

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Maternal posttraumatic stress disorder, depression and alcohol dependence and child behaviour outcomes in HIV infected mother-child dyads: a longitudinal study
AUTHORS	Nöthling, Jani; Martin, Cherie; Laughton, Barbara; Cotton, Mark; Seedat, Soraya

VERSION 1 - REVIEW

REVIEWER	Debra A. Murphy, Ph.D. Professor in Residence Department of Psychiatry, University of California Los Angeles United States
REVIEW RETURNED	13-Aug-2013

THE STUDY	<p>This study assessed 70 mother-child dyads infected with HIV to investigate maternal PTSD and child behavior outcomes in an HIV vertically infected sample. The authors found that children of mothers with depression were significantly more likely to display behavior problems than children of mothers without depression. Maternal PTSD did not significantly predict child outcomes.</p> <p>The writing is very clear; results are presented well. However, there are a number of issues that limit enthusiasm for this paper These will briefly be described, with some suggestions for improvement.</p> <ol style="list-style-type: none">1. There is not rationale/justification presented for the assessment time points (12 months postpartum and 3 1/2 years of age); the authors should explain why these time points were selected.2. There are a number of potential confounds for this relatively small sample size: two different cites, the fact that infants were randomized to early therapy for either 40 or 96 weeks followed by planned treatment or deferred therapy, changes in caregivers (which can influence measures, since caregivers are serving as the informant for child behavior as well as their own, etc. The authors should better discuss how these were controlled for and/or plausible rationale for impact in the discussion.3. Probably the main issue related to this study is that the finding is not new (that children of others with depression were significantly more likely to exhibit behavior problems than children of mothers without depression); we have known this for many years now. The authors note that sample characteristics make their finding important, since this is the first study investigating maternal PTSD effects in a vertically transmitted HIV infected child population, however, that was not the significant finding. Perhaps had the investigators been able to explore how their children compare in
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	severity to general population samples where depressed mothers have behavior problem children, they might be adding more information to the literature. Alternatively, this might be better as a brief report.
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REVIEWER	Dr Simone Honikman Director Perinatal Mental Health Project Senior Researcher University of Cape Town South Africa I declare no competing interests with the CHER study of the sub-study referred to for this manuscript, or their authors.
REVIEW RETURNED	15-Oct-2013

THE STUDY	The limitations are not adequately articulated - this is discussed more fully in the file I have attached. Details with respect to irrelevant references and suggested current references are supplied in the file attached for general comments.
RESULTS & CONCLUSIONS	Insufficient reference to previous evidence and certain types of evidence - elucidated in the attachment for comments section.
REPORTING & ETHICS	No reporting statement or checklist was provided. The study in the article is not a randomised controlled trial although it was nested within a broader RCT study. It is not stated whether the committee who approved the study was a research ethics committee. It is stated that the committee is the "Committee for Health Research". If this is a misnomer and the committee is the same as the Health Research Ethics Committee of the University of Stellenbosch, it is not clear whether the nested study received separate ethics approval or approval as an amendment to the approval granted for the broader CHER RCT. A proportion of the mother/caregiver participants were between 16 and 19 years of age. The ethical and statutory considerations of including this group require mention.
GENERAL COMMENTS	This is an original, fascinating and relevant article that highlights an important aspect of psychiatric comorbidity with HIV infection, among mothers. Some comments follow; Introduction In this section, it may be useful to cite background prevalence rates of each of PTSD, depression and alcohol use disorder (AUD) for South Africa as well as those rates for perinatal or maternal populations (although they are cited for HIV positive adults in your discussion section). Similarly, in order to contextualise the study better, it may be useful to cite any data pertaining to background rates of child behavioural problems in South Africa or other low and middle income settings. The primary aim is inaccurately stated as the study methods were

not designed to investigate impact and long-term effects of maternal trauma and PTSD on child behaviour. That would require a design that explored causal mechanisms. Rather, this study explored **associations** between maternal mental health problems and child behaviours.

Methods

It is not clear whether the end date of the study for this paper is the same as the end date of the broader trial.

