Meta-analysis found high rates of post-traumatic stress disorder and associated risk factors in parents following paediatric medical events

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Short title: Parental trauma after paediatric medical events.

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CONFLICTS OF INTEREST

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ABBREVIATION

PTSD, post-traumatic stress disorder
ABSTRACT

Aim: This meta-analysis identified how prevalent parental post-traumatic stress disorder (PTSD) was after their children’s medical events and evaluated the risk factors that increased the likelihood of PTSD.

Methods: The MEDLINE, PsycINFO and PTSDpubs databases were searched for papers published in English from 1980 to June 2018. The prevalence of parental PTSD was pooled across the studies and risk factors were extracted if PTSD symptoms were correlated with other research variables or when the authors had conducted between group analyses of PTSD. We also explored the effects of the assessment method, parental gender and medical events and the risk of bias.

Results: The 54 studies that were identified had a pooled PTSD prevalence rate of 30.3% (95% confidence interval 25.3-35.5%). Childhood cancer cases yielded the highest rates of parental PTSD. A total of 33 potential risk factors were identified. The risk factors with medium to large effects were: co-morbid parental psychological responses and functioning, acute stress responses, child behavioural functioning, uncertainty about the child’s illness and negative coping strategies. The findings are discussed within the context of high heterogeneity.

Conclusion: The prevalence of parental PTSD after paediatric medical events was relatively high and 33 risk factors were identified.

KEY WORDS: medical events, parents, post-traumatic stress disorder, prevalence, risk factors
KEY NOTES

- This meta-analysis examined the prevalence of parental post-traumatic stress disorder (PTSD) following paediatric medical events and identified the associated risk factors.
- We searched key databases from 1980-2018 and found 54 studies that showed a pooled PTSD prevalence rate of 30.3% and 33 wide-ranging risk factors.
- PTSD was particularly common after cancer and the parental risk factors with the largest effects were anxiety, depression and stress.
INTRODUCTION

Indirect exposure to trauma, such as learning that a loved one has been exposed to trauma, can lead to post-traumatic stress disorder (PTSD).\textsuperscript{1} According to diagnostic manuals, traumatic events include chronic conditions, such as cancer and type 1 diabetes, and being admitted to a paediatric intensive care unit.\textsuperscript{1} Parents can develop PTSD after their child receives a medical diagnosis or undergoes invasive medical procedures.

Research has shown that when parents are traumatised by paediatric medical events this can increase the risk of their child developing PTSD or experiencing trauma responses without a psychiatric diagnosis.\textsuperscript{2} In addition, most children rely on their parents as primary caregivers to meet their basic care needs. This is particularly important if the child is recovering from trauma exposure, as this can lead to PTSD and many other difficulties, such as depression, anxiety and self-harm.\textsuperscript{3} PTSD can impede family functioning\textsuperscript{4} and qualitative research has suggested that parental PTSD can have an impact on parenting practice.\textsuperscript{5} Parents may not realise that their child is experiencing trauma responses if they are also experiencing PTSD.\textsuperscript{6} Parental PTSD has a significant impact on their own general functioning and mental wellbeing and has cost implications for wider societies and health services.\textsuperscript{7}

A previous meta-analysis\textsuperscript{8} compared PTSD between parents whose children did, or did not, have a chronic medical condition. A large effect size difference was identified (Hedges’ $g = 0.85$), indicating that the parents of children with chronic conditions were more likely to experience PTSD. Another meta-analysis of 16 studies found that 22.8% of parents developed PTSD following their child’s chronic illness.\textsuperscript{9} In addition, a study by Pinquart\textsuperscript{8} identified several significant factors that increased the risk of parental PTSD when their child had a chronic illness. These included medical factors, such as illness severity, treatment duration and intensity and time since diagnosis or treatment. Mothers were more likely
develop trauma responses than fathers and child PTSD was significantly associated with parental PTSD.

Understanding the prevalence of parental PTSD after paediatric medical events is important if we are to develop appropriately resourced services for this population. The aim of this study was to use meta-analysis principles to update earlier reviews and identify the prevalence of parental PTSD following paediatric medical events. We also aimed to calculate the prevalence rates between subpopulations, for example diseases related to cancer or in particular medical settings. Prior empirical studies suggested variations in the prevalence of parental PTSD, depending on the child’s medical event. To help us identify parents at risk of PTSD, we adopted a data-driven approach without limiting the search to particular factors, such as previous research. Therefore, risk factor estimates reported in two or more studies were pooled for analysis. A search of the International Prospective Register of Systematic Reviews database showed no similar review studies had been completed and the current meta-analysis was registered on 31 July 2018 (CRD42018099578).

