The burden of mental ill health associated with childhood maltreatment in the UK, using The Health Improvement Network database

chandan, Joht; Thomas, Tom; Gokhale, Krishna; Bandyopadhyay, Siddhartha; Taylor, Julie; Nirantharakumar, Krishnarajah

[Link to publication on Research at Birmingham portal](#)

The burden of mental ill health associated with childhood maltreatment in the United Kingdom: A retrospective cohort study using 'The Health Improvement Network' database

Running Title: The association between childhood maltreatment and mental ill health

Author Names:

Joht Singh Chandan, Tom Thomas, Krishna Gokhale, Siddhartha Bandyopadhyay*, Julie Taylor*, Krishnarajah Nirantharakumar*

*Equal Contribution

Authors Addresses and Positions:

Dr Joht Singh Chandan MBBS
Academic Clinical Fellow in Public Health
Institute of Applied Health Research, College of Medical and Dental Sciences, University of Birmingham, B152TT

Dr Tom Thomas MBBS
Clinical Research Fellow
Institute of Applied Health Research, College of Medical and Dental Sciences, University of Birmingham, B152TT

Mr Krishna Margadhamane Gokhale MSc
Research Fellow
Institute of Applied Health Research, College of Medical and Dental Sciences, University of Birmingham, B152TT

Professor Siddhartha Bandyopadhyay PhD (Full Professor)
Professor of Economics and Director of the Centre of Crime, Justice and Policing
The Department of Economics, University of Birmingham, B152TT

Corresponding author:
Professor Julie Taylor PhD (Full Professor)
Professor of Child Protection
School of Nursing, College of Medical and Dental Sciences, University of Birmingham, B152TT
Birmingham Women's and Children's Hospitals NHS Foundation Trust, Birmingham.
j.taylor.1@bham.ac.uk

Dr Krishnarajah Nirantharakumar MD
Senior Clinical Lecturer & UKRI Innovation Clinical Fellow
Midlands Health Data Research UK & Institute of Applied Health Research, College of Medical and
Dental Sciences, University of Birmingham, B152TT

STRUCTURED ABSTRACT

Background: Childhood maltreatment is a global public health, human rights and moral issue that is associated with a vast mental health burden. This study explores the association of childhood maltreatment with the development of mental ill health and initiation of new prescriptions for mental ill health.

Methods: Retrospective cohort study using the UK primary care database, 'The Health Improvement Network' between 1st January 1995- 31st December 2018. 217 758 patients of all ages who had experienced childhood maltreatment or related concerns (exposed patients) were matched to 423 410 unexposed patients. Outcomes of interest were depression, anxiety or serious mental illness or initiation of a prescription drug used to treat mental ill health. The average age at cohort entry was 12 years and length of follow-up was 2.7 years.

Outcomes: At study entry, the exposed cohort had an increased likelihood of having experienced mental ill health (OR 3·07; 95% CI 3·00-3·15) and mental ill health related prescription (OR 1·27; 95% CI 1·23-1·31) compared to the unexposed group. In keeping with previous literature, of individuals without pre-existing mental ill health, the exposed group developed 11 665 new diagnoses (Incidence Rate (IR) 16·8 per 1 000 person years) compared to 15 301 (IR 8·3 per 1 000 person years) in the unexposed group. This translated to an adjusted IRR 2·14 (95% CI 2·08-2·19). There were 30 911 new prescriptions (IR 46·5 per 1 000 person years) within the exposed group compared to 36 390 (IR 20·5 per 1 000 person years) in the unexposed group (IRR 2·44 (95% CI 2·40-2·48)). The relationship with the development of mental ill health became even more apparent when examining the officially confirmed cases of maltreatment.

Interpretation: Childhood maltreatment is thought to affect one in three children; therefore, a doubling of the risk of developing mental ill health among these individuals represents a substantial contribution to the mental ill health burden in the UK. It is imperative that public health approaches, including those aimed at preventing and detecting childhood maltreatment and its associated negative consequences, are implemented in order to prevent mental ill health.