I would suggest putting the terms 'maternal' and 'mother' in quotation marks separated by the word 'or'. Page 6, line 10

It is stated that maternal assessments were completed at 10-12 months (page 6, line 43), yet on page 7, line 5, it is stated that these assessments occurred at five different time points. From the data, it appears that a single assessment was made for both mothers and infants. I would suggest that the several limitations of this 'once-off' assessment approach need to be clearly articulated in the discussion section. It has been well documented that maternal depression or anxiety antenatally, or within the first 12 months postpartum, are associated with a range of negative child behavioural outcomes, many of which persist, even when maternal symptoms resolve, as is a common natural course of events. In addition to the impact of maternal mental health or ill-health, several confounding factors or events occurring between 12 and 42 months may account for child behavioural outcomes.

The lack of clarity regarding research ethics committee approval and inclusion of adolescent mother participants has already been mentioned in the score sheet.

I suggest capitalising all the letters for the AUDIT as it is an acronym.

Page 7: the grammar of the first sentence, second paragraph is a bit cumbersome.

The fact that the status of maternal physical health was unknown is another important limitation that requires mention. This is relevant, given the fact that physical health status and mental health status have been shown to be associated, and may be particularly so for those with HIV infection. HIV-associated neurocognitive impairments in the mother may impact on behavioural outcomes of the children through negative patterns of engagement with offspring.

The references cited for cross-cultural adaptability of the Harvard Trauma Scale are not relevant to the South African population (Indo-Chinese refugees and Urdu-speakers). I would suggest searching for use and testing of the scale in the South African context. Suggested reference below;

Reliability of self report questionnaires for epidemiological investigations of adolescent mental health in Cape Town, South Africa, Rothon et al; *Journal of Child and Adolescent Mental Health* 2011, Volume 23, Number 2, pp. 119-128(10)

Similarly, the reference cited for utility of the Sheehan Disability Scale, does not adequately convince of validity or reliability in the South African setting as it refers to a US group of participants with bipolar disorder.

Results

I would suggest stating the 10-12 month infant immunodeficiency status data before stating that data for the 42 month assessment.

The phrases 'prevalence rate for all maternal psychiatric disorders' used on page 12, line 47 and 'overall prevalence of maternal psychiatric disorders' page 17, lines 25-26 are misleading on two accounts: the rates were for the three disorders only, and these disorders were not confirmed by diagnostic interview or clinician assessment (although the latter is acknowledged as a limitation). It may be more accurate to refer to symptoms or features or screen positive rates.

Discussion

In addition to contrasting the study findings to rates of the disorders in HIV infected samples, it would be interesting to refer to findings in maternal samples at 10-12 months, or those antenatally, which may too have an impact on later child developmental outcomes.

Although the infants were relatively healthy at the time of the assessment, it appears that this was not the case at the 10-12 month maternal assessment period. The evidence of prior immune-compromise ought to be taken in to account with respect to potential HIV-related insult to the developing infant brain such as HIV encephalopathy and CNS infections.

The discussion may be strengthened by including an exploration of possible causal mechanisms behind the study's findings, as well as the myriad potential confounding influences on infant behaviours in the study setting.

I suggest reference to the recent article below.

Trauma and posttraumatic stress disorder in South Africa: analysis from the South African Stress and Health Study. Atwoli et al; *BMC Psychiatry* 2013 Volume 13 Issue 1, pp. 1 -12

There are two typographical errors in the body of the paper– page 4, line 11 and page 10, line 28. There are several typographical errors in the reference section.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Comments

Reviewer: Debra A. Murphy, Ph.D.
Professor in Residence
Department of Psychiatry,
University of California Los Angeles
United States

This study assessed 70 mother-child dyads infected with HIV to investigate maternal PTSD and child behavior outcomes in an HIV vertically infected sample. The authors found that children of mothers with depression were significantly more likely to display behavior problems than children of mothers without depression. Maternal PTSD did not significantly predict child outcomes.

The writing is very clear; results are presented well. However, there are a number of issues that limit enthusiasm for this paper. These will briefly be described, with some suggestions for improvement.