METHOD

Study selection

Papers from peer-reviewed, English-language journals that were published between 1980 and June 2018 were considered for inclusion. Human study filters were applied to databases in order to exclude any animal studies. The following databases were searched: PsycINFO, MEDLINE and PTSDpubs, which is managed by the National Centre for PTSD. The search terms can be found in Table S1.

PTSD met the criteria if it followed a structured clinical interview. We also included reliable PTSD self-report questionnaire scores that were above the clinical cut-off and indicated moderate to severe PTSD or PTSD that was determined by a diagnostic algorithm.
The definition of PTSD has changed since it was first established as a diagnosis in 1980. Data were only included, if the current method of assessing PTSD met the criteria listed above at the time of data collection for each study. Of the 54 studies in this meta-analysis, 51 used the definition of PTSD in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders\textsuperscript{10} and three used the definition from the third edition.\textsuperscript{11} Only prevalence and risk factors for current PTSD were included. Risk factors were operationalised as variables that had a reported correlation with PTSD scores or when PTSD was present for a proportion of the sample based on a variable, such as child gender.

**Inclusion and exclusion criteria**

Studies were included if they reported prevalence rates of parental PTSD that related to a medical event that affected a child aged 0-18 years. The term parents is used for the child’s main primary carer and mother and father are used to describe gender differences. A medical event was defined as a chronic illness or a medical procedure that required the child to have on-going treatment by a hospital or equivalent medical team. It did not include typical primary care services, such as general practice. This paper excludes research on single incident traumas, such as road traffic accidents, assaults and burns, which were unrelated to a chronic illness or medical condition requiring on-going treatment. These will be presented in a separate paper. Some of the studies we included presented data on mixed trauma samples. For example, one study presented data on chronic illnesses, including type 1 diabetes and cancer, and unintentional injuries without a chronic illness, but did not distinguish between PTSD rates for these two categories. We also discussed studies researching paediatric or neonatal intensive care units, which could be either a chronic medical event or a single incident. We decided to include such studies in the analysis, but also conduct a sensitivity analysis to account for any ambiguities. Analyses were re-run to exclude studies if the
temporal length of medical events was unclear or if PTSD rates resulted from a mixture of chronic medical events and single traumas.

Research articles were excluded if the mean age of the sample exceeded 18 years, acute stress disorders were assessed or PTSD was only assessed within one month of a medical event. We also excluded the parents’ reactions to their own traumas, studies that included children who died, due to the complication of grief-related trauma, medical events during birth or pregnancy or where the parents perpetrated the trauma. Studies that reported insufficient statistical data to calculate effect sizes for risk factors were also excluded. In addition, this analysis did not include randomised controlled trials, treatment or intervention studies, systematic reviews, meta-analyses, theses and dissertations, book chapters, qualitative research, single case reviews or case studies.

Risk of bias

Established research quality tools\textsuperscript{12-15} were used to identify 12 questions to assess the potential risk of bias. These included the sample, non-response rates and reasons, sample representativeness, recruitment procedures, inclusion and exclusion criteria, appropriate PTSD and risk factor assessments and the sample size and statistical testing. We also looked at whether an appropriate clinician undertook the assessment and how much time had elapsed between the traumatic incident and the assessment. Each question was rated on a three-point scale, from zero to two, and the total scores categorised the risk of bias: low was 17-24, moderate was 9-16 and high was 0-8. Inter-rater reliability was assessed for a third of the studies (n=17) by two authors (AB, LW). The aim was to reach 80% agreement with inter-rater scoring, which has been suggested to be the minimum acceptable level.\textsuperscript{16} They achieved an intra-class correlation of 96.8% for the risk of bias, with a 95% confidence interval (95% CI) of 91.6-98.8%.
Data extracted from each study

A number of study variables were examined, namely the author, year of publication, study design, child and parent sample sizes, health setting, country and population. The participant data were: the ages and genders of the children and parents, the type of medical event and the time that had elapsed since the event. The PTSD assessment data were: the amount of time between the event and the assessment, follow-up assessments, assessment methods and measures and the number of parents meeting the cut-off and diagnostic criteria for PTSD. The potential risk factors were: the type of risk factor, how it was measured and assessed and the statistical data. The first author read each paper twice and extracted the data each time.

