of adversity differ somewhat from the other phases. In this phase both maternal and child reports are used. Appendix B presents the correlation matrix of measures of adverse life events at FCV, 5, 14 and 21-year follow-ups. Adversity scores at each data collection phase are significantly correlated with adversity experienced at other phases.

Measurement of Depression

Maternal experiences of depression were measured using the depression subscale of Delusions-Symptoms-States Inventory (DSSI) of Bedford and Foulds (1977). This is a seven-item subscale based on a hierarchical model of mental illness. It was developed by psychiatrists using DSM criteria. The subscale has high reliability and has been validated

against patient groups receiving treatment (Bedford and Deary, 1999; Bedford et al., 1976). In a recent study the DSSI depression subscale was validated against DSM-IV criteria based upon CIDI diagnoses of past 12 months depression in a large population sample (Najman et al., 2016). For those scoring four or more symptoms on the DSSI, over half met the DSM-IV criteria for depression in the last year. Depression in offspring (at 30 years of age) was measured using the Composite International Diagnostic Interview (CIDI-3) with DSM-IV criteria used to determine lifetime ever depression. The CIDI has been widely used to detect psychopathology in community and population-based samples. Details of the validity and reliability of the CIDI have been reported in a number of studies (Haro et al., 2006; Wittchen, 1994).

Additional variables were selected as covariates on the basis that they were likely to be related to adversity and depression in the offspring. All these variables were recorded at the 30-year follow-up. These covariates are marital status, employment status, income of participant and partner. Finally, we additionally adjust for offspring reports of adverse life experiences at the 30-year follow-up.

Data analysis strategy

Figure 1 sets out the research design and includes details of the covariates included in the fully adjusted model.

(FIGURE 1 ABOUT HERE)

First we present details of the mother's experiences of depression and adversity over the reproductive life course. Second, we use generalised estimating equations (GEE) with lag to examine family adversity as a predictor of subsequent maternal depression and then depression as a predictor of subsequent adversity. We use multivariable generalised

estimating equations with modified Poisson regression to estimate the adjusted relative risks and 95% confidence intervals for depression predicting adversity and adversity predicting depression. Poisson regression with robust variance estimates are used to produce more conservative standard errors of parameter estimates (Yelland et al., 2011; Zou, 2004). Finally, we use maternal trajectories of depression and adversity to predict offspring DSM-IV lifetime ever depression. Here we specifically examine the extent to which a maternal history of depression and family history of adversity independently predict offspring depression. Three sets of multinominal logistic regression models are presented. The first is the unadjusted model, the second provides adjustment for depression or adversity respectively, and the third model adjusts for a range of covariates at the 30-year offspring follow-up, including offspring experiences of adverse life events preceding this follow-up.

RESULTS

In Table 1 we present the GEE multivariable model; firstly, for adversity predicting subsequent depression, and then for depression predicting subsequent adversity. All prediction models involve a time lag with adversity predicting subsequently occurring depression and depression predicting subsequently occurring adversity.

(TABLE 1 ABOUT HERE)

Adversity consistently predicts subsequently occurring depression, and excluding those women who were depressed at FCV makes no material difference to the findings. Adjustment for number of covariates also makes no material difference to the findings. In all instances prior adversity predicts subsequent depression. An almost identical pattern of results is evident when we consider the extent to which depression predicts subsequent experiences of adversity. Excluding women with prior experiences of adversity does not materially affect the findings, nor does adjustment for a number of covariates. The data are consistent in

suggesting the existence of bi-directional causal pathways and also in suggesting that the magnitude of the association is similar for each hypothesised causal pathway.

(TABLE 2 ABOUT HERE)

In table 2 we provide details of the criteria used to determine the selected trajectory groups (for depression and adversity) and the statistical criteria used to select the preferred groups. The DSSI-derived trajectories have been validated using CIDI/DSM-IV depression diagnoses (Najman et al., 2016). Some 47.7% of women in this study experience few, occasional or no symptoms of depression over the 27 years following the birth of the study child. A second group of women, 43.7% of the sample, report occasionally experiencing symptoms of depression over the 27-year time period. By contrast, we find 8.5% of women in this study are characterised by a high/escalating trajectory of depression. Adversity trajectory group membership is based upon a count of the number of life events reported. The low adversity trajectory group comprises 30.8% of women in the sample. Women in the low adversity trajectory group appear to occasionally experience adverse events, and there appears to be a peak of these experiences at the 14-year follow-up. The mid-adversity trajectory group comprises 55.5% of the sample and appears to consistently experience about twice as many life events as the low-adversity trajectory group. The high-adversity trajectory group (13.7% of the sample) report experiencing many adverse life events at each phase of the study. For the women in this study adversity experiences appear to increase in the years following the birth of the study child and then decline once the child reaches the mid to late adolescent years.