Reviewer's comment:

There is not rationale/justification presented for the assessment time points (12 months postpartum and 3 1/2 years of age); the authors should explain why these time points were selected.

Authors' response:

The following was added to the methods section:

"The assessments completed at 12 months postpartum were used in the current analysis. This was deemed a salient period for examining PTSD in new mothers and was intended to decrease the risk of confounding by postpartum depression, as the risk for postpartum depression is highest within the first year after giving birth."

"Child behaviour was assessed at 42 months postpartum using the Child Behaviour Checklist (CBCL). This time point was selected based on completeness of data and in an effort to measure the long-term effects of maternal mental health."

Reviewer's comment:

There are a number of potential confounds for this relatively small sample size: two different sites, the fact that infants were randomized to early therapy for either 40 or 96 weeks followed by planned treatment or deferred therapy, changes in caregivers (which can influence measures, since caregivers are serving as the informant for child behavior as well as their own, etc. The authors should better discuss how these were controlled for and/or plausible rationale for impact in the discussion.

Authors' response:

The following was added to the discussion section: "In eight cases, there was a change in the caregiver completing the maternal assessment at 12 months compared with the caregiver completing the child assessment at 42 months. The change in caregiver may have, in itself, contributed to behaviour problems. Caregivers may have had a limited sense of the child's temperament (owing to the short period of caring for the child) leading to inaccurate representation of the child's behaviour. Several confounding factors, apart from maternal mental health, may have influenced child behaviour problems. Maternal physical health, child physical health, change in child's medication (assigned treatment arm), socio-economic stressors and parenting styles were not measured in this study and may have contributed to child behaviour problems. Future studies should assess these factors as potential confounders. Maternal mental health at only one time point (12 months postpartum) was included in this analysis. Intervening maternal and/or child factors e.g. effects of HIV-related CNS infections or encephalopathy on the developing brain between 12 and 42 months may have contributed to child behavioural outcomes."

Reviewer's comment:

Probably the main issue related to this study is that the finding is not new (that children of others with

depression were significantly more likely to exhibit behavior problems than children of mothers without depression); we have known this for many years now. The authors note that sample characteristics make their finding important, since this is the first study investigating maternal PTSD effects in a vertically transmitted HIV infected child population, however, that was not the significant finding. Perhaps had the investigators been able to explore how their children compare in severity to general population samples where depressed mothers have behavior problem children, they might be adding more information to the literature. Alternatively, this might be better as a brief report.

Authors' response:

The following was added to the introduction which we feel strengthens the paper:

“The prevalence of psychiatric disorders in the general South African population is relatively high compared to other countries, with an estimated lifetime prevalence of 30.3% and 12-month prevalence of 16.5%.[1] Depression, alcohol abuse and posttraumatic stress disorder (PTSD) are commonly diagnosed disorders with a 12-month prevalence rate of 4.9%, 4.5% and 0.7% respectively. [1,2] Among South Africans, alcohol abuse has a lifetime prevalence rate of 11.4% followed by depression at 9.8% and PTSD at 2.3%. [1,2] Postpartum depression is also prevalent in South Africa. High prevalence rates of 28% and 34.7% have been reported among new mothers. [3]”
“Prevalence rates of 16% - 30% and 7% - 31% for externalising behaviour problems and internalising behaviour problems respectively have been identified among preschool children in low income families.”

The following was added to the discussion which we feel strengthens the paper:

“The prevalence of psychiatric disorder was also considerably higher than rates documented in the general South African population [1] Previous studies have found a high prevalence (28%-34.7%) for postpartum depression in low income populations in South Africa. We found a higher prevalence rate of 50% among this sample for depression. The added emotional and physical load of HIV infection and caring for a child infected with HIV seems to contribute considerably to psychiatric disease burden. The high prevalence rate of psychiatric disorder, especially PTSD, could possibly be biased by female gender, a previously identified risk factor for PTSD in HIV infected individuals.[20]”
“The prevalence rate of externalising behaviour problems is considerably higher than previously reported rates of 16%-30%. The prevalence rate for internalising behaviour problems corresponds with those identified in previous studies (7%-31%). The children in this sample are therefore at greater risk of displaying externalising behaviour problems and consequently psychiatric disorders associated with externalising behaviour problems later in life. [17,16]”
“Fatigue and emotional burnout associated with depression may lead to poor mother-child interaction in early infancy and consequently to insecure infant attachment and behavioural problems [3,70]. The added burden of caring for an ill child, guilt associated with transmission of HIV to the child and stressors associated with living in poverty may further intensify depressive symptoms. [71,72]”
“Similar to depression, maternal PTSD may lead to poor mother child interaction. Parental anxiety is associated with an over involved parenting style and negative parental attitudes during interaction with children. [73] Children may model parent's anxious behaviour; parental vigilance, intrusion and discouragement of independent problems solving may lead to a limited sense of competence and autonomy in the children which, in turn, can lead to anxiety within the child. [74] Maternal antenatal anxiety may have adverse consequences on child neurodevelopment and subsequent behavioural and emotional problems. [75]”

Reviewer 2: Comments

Reviewer: Dr Simone Honikman

Director Perinatal Mental Health Project Senior Researcher University of Cape Town South Africa

I declare no competing interests with the CHER study of the sub-study referred to for this manuscript, or their authors.

No reporting statement or checklist was provided. The study in the article is not a randomised

controlled trial although it was nested within a broader RCT study.

It is not stated whether the committee who approved the study was a research ethics committee. It is stated that the committee is the "Committee for Health Research". If this is a misnomer and the committee is the same as the Health Research Ethics Committee of the University of Stellenbosch, it is not clear whether the nested study received separate ethics approval or approval as an amendment to the approval granted for the broader CHER RCT.

A proportion of the mother/caregiver participants were between 16 and 19 years of age. The ethical and statutory considerations of including this group require mention.

This is an original, fascinating and relevant article that highlights an important aspect of psychiatric comorbidity with HIV infection, among mothers.

Some comments follow:

Introduction

Reviewer's comment:

In this section, it may be useful to cite background prevalence rates of each of PTSD, depression and alcohol use disorder (AUD) for South Africa as well as those rates for perinatal or maternal populations (although they are cited for HIV positive adults in your discussion section).

Authors' response:

The following information was added to the introduction: "The prevalence of psychiatric disorders in the general South African population is relatively high compared to other countries, with an estimated lifetime prevalence of 30.3% and a 12-month prevalence of 16.5%. [1] Depression, alcohol abuse and posttraumatic stress disorder (PTSD) are commonly diagnosed disorders with a 12-month prevalence rate of 4.9%, 4.5% and 0.7% respectively. [1,2] Alcohol abuse has a lifetime prevalence rate of 11.4% followed by depression with 9.8% and PTSD with 2.3%. [1,2] Postpartum depression is also prevalent in South Africa. High prevalence rates of 28% and 34.7% have been reported among new mothers. [3]"

Reviewer's comment:

Similarly, in order to contextualise the study better, it may be useful to cite any data pertaining to background rates of child behavioural problems in South Africa or other low and middle income settings.

Authors' response:

The following information was added to the introduction: "Prevalence rates of 16% - 30% and 7% - 31% for externalising behaviour problems and internalising behaviour problems respectively, have been identified among preschool children in low income families. [15]"

Reviewer's comment:

The primary aim is inaccurately stated as the study methods were not designed to investigate impact and long-term effects of maternal trauma and PTSD on child behaviour. That would require a design that explored causal mechanisms. Rather, this study explored associations between maternal mental health problems and child behaviours.

Authors' response:

The primary aim was reworded: "The primary aim of this study was to investigate the impact of maternal trauma exposure and PTSD at a specific time point (12 months postpartum) and the association thereof with child behaviour (at three and a half years of age) in mother-child dyads, infected with HIV, while controlling for the effects of depression."

Methods

Reviewer's comment:

It is not clear whether the end date of the study for this paper is the same as the end date of the broader trial.