Funding: No funding

Keywords: childhood maltreatment, depression, anxiety, schizophrenia, bipolar disease, epidemiology

RESEARCH IN CONTEXT

Evidence before this study

A systematic literature search on Pubmed from database inception to May 2019 was conducted. The broad terms included were "child abuse" OR "child maltreatment" OR "adverse childhood experience*" AND "mental illness" OR "mental ill health" OR "depression" OR "anxiety" OR "serious mental illness" OR "schizophrenia" OR "bipolar" OR psychos*". There were no age or language restrictions. We reviewed reference lists and forward citations of all articles pertinent to the study objectives. We identified a large body of data derived from cross-sectional and case-control studies demonstrating an association between childhood maltreatment and recurrent depressive episodes, anxiety, eating disorders, post-traumatic stress, sleep disorders and suicide attempts. A 2016 review identified only eight global cohort studies based in the US, New Zealand and Australia which reported a positive association between exposure to any type of maltreatment and subsequent development of depression and anxiety. A more recent review exploring the development of depression and anxiety following adverse childhood experiences, only identified one European cross-sectional study. We also identified, a Swedish birth cohort and a Danish registry study demonstrating positive associations between adverse childhood experiences and childhood maltreatment with the development of depression respectively. No other global cohort studies have examined the relationship between childhood maltreatment and the subsequent development of schizophrenia, bipolar disorder or psychosis. Additionally, apart from the previously mentioned Swedish birth cohort study which also demonstrated a positive association between adverse childhood experiences and the future use of psychotropic drugs, there were no other global cohort studies examining the association between childhood maltreatment and the initiation of mental ill health prescriptions.

Added value of this study

To our knowledge, this is the first attempt to synthesise data exploring the relationship between childhood maltreatment and the development of mental ill health (stratified by depression, anxiety and SMI (defined as psychoses, schizophrenia and bipolar disorder in the Quality Outcomes Framework)), by both diagnosis (documented by clinical code) and prescription in a UK retrospective cohort derived from medical records. By using a large UK primary care dataset between 1995 and 2018, we identified a doubling in the risk of developing mental ill health and a higher odds ratio of having a history of mental ill health at study entry in individuals who had been exposed to childhood maltreatment compared to those with no such recorded exposure. Considering, childhood maltreatment is thought to affect one in three children, our study clearly highlights a large burden of mental ill health in the UK that could be attributable to childhood maltreatment. There is also a substantial risk of requiring prescription treatment for mental ill health in the cohort of those who have experienced childhood maltreatment.

Implications of all the available evidence

Our findings along with evidence from other global studies demonstrates the substantial burden of mental ill health following child maltreatment. The findings are impactful for the UK, as they demonstrate how imperative it is that public health approaches, including those aimed at preventing and detecting childhood maltreatment and its associated negative consequences, are urgently implemented in order to reduce the burden of mental ill health.

INTRODUCTION

Childhood maltreatment, defined as any form of physical, sexual or emotional abuse and neglect, is a global public health and human rights issue affecting more than one in three children (<18 years old).[1] The downstream effects of childhood adversity either in the form of childhood maltreatment or living in a dysfunctional household have been demonstrated in multiple studies exploring the long term effects of adverse childhood experiences.[3] The effect of childhood maltreatment on mental health has been demonstrated in previous meta-analyses.[4–7]

Reviews of observational data have demonstrated an association between childhood maltreatment and recurrent depressive episodes.[4] Childhood sexual abuse has been associated with the development of depression, anxiety, eating disorders, post-traumatic stress, sleep disorders, and suicide attempts.[5,6,9] However, these reviews largely consisted of cross-sectional and case-control studies where individuals recalled their experiences and therefore were prone to recall bias.[10] A meta-analysis[7] tried to mitigate this bias by identifying only cohort studies where exposure and outcome were not recalled by the participants. That review identified 8 studies done in the USA, New Zealand and Australia which demonstrated a pooled odds ratio (OR) between exposure to any type of maltreatment and subsequent development of depression to be 2·03 (95% CI 1·37-3·01) and of anxiety to be 2·70 (95% CI 2·10-3·47). The generalisability of its findings were limited by the lack of cohort studies exploring this association in other global regions, a limitation accepted in another review on the topic with cohorts originating from North America.[11] Considering the variation in population structure, available support during early years and child protection systems, it is not clear whether these results would be generalisable to the UK.[12] The authors[11] also state that the use of cohorts which utilise routinely collected data might mainly identify severely affected patients who have made it to the point of requiring assistance, possibly underestimating their pooled effect size. An alternative approach is to broaden the definition of maltreatment through including the household dysfunction elements of adverse childhood experiences. A meta-analysis[3] identified a similarly positive risk with the diagnosis of depression (OR 4·40 (95% CI 3·54-5·46)) and anxiety (OR 3·70 (95% CI 2·62-5·22)) in adulthood for those who had four or more adverse childhood experiences. However, this meta-analysis also mostly consisted of North American studies with one cross-sectional European study included from Finland (n=4 076).[13] A birth cohort study of Swedish children noted additional markers of household adversity (excluding physical, sexual or emotional abuse, neglect and living in a household with domestic abuse) and found that they were associated with depression and future use of psychotropic medications.[14,15] A study of individuals on a Danish national register who had experienced childhood abuse found an increased risk of developing unipolar depression, however, the study did not explore the association with anxiety or SMI and had a relatively small sample