For depression the optimum Baysian Information Criteria involves a three-group solution. The average posterior probabilities exceed the minimum criteria suggesting that the groups are distinct. Trajectory group 3 is of women who have persistently high symptom levels of

depression over a 27-year period. The three-group solution for adversity is also the best fitting model with 13.7% of the sample comprising women who report a persistently high level of family adversity over a 21-year period following the birth of the study child.

(TABLE 3 ABOUT HERE)

In the unadjusted model (Table 3) depression trajectory group membership of the mother predicts CIDI/DSM-IV lifetime ever depression in offspring (unadjusted). This is no longer the case once there is adjustment for maternal reports of adversity over the first 21 years following the birth of the child. On the other hand, adversity trajectory group membership predicts offspring lifetime ever depression, even after adjustment for maternal depression trajectory group membership and a range of covariates including experiences of adversity reported by the offspring at 30 years of age.

(TABLE 4 ABOUT HERE)

Table 4 presents adversity and trajectory group membership by number of lifetime episodes of CIDI/DSM-IV depression experienced by offspring to 30 years of age. For maternal depression trajectories there are no significant associations with offspring depression after adjustment for maternal adversity trajectory group membership. By contrast the high adversity trajectory group experiences more multiple episodes of offspring depression even after adjustment for maternal depression trajectory group membership. After additional adjustment for a range of offspring confounders, these associations are only significant for those offspring with a history of 1-2 lifetime ever episodes of depression.

(TABLE 5 ABOUT HERE)

Table 5 presents the association between maternal trajectory groups and age of first episode of depression in offspring. The unadjusted associations suggest some broadly based association with maternal depression and adversity trajectory group membership predicting both young (up to 15 years) and older (20+ years) first onset of offspring depression.

Adjustment, respectively, for maternal depression and adversity trajectory group membership attenuates most associations with offspring age of first onset of depression. Additional adjustment suggests that the high maternal depression and family adversity trajectory groups have offspring who have a younger age of first onset of depression. Both maternal depression and maternal adversity trajectory groups are independently associated with younger age of onset of offspring depression.

DISCUSSION

Maternal reports of some symptoms of depression and some experiences of adversity (life events) appear to be common in the life course of women who have given birth to a child. Most women report experiencing some (repeated) events such as marital problems, financial difficulties and changes in their employment situation. In that sense the majority of women experience repeated exposure to a range of potentially stressful events over the period they are rearing their child. The findings from the trajectory groups' analyses suggest that patterns of both maternal depression and family adversity are persistent over all of the child's early life course. While only about one in every seven mothers experiences a reproductive life course characterised by repeated levels of high adversity, the majority of mothers experience moderate and repeated experiences of adversity. By contrast, while most mothers experience some symptoms of depression over the period of time they are rearing their child, only about one in ten women reports persistent and recurrent levels of clinically-significant depression.

The correlation between adversity and depression trajectory group membership is 0.3 (Kendall Tau B, p<.001). This is a modest correlation and suggests that while there is some persistence in experiences of maternal depression and family adversity over the life course,

there are many women who are in the high adversity trajectory group who experience

moderate or low levels of depression. The reverse is also the case.

It is difficult to account for the finding that a majority of mothers experience repeated levels

of moderate adversity, but a relatively small proportion of these mothers become depressed.

It is likely that a small proportion of mothers have a genetic (Caspi, et al., 2003; Caspi, et al.,

2010) or other biological vulnerability (Beck, 2008) to depression. While the majority of

mothers experiencing adversity appear to be relatively unaffected, a smaller sub-group

experience high rates of repeated episodes of depression (Najman et al., 2016). It is this group

of women in particular who may engage in behaviours which increase their level of life

adversities, and subsequent experiences of depression.

Over the 21 years of follow-up the data are consistent with a pattern of reciprocal causation.

Those who experience persistently high levels of depression over their life course are

disproportionately more likely to also experience high levels of adversity over an extended

part of their reproductive life course. Studies which attribute depression to life adversities (or

vice versa) may be misleading in so far as they fail to identify what is a bi-directional

association which persists over an extended part of the reproductive life course and which is

likely to affect offspring mental health.