Authors' response:

The end date for this study is not the same as the end date for the broader trial. Sentences were reworded to make this clearer, e.g. "Seventy mother-child dyads infected with HIV participated in this study. Data was collected between 2006 and 2010."

Reviewer's comment:

I would suggest putting the terms 'maternal' and 'mother' in quotation marks separated by the word 'or'. Page 6, line 10

Authors' response:

Changed to: " 'Maternal' or 'mother' within the context of this study therefore refers to either the biological mother or primary caregiver of the child."

Reviewer's comment:

It is stated that maternal assessments were completed at 10-12 months (page 6, line 43), yet on page 7, line 5, it is stated that these assessments occurred at five different time points. From the data, it appears that a single assessment was made for both mothers and infants. I would suggest that the several limitations of this 'once-off' assessment approach need to be clearly articulated in the discussion section. It has been well documented that maternal depression or anxiety antenatally, or within the first 12 months postpartum, are associated with a range of negative child behavioural outcomes, many of which persist, even when maternal symptoms resolve, as is a common natural course of events. In addition to the impact of maternal mental health or ill-health, several confounding factors or events occurring between 12 and 42 months may account for child behavioural outcomes.

Authors' response:

Maternal assessments were completed at five different time periods. Maternal assessments completed at 12 months postpartum and child assessments completed at 42 months were used in the analyses for this paper. The time periods were used for the following reasons (added to methods section):

"The assessments completed at 12 months postpartum were used in the current analysis. This was deemed a salient period for examining PTSD in new mothers and was intended to decrease the risk of confounding by postpartum depression, as the risk for postpartum depression is highest within the first year after giving birth."

"Child behaviour was assessed at 42 months postpartum using the Child Behaviour Checklist (CBCL). This time point was selected based on completeness of data and in an effort to measure the long-term effects of maternal mental health."

The following was added to the limitations of the study:

"Several confounding factors, apart from maternal mental health, may have influenced child behaviour problems. Maternal physical health, child physical health, change in child's medication (assigned treatment arm), socio-economic stressors and parenting styles were not measured in this study and may have contributed to child behaviour problems. Future studies should assess these factors as potential confounders. Maternal mental health at only one time point (12 months postpartum) was included in this analysis. Intervening maternal and/or child factors e.g. effects of HIV-related CNS infections or encephalopathy on the developing brain between 12 and 42 months may have contributed to child behavioural outcomes."

Reviewer's comment:

The lack of clarity regarding research ethics committee approval and inclusion of adolescent mother

participants has already been mentioned in the score sheet.

Authors' response:

The study was approved by the Health Research Ethics Committee. The following was added to the methods section: "The study under investigation was approved by the Health Research Ethics Committee of Stellenbosch University in Cape Town, South Africa."

While the South African National Health Act requires parental consent (in addition to participant assent) for adolescents less than 18 years to be enrolled in research studies, a waiver of parental consent was granted by the ethics committee to include adolescent mothers aged 16-18 years.

Reviewer's comment:

I suggest capitalising all the letters for the AUDIT as it is an acronym.

Authors' response:

Audit was changed to AUDIT throughout the paper.

Reviewer's comment:

Page 7: the grammar of the first sentence, second paragraph is a bit cumbersome.

Authors' response:

The sentence was changed to the following:

"Child behaviour was assessed at 42 months postpartum using the Child Behaviour Checklist (CBCL). This time point was selected based on completeness of data and in an effort to measure the long-term effects of maternal mental health."

"The child had to be in the care of the caregiver for at least six months prior to the assessments to qualify as a suitable participant."

Reviewer's comment:

The fact that the status of maternal physical health was unknown is another important limitation that requires mention. This is relevant, given the fact that physical health status and mental health status have been shown to be associated, and may be particularly so for those with HIV infection. HIV-associated neurocognitive impairments in the mother may impact on behavioural outcomes of the children through negative patterns of engagement with offspring.