When the prevalence of PTSD was measured in multiple ways, clinical interview data superseded self-reports. Continuous PTSD scores were extracted for risk factor estimates, where possible, rather than dichotomous outcomes. For longitudinal studies, the time of the first PTSD assessment at, or closest to, four weeks after the medical event was used. We included the risk factors assessed prior to, or at the same time as, the PTSD assessment, but those conducted after the PTSD assessment were excluded. Studies that had multiple effect sizes for the same risk factor were combined using Fisher’s Z transformation.17

When prevalence rates were identified, only one prevalence rate from each study was included. This was the one with the largest sample size or the PTSD assessment that was carried out closest to four weeks after the event. When effect size estimates of the same risk factor were included in more than one paper, the one from the largest sample was used. Once all the risk factor values had been extracted, any variables that only appeared in one study were removed. An effect size of zero was extracted when studies reported non-statistically significant findings for potential risk factors and no effect size was provided. These accounted for 56 (16.7%) of the effect sizes. We acknowledge that this conservative strategy
probably underestimated the true effect sizes\textsuperscript{18}, but excluding non-significant results could have overestimated the combined effect sizes that were included.\textsuperscript{19}

**Data synthesis**

The prevalence analysis was carried out with OpenMeta[Analyst] (Brown University, Rhode Island, USA),\textsuperscript{20} which uses the metaphor package in \textit{R} (R Foundation for Statistical Computing, Vienna, Austria).\textsuperscript{21} For the risk factor analysis, we used MAVIS, version 1.1.3 (University of California, California, USA).\textsuperscript{22} An arcsine of square root proportion random-effects model was used for the prevalence and risk factor meta-analyses,\textsuperscript{23-24} because of the expected heterogeneity of the studies. Variations were found in the methodological, statistical and clinical aspects of the studies. Arcsine transformation prevents the confidence intervals of prevalence estimates from falling below zero. Heterogeneity was assessed among the meta-analyses by inspecting forest plots as well as Cochran’s \( Q \) test\textsuperscript{25} and the I\textsuperscript{2} statistic.\textsuperscript{26}

A separate meta-analysis was conducted for each risk factor. We used Pearson’s correlation coefficient (\( r \)) as the effect size, based on a previous meta-analysis.\textsuperscript{27} Higher values of \( r \) represent a stronger positive association with PTSD symptomology. Effect sizes were considered to be small (0.1), medium (0.3) or large (0.5).\textsuperscript{28}

**Subgroup and moderator analyses**

Sub-group analysis identified the prevalence of parental PTSD for each paediatric medical event: admission to a paediatric or neonatal intensive care unit, transplants, type 1 diabetes and cancer, including tumours and malignancies. The typing of these medical events was based on the definitions used by each study. If a sub-population did not fit within a type, they were excluded from the sub-group analysis. The typing of medical events was based on the psychological provision and service design of paediatric services in the UK. Where possible, studies that investigated multiple medical events, and reported separate prevalence rates, were separated for the purposes of the sub-group analyses. Studies that only
investigated mothers or fathers, or those that presented separated prevalence rates for parents, were included. Moderator analyses were undertaken with regard to parental gender and the type of PTSD and self-reports and interview assessments were compared.

**Sensitivity analysis**

Sensitivity analysis identified results skewed by studies with a high risk of bias and those data were removed from the prevalence and any risk factor meta-analyses. Medical events were removed from the sensitivity analysis if there was any doubt about whether they fell within the remit for the analysis, as discussed above.

**RESULTS**

We identified 13,247 papers after duplicates had been removed and two authors (AB, LW) reviewed the titles and abstracts against the inclusion and exclusion criteria. They then carried out full text reviews of 228 papers and selected 54 studies. Figure 1 shows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart for this process.

The total sample size was 6,743 (range 10 to 474). The studies contained 45 prevalence rates of parental PTSD and 52 studies reported risk factors, yielding 359 effect sizes.

**Characteristics of the studies**

Table S2 lists the characteristics of the 54 studies included in the meta-analysis and the studies with duplicate samples are labelled.

**PTSD prevalence**

A total of 45 studies reported prevalence rates, which resulted in a pooled prevalence of parental PTSD following paediatric medical events of 30.3% (95% CI 25.3 to 35.5%).
However, this was significantly heterogeneous ($Q(44)=684.250$, $p<0.001$, $I^2 = 93.57\%$). The prevalence rates for PTSD ranged from 7.27% to 75.5%.

**Moderator analysis of prevalence**

The sub-group analyses can be found in Table 1.

Firstly, the method of PTSD assessment was investigated. We found no statistically significant differences in the prevalence rate as a function of the assessment type: self-report ($k=39$) versus interview ($k=6$) ($\beta=-0.15$, 95% CI -0.31 to 0.02, $p=0.077$).