To what extent then do maternal life course trajectories of depression and adversity predict

offspring depression at the 30 year follow-up? While the unadjusted comparisons suggest that

both maternal depression and adversity predict offspring lifetime ever DSM-IV depression, it

appears that a lifetime history of exposure to adversity has a greater impact on offspring

depression than does a maternal history of depression. A maternal history of depression and adversity independently predict early age of first onset of depression. Findings from the Avon Longitudinal Study of Parents and Children (ALSPAC) are broadly consistent with those reported in this study (Barker et al., 2012; Barker, 2013) although the ALSPAC findings involve a shorter period of follow-up and different measures of offspring psychopathology.

While our findings suggest that the association between maternal depression and offspring depression is largely a consequence of the higher levels of adverse life events experienced by youth living in an environment which involves higher levels of maternal depression, it is apparent that the majority of children reared in such an environment do not experience a clinically significant depression. In seeking to understand why most mothers who experience multiple adversities do not experience depression we have pointed to evidence that some mothers appear to be more vulnerable to adverse experiences, and it is likely that the same explanation accounts for the findings relating to offspring depression.

Limitations

While a maternal history of depression and a family history of adversity independently predict offspring depression, the findings of this study should be interpreted with caution. Loss to follow-up has the potential to bias our findings.

We suggest there are three reasons why the potential bias associated with loss to follow-up, is unlikely to have produced misleading findings. Firstly, in previous papers from this study, we have used inverse probability weighting, multiple imputation and other strategies to adjust for attrition. In no instance has this adjustment materially affected our findings. Second we have tested the potential for bias by taking a known finding at FCV, say poverty and smoking, and

then removed cases lost to successive follow-ups, to assess the impact of biased loss for a known association. In almost every instance the findings remain the same. In occasional instances the reduction in sample size has an impact on the finding, but this then can be interpreted as a conservative outcome. Finally others have also noted that attrition (or biased recruiting) impacts on population estimates of a behaviour or other characteristics, but has very little impact on estimates of association within the sample (Deeg, 2002; Powers and Loxton, 2010).

The limited number of items measuring life events and/or life changes (adversity) are of concern. Others have sometimes used a larger list of adversities. The fact that adversity experiences tend to be clustered – suggests the domain of adversity experiences is very large and that lists of possible exposures can be interpreted as comprising a sample from the broader range of possible adversities. We have used a list of adversities which assess the key life domains of marital relationships, work and employment, financial problems and those adversities associated with health or contact with the criminal justice system. While a more exhaustive list of life adversities could be used we have selected the more commonly experienced life adversities as suggested in appendix A. It should also be noted that while the list of adversities is similar for the FCV, 5 and 14 year data collections (all are maternal reports), the list at the 21 year follow-up comprises a combination of maternal and offspring reports. An identical list was simply not available at the 21 year follow-up.

Another limitation of this study is the absence of a measure of paternal depression. In this study only very limited information about the father was obtained. It is possible that paternal depression could impact on offspring although mothers tend to have more contact with children and have higher rates of depression than do men. Of course, family adversities

reflect the experiences of both parents and the findings of this study suggest they make the major contribution to offspring depression.

Finally, there is the issue of whether the association between maternal depression, family adversities and offspring depression is likely to be causal. Certainly the association has many of the characteristics of a causal one (temporal sequence, strong association, associations are plausible). However there remains the possibility of an uncontrolled variable which might account for the associations we have observed. For example there may be genetic or other biological factors, which we have not measured. The observation that maternal depression is not a strong or independent predictor of offspring depression would reduce the likelihood of genetic factors accounting this component of our findings. It is also difficult to think of a genetic basis for family experiences of adversity. With those caveats acknowledged the findings point to a bidirectional causal association between depression and life adversities within families, and their intergenerational transmission, particularly in the case of family adversities and offspring depression. Our findings raise the possibility that maternal depression predicts offspring depression, in part because family adversities are implicated for both maternal depression and offspring depression.

CONCLUSION

Not a great deal is known about the generational factors that may contribute to the development of depression in children, particularly when these children reach adulthood. Maternal depression and family based life adversities have both been suggested as possible causes of offspring depression.

Distinguishing between the impact of maternal depression and maternal reports of life experiences of adversity has been difficult, in part because these appear to co-occur and be related to each other over the entire maternal reproductive life course. Despite this we find that while both maternal depression and family adversities predict the onset of depression in adult offspring. We also find the impact of family adversities appear to be the stronger independent predictor. This suggests that a family history of adversities might be a primary cause of offspring depression. Such life adversities as a family history of marital conflict and breakdown, family poverty and contacts with police and the criminal justice system appear to have long term consequences for children. Policy responses will need to focus upon the family life of children as they are being reared and aim to reduce either the number or consequences of these family based life adversities.