Authors' response:

The following was added to the limitation:

"Several confounding factors, apart from maternal mental health, may have influenced child behaviour problems. Maternal physical health, child physical health, change in child's medication (assigned treatment arm), socio-economic stressors and parenting styles were not measured in this study and may have contributed to child behaviour problems. Future studies should assess these factors as potential confounders. Maternal mental health at only one time point (12 months postpartum) was included in this analysis. Intervening maternal and/or child factors e.g. effects of HIV-related CNS infections or encephalopathy on the developing brain between 12 and 42 months may have contributed to child behavioural outcomes."

Reviewer's comment:

The references cited for cross-cultural adaptability of the Harvard Trauma Scale are not relevant to the South African population (Indo-Chinese refugees and Urdu-speakers). I would suggest searching for use and testing of the scale in the South African context. Suggested reference below; Reliability of self-report questionnaires for epidemiological investigations of adolescent mental health in Cape Town, South Africa, Rothon et al; Journal of Child and Adolescent Mental Health 2011, Volume 23, Number 2, pp. 119-128(10)

Authors' response:

The following was added to the methods section: "The HTS has shown strong test-retest reliability

among a South African, adolescent sample. [39]"

The reference to Mollica et al. (1992) and Halepota and Wasif (2001) were replaced with: "Rothon C, Stansfeld, SA, Mathews C, et al. Reliability of self-report questionnaires for epidemiological investigations of adolescent mental health in Cape Town, South Africa. *Journal of Child and Adolescent Mental Health* 2011; 23(2), 119-128."

Reviewer's comment:

Similarly, the reference cited for utility of the Sheehan Disability Scale, does not adequately convince of validity or reliability in the South African setting as it refers to a US group of participants with bipolar disorder.

Authors' response:

The following was added to the methods section: "The SDS is frequently used in clinical trials in psychiatry and has shown good reliability in an HIV infected, South African sample." [65]

The reference to Arbuckle et al. (2009) was replaced with the following: Troeman CE, Spies G, Cherner M, et al. Impact of childhood trauma on functionality and quality of life in HIV-infected women. *Health and Quality of Life Outcomes* 2011; 9:84.

Results

Reviewer's comment:

I would suggest stating the 10-12 month infant immunodeficiency status data before stating that data for the 42 month assessment.

Authors' response:

The 10-12 month infant immunodeficiency data was swapped around with the 42 month data: "The prevalence of infant immunodeficiency was relatively high at 10 to 12 months postpartum with 47.1% (range: 15.4%-54.5%) and 40% (range: 574-3777) showing mild to severe immunodeficiency based on CD4 percentages and absolute counts respectively. At 42 months, the majority of the children did not have CD4 percentages (91.4%, range: 16.3%-53.6%) or absolute counts (100%, range: 468-3267) indicative of immunodeficiency."

Reviewer's comment:

The phrases 'prevalence rate for all maternal psychiatric disorders' used on page 12, line 47 and 'overall prevalence of maternal psychiatric disorders' page 17, lines 25-26 are misleading on two accounts: the rates were for the three disorders only, and these disorders were not confirmed by diagnostic interview or clinician assessment (although the latter is acknowledged as a limitation). It may be more accurate to refer to symptoms or features or screen positive rates.

Authors' response:

The following was added / changed on page 12, line 47: "The prevalence rate for all measured maternal psychiatric disorders (based on self-report data) was 27.6%. Depression was the most prevalent disorder at 50% (n = 35), followed by PTSD with 22.9% (n = 16), alcohol abuse with 7.1% (n = 5) and alcohol dependence with 2.9% (n = 2)."

The following was added / changed on page 17, line 25-26: "The overall prevalence of maternal psychiatric disorders, based on self-report data, was 27.6%."

Discussion

Reviewer's comment:

In addition to contrasting the study findings to rates of the disorders in HIV infected samples, it would be interesting to refer to findings in maternal samples at 10-12 months, or those antenatally, which may too have an impact on later child developmental outcomes.