Secondly, the prevalence for each medical event type was calculated using sub-group analyses. Figure 2 demonstrates that paediatric cancer yielded the highest rate of parental PTSD ($k=19$, 40.7%) compared to all other medical event types combined, excluding cancer ($k=27$, 21.1%). A *post-hoc* analysis found that parental PTSD following paediatric cancer was significantly higher when it was compared with all the other paediatric medical events ($\beta=0.20$, 95% CI 0.11 to 0.30, $p<0.001$).

Thirdly, we analysed the prevalence rates between mothers and fathers, wherever possible, and this showed no statistically significant differences in prevalence as a function of gender ($\beta=-0.10$, 95% CI -0.23 to 0.04, $p=0.152$).

**Sensitivity analysis of prevalence**

A sensitivity analysis was conducted on the five studies that were rated as having a high risk of bias. Meta-regression identified no statistically significant differences between studies rated as poor quality and the other studies that were included ($\beta=0.07$, 95% CI -0.13 to 0.27, $p=0.495$).

Secondly, 12 studies were removed because there was ambiguity that the medical event did not fully meet the inclusion criteria. Meta-regression was used to compare the prevalence rates for these studies to the other studies and this did not identify any statistically significant differences ($\beta=0.11$, 95% CI -0.01 to -0.2), $p=0.065$).
**Risk factor estimates**

A total of 33 risk factors were reported in two or more studies and the main findings for each individual meta-analysis are presented in Table 2. The risk factor recovery was defined as how well the child recovered from their medical event and included factors such as functionality and quality of life. We found 19 statistically significant risk factors, but illness severity did not reach small effect size. Risk factors that were considered small in effect included: length of hospital stay, treatment or condition length, relapse and readmission, medical complications, recovery, child PTSD, being a mother, perceived social support and previous trauma or adverse life effects. Risk factors that reached a medium effect size included: child behavioural difficulties, parental uncertainty about the child’s illness and the use of negative coping strategies, including avoidance, disengagement, substance use and emotion-focused or passive coping. Risk factors with large effects included: diagnosis of acute stress disorder, depressive symptoms, anxiety symptoms, general psychological distress, stress and a partner having PTSD.

**Sensitivity analysis of risk factor estimates**

The sensitivity analysis was conducted by removing the risk factor estimates from papers with a high risk of bias. This analysis showed that the illness severity risk factor was no longer statistically significant. In addition, the child depression risk factor could no longer be computed, because only one effect estimate remained.

The same process was used to remove risk factor estimates that did not appear to fully meet the inclusion criteria of the study. This process identified three main changes. Firstly, illness severity was no longer statistically significant. Secondly, poor family functioning increased to a medium effect size (0.30) and was significant (p<0.001). Finally, the following risk factors could not be entered into the meta-analysis, because all the effect sizes were no longer included or only one effect size remained. These were acute stress disorder, medical
complications, recovery, family psychiatric history, use of positive coping strategies, post-
traumatic growth, having a partner with PTSD and prior hospitalisation. Therefore, caution
should be taken when interpreting these as risk factors for parents developing PTSD after a
paediatric medical event.

DISCUSSION

This meta-analysis found that the overall prevalence of parental PTSD following their
child’s medical event was 30.3%. However, there was significant heterogeneity across these
studies, which was not surprising given the various clinical and methodological differences
between the studies. This review identified a higher prevalence rate than previous meta-
analyses.

Prevalence rates between different paediatric conditions varied considerably. For
example, three studies found that type 1 diabetes had a prevalence of 18.2%, with relatively
low heterogeneity. In contrast, 19 cancer studies had a high prevalence of 40.7%, with higher
heterogeneity. Cancer diagnoses resulted in significantly higher rates of parental PTSD than
other medical events. This was also the case when cancer diagnoses were compared with
parental PTSD due to children being admitted to a paediatric or neonatal intensive care unit.
This contradicts research that found that the parents of children with, and without, cancer did
not have different levels of PTSD.

In order to evaluate why cancer yielded more parental PTSD than other medical
events, the risk factors with higher effect sizes were considered. Parental uncertainty was a
risk factor with a medium effect size. We hypothesised that there may have been considerable
amounts of uncertainty around cancer diagnoses than other paediatric medical events, such as
the prognosis and treatment success. Indeed, parental PTSD was associated with measures of
uncertainty in this meta-analysis, which could explain why cancer resulted in higher
prevalence rates of parental PTSD. In fact, four out of the five risk factor estimates used for parental uncertainty came from cancer research. The impact that uncertainty had on parental PTSD as a result of other paediatric medical events needs further study. In particular, we need to understand whether this is a psychological mechanism that promotes greater worry or genuine uncertainty around the future course of the child’s condition or a combination of both.