REFERENCES

AIHW, 2010. Patterns of Drug Use Australia, 2010 National Drug Strategy Household Survey Report. Australian Institute of Health and Welfare, Canberra, pp. 46-76.

Barker, E.D., 2013. The duration and timing of maternal depression as a moderator of the relationship between dependent interpersonal stress, contextual risk and early child dysregulation. Psychological Medicine 43, 1587-1596.

Barker, E.D., Copeland, W., Maughan, B., Jaffee, S.R., Uher, R., 2012. Relative impact of maternal depression and associated risk factors on offspring psychology. The British Journal of Psychiatry 200,124-129.

Baune, B., 2015. Cognitive functioning in major depressive disorder. Research Review Educational Series 2015.

Beck, A.T., 2008. The Evolution of the Cognitive Model of Depression and its Neurobiological Correlates. American Journal of Psychiatry 165:969-977.

Bedford, A., Deary, I.J., 1999. The Delusions-Symptoms-States Inventory (DSSI): construction, applications and structural analyses. Personality and Individual Differences 26(3), 397-424.

Bedford, A., Foulds, G.A., Sheffield, B.F., 1976. A new personal disturbance scale (DSSI/sAD). British Journal of Social and Clinical Psychology 15(4), 387-394.

Brown, G.W., Moran, P., 1994. Clinical and psychological origins of chronic depressive episodes 1: A community survey. British Journal of Psychiatry 165(447-456).

Caspi, A., Sugden, K., Moffitt, T.E. et al., 2003. Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene. Science 301(5631):pp386-389.

Caspi, A., Hariri, A.R., Holmes, A. et al., 2010. Genetic Sesitivity to the Environment: The Case of the Serotonin Transporter Gene and its Implications for Studying Complex Diseases and Traits. American Journal of Psychiatry 167:509-527.

Chun, C.-A., Cronkite, R.C., Moos, R.H., 2004. Stress generation in depressed patients and community controls. Journal of Social and Clinical Psychology 23(3), 390-412.

Davila, J., Bradbury, T.N., Cohan, C.L., Tochluk, S., 1997. Marital Functioning and Depressive Symptoms: Evidence for a Stress Generation Model. Journal of Personality and Social Psychology 73(4), 849-861.

Deeg, D.J.H., 2002. Attrition in longitudinal population studies: Does it affect the generalizability of the findings?: An introduction to the series. Journal of Clinical Epidemiology 55(3), 213-215.

Dekel, R., Goldblatt, H., 2008. Is There Intergenerational Transmission of Trauma? The Case of Combat Veterans' Children. American Journal of Orthopsychiatry 78(3), 281-289.

Flynn, M., Abaied, J., Groot, A., Thompson, R., Rudolph, K., 2009. Why is Past Depression the Best Predictor of Future Depression? Stress Generation as a Mechanism of Depression Continuity in Girls. Journal of Clinical Child & Adolescent Psychology 38(4), 473-485.

Goff, D.C., Sullivan, L.M., McEvoy, J.P., Meyer, J.M., Nasrallah, H.A., Daumit, G.L., Lamberti, S., D'Agostino, R.B., Stroup, T.S., Davis, S., Lieberman, J.A., 2005. A comparison of ten-year cardiac risk estimates in schizophrenia patients from the CATIE study and matched controls. Schizophrenia Research 80(1), 45-53.

Goodman, S.H., 2007. Depression in mothers. Annual review of clinical psychology 3(1), 107-135.

Goodman, S.H., Rouse, M.H., Connell, A.M., Broth, M.R., Hall, C.M., Heyward, D., 2011. Maternal depression and child psychopathology: a meta-analytic review. Clinical child and family psychology review 14(1), 1-27.

Green, J.G., Zaslavsky, A.M., Kessler, R.C., Sampson, N.A., Gruber, M.J., McLaughlin, K.A., 2010. Childhood Adversities and Adult Psychiatric Disorders in the National Comorbidity Survey Replication II: Associations With Persistence of DSM-IV Disorders. Archives of General Psychiatry 67(2), 124-132.

Hammen, C., 1991. Generation of Stress in the Course of Unipolar Depression. Journal of Abnormal Psychology 100(4), 555-561.

Hammen, C., 1996. Stress, families, and the risks for depression, in: Freeman, H.L., Mundt, C. (Eds.), Interpersonal factors in the origin and course of affective disorders. RCPsych Publications.