Authors' response:

The following was added to the discussion section: "The prevalence of psychiatric disorder was also

considerably higher than rates documented in the general South African population [1] Previous studies have found a high prevalence (28%-34.7%) for postpartum depression in low income populations in South Africa. We found a higher prevalence rate of 50% among this sample for depression. The added emotional and physical load of HIV infection and caring for a child infected with HIV seems to contribute considerably to psychiatric disease burden. The high prevalence rate of psychiatric disorder, especially PTSD, could possibly be biased by female gender, a previously identified risk factor for PTSD in HIV infected individuals. [20] The low rate of alcohol dependence might be due to the use of prenatal alcohol exposure as an exclusion criterion for participation in the study.”

Reviewer’s comment:

Although the infants were relatively healthy at the time of the assessment, it appears that this was not the case at the 10-12 month maternal assessment period. The evidence of prior immune-compromise ought to be taken in to account with respect to potential HIV-related insult to the developing infant brain such as HIV encephalopathy and CNS infections.

Authors’ response:

The following was added to the limitations section: “Several confounding factors, apart from maternal mental health, may have influenced child behaviour problems. Maternal physical health, child physical health, change in child’s medication (assigned treatment arm), socio-economic stressors and parenting styles were not measured in this study and may have contributed to child behaviour problems. Future studies should assess these factors as potential confounders. Maternal mental health at only one time point (12 months postpartum) was included in this analysis. Intervening maternal and/or child factors e.g. effects of HIV-related CNS infections or encephalopathy on the developing brain between 12 and 42 months may have contributed to child behavioural outcomes. ”

Reviewer’s comment:

The discussion may be strengthened by including an exploration of possible causal mechanisms behind the study’s findings, as well as the myriad potential confounding influences on infant behaviours in the study setting.

Authors’ response:

The following was added to the discussion section:

“The prevalence rate of externalising behaviour problems is considerably higher than previously reported rates of 16%-30%. The prevalence rate for internalising behaviour problems corresponds with those identified in previous studies (7%-31%). The children in this sample are therefore at greater risk of displaying externalising behaviour problems and consequently psychiatric disorders associated with externalising behaviour problems later in life. [17,16]”

“Fatigue and emotional burnout associated with depression may lead to poor mother-child interaction in early infancy and consequently to insecure infant attachment and behavioural problems [3,70]. The added burden of caring for an ill child, guilt associated with transmission of HIV to the child and stressors associated with living in poverty may further intensify depressive symptoms. [71,72]”

“Similar to depression, maternal PTSD may lead to poor mother child interaction. Parental anxiety is associated with an overinvolved parenting style and negative parental attitudes during interaction with children. [73] Children may model parent’s anxious behaviour; parental vigilance, intrusion and discouragement of independent problems solving may lead to a limited sense of competence and autonomy in the children which, in turn, can lead to anxiety within the child. [74] Maternal antenatal anxiety may have adverse consequences on child neurodevelopment and subsequent behavioural and emotional problems. [75]”

“In eight cases, there was a change in the caregiver completing the maternal assessment at 12 months compared with the caregiver completing the child assessment at 42 months. The change in caregiver may have, in itself, contributed to behaviour problems, Caregivers may have had a limited sense of the child’s temperament (owing to the short period of caring for the child) leading to inaccurate representation of the child’s behaviour. Several confounding factors, apart from maternal mental health, may have influenced child behaviour problems. Maternal physical health, child physical

health, change in child's medication (assigned treatment arm), socio-economic stressors and parenting styles were not measured in this study and may have contributed to child behaviour problems. Future studies should assess these factors as potential confounders. Maternal mental health at only one time point (12 months postpartum) was included in this analysis. Intervening maternal and/or child factors e.g. effects of HIV-related CNS infections or encephalopathy on the developing brain between 12 and 42 months may have contributed to child behavioural outcomes”

Reviewer's comment:

I suggest reference to the recent article below.

Trauma and posttraumatic stress disorder in South Africa: analysis from the South African Stress and Health Study. Atwoli et al; BMC Psychiatry 2013 Volume 13 Issue 1, pp. 1 -12

Authors' response:

The reference was added to the paper.

Reviewer's comment: There are two typographical errors in the body of the paper– page 4, line 11 and page 10, line 28. There are several typographical errors in the reference section.

Authors' response: Typographical errors in the body and reference section have been corrected.