We considered the effects of self-reports and interview assessment types and parental gender in order to explore the sources of heterogeneity, but they were not significant moderators. However, we did note the limited power of these analyses, particularly in relation to assessment type, as most studies used self-report questionnaires to identify parents with clinically significant PTSD. The high prevalence of parental PTSD may have been due to the small number of studies that used clinical interviews. Although assessment type was not a statistically significant moderator, there were apparent differences in the pooled prevalence rates that may have been significant with greater power. For example, the self-report assessment yielded a 31.9% prevalence compared to 18.1% for the interview assessments. The meta-analysis of gender as a risk factor provided better statistical power and yielded a statistically significant, but small, effect. This may not be surprising as research has shown that adult PTSD rates are higher among females. Indeed, many of our findings were similar to the wider literature on the correlates of PTSD in adults.

Interestingly, studies explored risk factors that yielded large effect sizes and showed a strong relationship with parental PTSD, including co-morbid psychological and functioning variables, such as depression, anxiety, general distress and stress. Research has demonstrated that parental distress and pre-trauma psychopathology predict later adult PTSD symptoms. Typically, psychopathology was measured after trauma, which only provided a cross-sectional picture of parental psychological reactions to their child’s medical event. This
means that our findings may reflect comorbid associations rather than evidence of risk factors per se. It is well known that PTSD is comorbid with other presentations, such as depression and anxiety, and our parental findings agreed. It has also been argued that PTSD can resemble a more general psychopathological reaction to trauma\textsuperscript{36}, which could help to explain the high correlations between PTSD and other psychological difficulties. It is possible that changes to parents’ general psychological functioning in response to children’s medical events can be explained by overlapping constructs. Moreover, the shared method variance of those psychological constructs could better explain the large effects found in these risk factors. Indeed, some items included in self-report measures of PTSD and depression are similar, such as sleep and irritability, while other items are more distinct. Studies that measure parents’ psychological functioning before and after paediatric medical events, and more longitudinal research, may shed greater light on this.

Medical risk factors were significant, yet small in effect, which were similar to a review\textsuperscript{8} that found similar medical factors with small effects. The difference in the current meta-analysis was that illness severity was significant, but small in effect, and should be interpreted with caution, given the sensitivity analysis. Medical factors have varied with regard to their strength as risk or protective factors,\textsuperscript{37} highlighting the importance of not relying on medical treatment or prognostic factors as a reliable indicator of possible parental PTSD.

Although small in effect, child PTSD, being a mother, perceived social support and previous trauma were all associated with parental trauma responses to their child’s medical event. This may not be surprising as social support is well known to play a role in PTSD after various types of trauma.\textsuperscript{38} The parents’ emotional reactions during the medical event were not statistically significant, but were only measured in four studies and mainly using questionnaires that lacked validity and reliability. Cognitive models of PTSD in adults\textsuperscript{39} and
the model of Paediatric Medical Traumatic Stress\textsuperscript{37} have highlighted the role that subjective appraisals of traumas and medical events played in the development of PTSD. This suggests that subjective appraisals of life-threatening experiences should be further studied to identify the impact that such appraisals have on whole family functioning and the risk level of trauma responses.

This meta-analysis demonstrates that a high number of parents developed PTSD when their children experienced a medical event and that there were high rates of comorbid anxiety and depression. These findings were consistent with standards for the psychosocial care of children with cancer,\textsuperscript{40} which stress that children and their families should have systematic mental health need assessments and be offered interventions. Clinicians need to be aware of the risk factors highlighted in the current study during any assessments or screening processes after paediatric medical events. We have indicated risk factors that could be explored and these could also inform the development of tools that highlight those families at increased risk of developing trauma responses. We focused on studies that highlighted subjective experiences, rather than medical variables that were significant, but often small, in effect.

**Limitations**

Several limitations should be considered. Only published research was included, the study was limited to papers published in English and the level of heterogeneity was significant. Several studies had a high risk of bias and we attempted to mitigate that effect with sensitivity analysis. Finally, the trajectory of the parents’ PTSD symptoms were not studied and the prevalence rates and risk factors may have differed over time.
CONCLUSION

This meta-analysis showed that a high percentage of parents developed PTSD following paediatric medical events. This was significant, as untreated PTSD can have serious complications for children, parents and families. Certain risk factors were identified, and these provide key indicators that can be used by paediatric clinical teams to highlight those families who are more likely to develop PTSD following paediatric medical events.

REFERENCES


**Figure Legends**

Figure 1: PRISMA flowchart of studies identified, screened and included in the final meta-analysis

Figure 2: Forest plot showing the prevalence of parental PTSD according to the type of paediatric medical event