Hammen, C., Shahar, G., 2006. Stress generation in depression: Reflections on origins, research, and future directions. Journal of Clinical Psychology 62(9), 1065-1082.

Haro, J.M., Arbabzadeh-Bouchez, S., Brugha, T.S., De Girolamo, G., Guyer, M.E., Jin, R., Lepine, J.P., Mazzi, F., Reneses, B., Vilagut, G., Sampson, N.A., Kessler, R.C., 2006. Concordance of the Composite International Diagnostic Interview Version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO World Mental Health Surveys. International Journal of Methods in Psychiatric Research 15(4), 167-180.

Holmes, T.H., Rahe, R.H., 1967. The social readjustment rating scale. Journal of psychosomatic research 11(2), 213-218.

Kessler, R.C., Berglund, P.A., Foster, C.L., Saunders, W.B., Stang, P.E., Walters, E.E., 1997. Social consequences of psychiatric disorders, II: Teenage parenthood. American Journal of Psychiatry 154(10), 1405-1411.

Kessler, R.C., Davis, C.G., Kendler, K.S., 1997. Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey. Psychological Medicine 27(5), 1101-1119.

Kessler, R.C., Foster, C.L., Saunders, W.B., Stang, P.E., 1995. Social consequences of psychiatric disorders, I: Educational attainment. The American Journal of Psychiatry 152(7), 1026.

Kessler, R.C., Heeringa, S., Lakoma, M.D., Petukhova, M., Rupp, A.E., Schoenbaum, M., Wang, P.S., Zaslavsky, A.M., 2008. Individual and societal effects of mental disorders on earnings in the United States: Results from the National Comorbidity Survey Replication. American Journal of Psychiatry 165(6), 703-711.

Kessler, R.C., Magee, W.J., 1993. Childhood adversities and adult depression: basic patterns of association in a US national survey. Psychological Medicine 23(3), 679-690.

Kessler, R.C., McLaughlin, K.A., Green, J.G., Gruber, M.J., Sampson, N.A., Zaslavsky, A.M., Aguilar-Gaxiola, S., Alhamzawi, A.O., Alonso, J., Angermeyer, M., Benjet, C., Bromet, E., Chatterji, S., De Girolamo, G., Demyttenaere, K., Fayyad, J., Florescu, S., Gal, G., Gureje, O., Haro, J.M., Hu, C.-Y., Karam, E.G., Kawakami, N., Lee, S., Lépine, J.-P., Ormel, J., Posada-Villa, J., Sagar, R., Tsang, A., Bedirhan Üstün, T., Vassilev, S., Viana, M.C., Williams, D.R., 2010. Childhood adversities and adult psychopathology in the WHO world mental health surveys. British Journal of Psychiatry 197(5), 378-385.

Kessler, R.C., Walters, E.E., Forthofer, M.S., 1998. The social consequences of psychiatric disorders, III: Probability of marital stability. American Journal of Psychiatry 155(8), 1092-1096.

Latoo, J., Omodunbi, O., Hindley, D., Derbyshire, A., Kane, R., 2015. Physical health of people with severe mental illness: Don't just screen… intervene. British Journal of Medical Practitioners 8(3).

Matthews, C.A., Reus, U.I., 2001. Assertive mating in the affective disorders: A systematic review and meta-analysis. Comprehensive Psychology 41(4), 257-262.

McLaughlin, K.A., 2012. Parent Psychopathology and Offspring Mental Disorders: Results from the WHO World Mental Health Surveys. British Journal of Psychiatry 200, 290-299.

Najman, J.M., Khatun, M., Mamun, A., Clavarino, A., Williams, G.M., Scott, J., O'Callaghan, M., Hayatbakhsh, R., Alati, R., 2014. Does depression experienced by mothers leads to a decline in marital quality: a 21-year longitudinal study. Social psychiatry and psychiatric epidemiology 49(1), 121-132.

Najman, J.M., Alati, R., Bor, W. et al., 2015. Cohort Profile Update: The Mater-University of Queensland Study of Pregnancy (MUSP). International Journal of Epidemiology 44(1):78-78f.

Najman, J.M., Plotnikova, M., Williams, G.M. et al., 2016. Trajectories of Maternal Depression: A 27 Year Population-Based Prospective Study. Epidemiology and Psychiatric Sciences online 19 January.

Paton, S., Kessler, R.C., Kardel, D., 1977. Depressive Mood and Adolescent Illicit Drug Use: A Longitudinal Analysis. 131 2, 267-289.

Powers, J., Loxton, D., 2010. The Impact of Attrition in an 11-Year Prospective Longitudinal Study of Younger Women. Annals of Epidemiology 20(4), 318-321.

Raposa, E.B., Hammen, C.L., Brennan, P.A., O'Callaghan, F., Najman, J.M., 2014. Early Adversity and Health Outcomes in Young Adulthood: The Role of Ongoing Stress. Health Psychology 33(5), 410-418.

Robson, D., Gray, R., 2007. Serious mental illness and physical health problems: A discussion paper. International Journal of Nursing Studies 44(3), 457-466.

Scharf, M., 2007. Long-term effects of trauma: Psychosocial functioning of the second and third generation of Holocaust survivors. Development and Psychopathology 19(2), 603-622.

Shih, J.H., Eberhart, N.K., 2008. Understanding the impact of prior depression on stress generation: Examining the roles of current depressive symptoms and interpersonal behaviours. British Journal of Psychology 99(3), 413-426.

Swann, W.B., Wenzlaff, R.M., Tafarodi, R.W., 1992. Depression and the Search for Negative Evaluations: More Evidence of the Role of Self- Verification Strivings. Journal of Abnormal Psychology 101(2), 314-317.

Turner, H.A., Butler, M.J., 2003. Direct and Indirect Effects of Childhood Adversity on Depressive Symptoms in Young Adults. Journal of Youth and Adolescence 32(2), 89-103.

Wade, T.J., Cairney, J., 2000. Major Depressive Disorder and Marital Transition among Mothers:: Results from a National Panel Study. The Journal of Nervous and Mental Disease 188(11), 741-750.

Wittchen, H.-U., 1994. Reliability and validity studies of the WHO-Composite International Diagnostic Interview (CIDI): A critical review. Journal of Psychiatric Research 28(1), 57-84.

Yelland, L.N., Salter, A.B., Ryan, P., 2011. Performance of the modified Poisson recession approach for estimating relative risk from clustered prospective data. American Journal of Epidemiology 174(8), 984-992.

Zou, G., 2004. A Modified Poisson Regression Approach to Prospective Studies with Binary Data. American Journal of Epidemiology 159(7), 702-706.

ACKNOWLEDGEMENT

Table 1: Comparison of Adversity Predicting Depression and Depression Predicting Adversity (with time lag)
(GEE model)

	Adversity Predicting Depression			Depression Predicting Adversity		
	With lag	With lag excluding prior depression	With lag excluding prior depression, adj for confounding*	With lag	With lag excluding prior adversity	With lag excluding prior depression, adj for confounding*
FCV to 5yr F/U	1.87 (1.58, 2.22)	1.72 (1.39, 2.14)	1.66 (1.33, 2.06)	1.44 (1.28, 1.63)	1.28 (1.02, 1.61)	1.23 (0.98, 1.56)
5yr F/U to 14yr F/U	1.64 (1.38, 1.94)	1.63 (1.33, 1.98)	1.62 (1.32, 1.98)	1.53 (1.36, 1.72)	1.60 (1.37, 1.87)	1.58 (1.35, 1.85)
14yr F/U to 21yr F/U	1.36 (1.12, 1.65)	1.46 (1.16, 1.83)	1.45 (1.53, 1.82)	1.65 (1.34, 2.02)	1.66 (1.25, 2.21)	1.60 (1.20, 2.13)

* Adjusted for maternal age, education, marital status and number of children

Table 2: Trajectory Models for Maternal Depression and Adversity

Depression Trajectory		Group Membership, %	BIC	Average Posterior Probability
Two groups solution	Traj 1	66.9	-23414.14	0.9334
	Traj 2	33.1		0.8998
Three groups solution	Traj 1	47.7	-23207.87	0.8772
	Traj 2	43.7		0.8444
	Traj 3	8.5		0.8688
Four groups solution	Traj 1	27.5	-23271.90	0.8130
	Traj 2	56.0		0.8892
	Traj 3	0.06		0.9776
	Traj 4	16.4		0.8597
Five group solution	Traj 1	46.1	-23139.25	0.8510
	Traj 2	16.6		0.6438
	Traj 3	2.0		0.8090
	Traj 4	30.1		0.8048
	Traj 5	5.2		0.8494
Adversity Trajectory				
Two groups solution	Traj 1	70.4	-29394.39	0.9050
	Traj 2	29.6		0.8412
Three group solution	Traj 1	30.8	-29319.20	0.7431
	Traj 2	55.5		0.7753
	Traj 3	13.7		0.7970

Table 3: Trajectories of maternal depression over 27 yrs. and adversity over 21 yrs. predicting offspring outcome at 30 years:
DSM-IV CIDI Major Depressive Disorder (lifetime ever) (Multinominal Logistic Regression)

Trajectory group membership		Odds Ratio and CI by DSM-IV Major Depressive Disorder (Lifetime)					
		Unadjusted model		Adjusted model 1*		Adjusted model 2**	
		No	Yes	No	Yes	No	Yes
Depression (n=2123)	Low	1	1	1	1	1	1
	Mid	1	**1.37 (1.10, 1.71)**	1	1.23 (0.99, 1.54)	1	1.10 (0.80, 1.52)
	High	1	**1.71 (1.20, 2.45)**	1	1.33 (0.92, 1.92)	1	1.33 (0.78, 2.27)
Adversity (n=2289)	Low	1	1	1	1	1	1
	Mid	1	**1.54 (1.21, 1.95)**	1	**1.48 (1.14, 1.90)**	1	**1.46 (1.02, 2.08)**
	High	1	**2.19 (1.58, 3.03)**	1	**1.97 (1.37, 2.83)**	1	**1.86 (1.09, 3.15)**

*Depression trajectories adjusted for adversity trajectories, and adversity trajectories adjusted for depression trajectories

** As above and additional adjustment for confounders (marital status, employment status, income of participant and partner and adversity/life events, all from the 30-year follow-up)

Table 4: Trajectories of maternal depression over 27 yrs. and adversity over 21 yrs. predicting offspring lifetime number of episodes depression (Multinominal Logistic Regression)

Trajectory group membership			Odds Ratio and CI by Lifetime number of episodes depression						
				Unadjusted model		Adjusted model 1*		Adjusted model 2**	
		No episodes	1-2 episodes	3+ episodes	1-2 episodes	3+ episodes	1-2 episodes	3+ episodes
Depression (n=2096)	Low	1	1	1	1	1	1	1
	Mid	1	1.14 (0.87, 1.49)	**1.38 (1.07, 1.77)**	1.04 (0.73, 1.49)	1.25 (0.89, 1.75)	0.99 (0.70, 1.40)	1.17 (0.83, 1.64)
	High	1	1.29 (0.82, 2.04)	1.51 (0.99, 2.32)	1.00 (0.53, 1.88)	1.23 (0.69, 2.12)	1.02 (0.56, 1.88)	1.34 (0.76, 2.35)
Adversity (n=2242)	Low	1	1	1	1	1	1	1
	Mid	1	1.07 (0.81, 1.41)	**1.58 (1.19, 2.20)**	1.12 (0.78, 1.62)	1.37 (0.95, 1.96)	1.11 (0.77, 1.61)	1.29 (0.89, 1.86)
	High	1	**1.81 (1.22, 2.66)**	**2.50 (1.71, 3.66_**	**1.96 (1.15, 3.34)**	**1.92 (1.13, 3.23)**	**1.95 (1.12, 3.41)**	1.66 (0.95, 2.90)

*Depression trajectories adjusted for adversity trajectories, and adversity trajectories adjusted for depression trajectories

** As above and additional adjustment for confounders (marital status, employment status, income of participant and partner and adversity/life events, all from the 30-year follow-up)
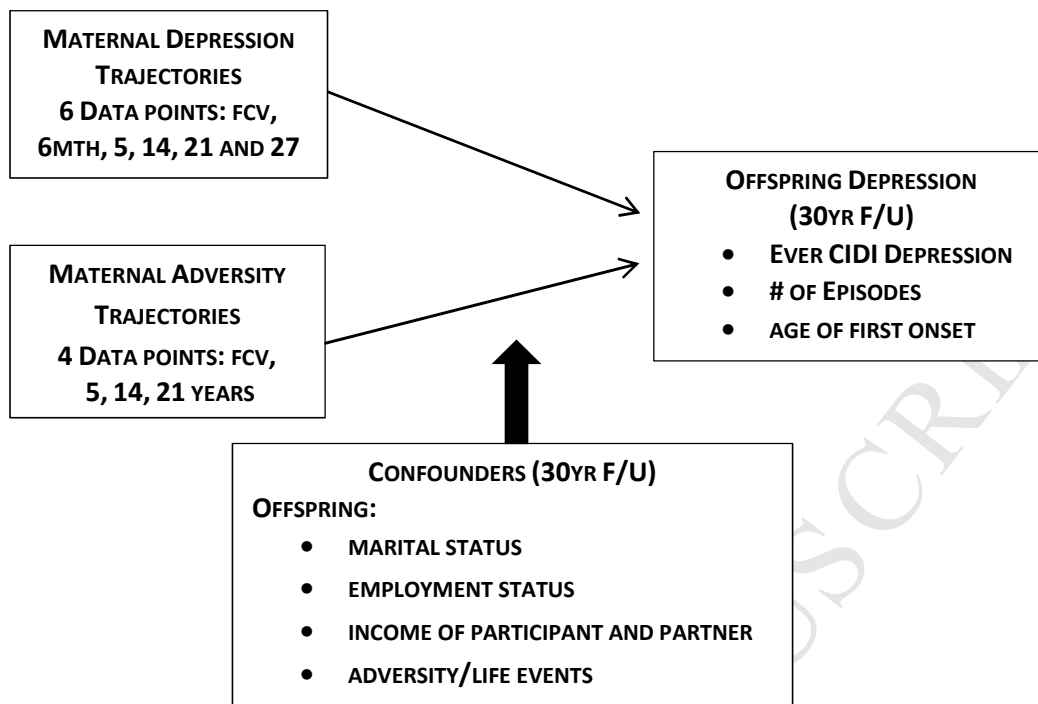
Table 5: Trajectory group membership of maternal depression over 27 yrs. and adversity over 21 yrs. predicting offspring age at first episode (Multinominal Logistic Regression)

Trajectory group membership		Odds Ratio and CI by Age at first episode									
			Unadjusted model			Adjusted model 1*			Adjusted model 2**		
		No episodes	20+ yrs.	16-19 yrs.	Up to 15 yrs.	20+ yrs.	16-19 yrs.	Up to 15 yrs.	20+ yrs.	16-19 yrs.	Up to 15 yrs.
Depression (n=1921)	Low	1	1	1	1	1	1	1	1	1	1
	Mid	1	**1.76 (1.26, 2.48)**	1.12 (0.78, 1.61)	1.33 (0.92, 1.92)	**1.65 (1.18, 2.30)**	0.96 (0.67, 1.37)	1.21 (0.83, 1.75)	**1.71 (1.16, 2.52)**	0.76 (0.49, 1.15)	1.18 (0.77, 1.81)
	High	1	1.24 (0.65, 2.37)	1.06 (0.55, 2.06)	**2.06 (1.19, 3.57)**	0.99 (0.52, 1.92)	0.80 (0.41, 1.54)	1.65 (0.94, 2.91)	0.89 (0.39, 2.03)	0.90 (0.44, 1.83)	**2.16 (1.16, 4.01)**
Adversity (n=2050)	Low	1	1	1	1	1	1	1	1	1	1
	Mid	1	1.30 (0.90, 1.87)	**1.62 (1.07, 2.46)**	**1.72 (1.12, 2.64)**	1.15 (0.73, 1.81)	1.58 (0.96, 2.60)	1.47 (0.88, 2.47)	1.11 (0.72, 1.71)	1.57 (0.98, 2.50)	1.42 (0.88, 2.30)
	High	1	**1.80 (1.07, 3.01)**	**2.43 (1.40, 4.22)**	**3.00 (1.73, 5.20)**	1.55 (0.80, 3.02)	**2.34 (1.13, 4.82)**	2.02 (0.98, 4.18)	1.37 (0.70, 2.67)	**2.57 (1.31, 5.03)**	1.55 (0.76, 3.14)

*Depression trajectories adjusted for adversity trajectories, and adversity trajectories adjusted for depression trajectories

** As above and additional adjustment for confounders (marital status, employment status, income of participant and partner and adversity/life events, all from the 30-year follow-up

Figure 1: Research Model

MATERNAL DEPRESSION TRAJECTORIES
6 DATA POINTS: FCV, 6MTH, 5, 14, 21 AND 27

MATERNAL ADVERSITY TRAJECTORIES
4 DATA POINTS: FCV, 5, 14, 21 YEARS

OFFSPRING DEPRESSION (30YR F/U)
- **EVER CIDI DEPRESSION**
- **# OF EPISODES**
- **AGE OF FIRST ONSET**

CONFOUNDERS (30YR F/U)
OFFSPRING:
- **MARITAL STATUS**
- **EMPLOYMENT STATUS**
- **INCOME OF PARTICIPANT AND PARTNER**
- **ADVERSITY/LIFE EVENTS**

ROLE OF FUNDING SOURCE