size.[16] A UK study using data from the Avon longitudinal study of parents and children attempted to explore this relationship but focussed specifically on the impact of bullying in conjunction with maltreatment reported by the child's mother (possibly under-reported) as a risk factor for depression and anxiety in young adults.[17] That study found no association between maltreatment alone and risk of anxiety or depression, but it included only 341 adults who had a past history of maltreatment. Few studies have explored the association between the development of serious mental illness (SMI: psychoses, schizophrenia and bipolar disorder) following childhood maltreatment. From those that exist, exposure to childhood maltreatment seems to predict unfavourable clinical outcomes in those with SMI,[18] suggesting the importance of early intervention in these children's lives to prevent adverse outcomes.

Thus, an improved global understanding of the impact of childhood maltreatment via analysis of other national cohorts is needed. Therefore, we conducted the first UK retrospective cohort study using 'The Health Improvement Network' (THIN) dataset exploring the association between officially confirmed childhood maltreatment and maltreatment related concerns (possible/suspected maltreatment) with the subsequent development of depression, anxiety and SMI.

METHODS

Study design, population and data source

This study is a population based, retrospective open cohort study using the THIN database. The study period was between 1st January 1995 and 31st December 2018. An open cohort study allows for patients to enter and exit the study at different time points, with each individual patient only contributing person years of follow-up from the time of cohort entry (index date) to the time they leave the cohort (exit date).

THIN database consists of a sample of UK electronic medical records taken from 787 general practices using the Vision software system. The database is representative of the UK population in terms of demographic structure and prevalence of key comorbidities.[19] Symptoms, examinations, and diagnoses in THIN are recorded using a hierarchical clinical coding system called Read codes.[20] The first coding level groups similar conditions together (e.g. E refers to mental disorders). Subsequent levels of the hierarchy add additional or more specific information (e.g. Eu2..00 Schizophrenia, schizotypal and delusional disorders, Eu20000 [X] Paranoid schizophrenia).

In this study we utilised medical records taken from all 787 general practices present in THIN during the study period. There were in total 11 831 850 patients who could have contributed from these practices. As entry into the database relies on use of Vision software, the number of contributing practices can vary over time. In order to reduce under-recording of events, general practices were included 12 months following their instalment of electronic practice records or from the practice's acceptable mortality recording date.[21]

Exposure and outcome definition

The purpose of this study was to compare exposed patients (those with a code identifying officially confirmed childhood maltreatment or a maltreatment related concern code) to unexposed patients (those without such codes) and then calculate their risk of developing mental ill health defined through Read codes (composite measure; anxiety, depression and SMI) or the requirement of an incident prescription of medication used to treat mental ill health (composite measure; anti-depressants, anxiolytics and anti-psychotics). In addition, this study also examined the odds ratio of having mental ill health (defined through Read codes and relevant prescription medications) at the point of cohort entry (baseline) between the exposed and unexposed groups.

Codes relating to officially confirmed exposure to child maltreatment and mental ill health were selected with the assistance of general practitioners and a public health clinician with a psychiatry background (read code selection methodology- appendix p2). Although there has been no prior published validation of these code lists, we anticipated depression and SMI to be well coded as they form part of the Quality Outcomes Framework,[22] (performance indicators linked to general practice payments in the UK). In addition, we expected anxiety to be well coded as previous studies have demonstrated a similar prevalence of anxiety measured in THIN database compared to pre-existing self-reported national survey data.[23,24] In order to act as an alternative form of validation for the diagnosis of mental ill health, we also explored prescriptions used to treat mental ill health as an outcome measure of interest. The prescription medication lists used to treat mental ill health were defined using the British National Formulary chapters specific to each condition.[25] Last, there have been recent attempts to improve the coding relating to childhood maltreatment in primary care[26]. Maltreatment related concern codes were adapted from previous research conducted using THIN and consist of codes designed to capture clinical concern relating to suspected or possible maltreatment[27].

Read code lists relating to exposure terms and outcomes are provided (Appendix p3).

Selection of unexposed group

Each exposed patient was matched with up to two unexposed control patients, who had no previously documented Read code relating to the exposure. Controls were taken from the same general practice and were matched by age at index date (+/- one year) and gender.

Follow-up period

The index date for those in the exposed group was the date of the first Read code relating to exposure or when they became eligible to enter the study for those with a previous history of exposure (prevalent cases). Therefore, prevalent cases could be adults at cohort entry (index date). However, their episode of maltreatment must have been recorded prior to their 18th birthday. To mitigate immortality time bias[28], the same index date was assigned to the corresponding unexposed patient. The follow-up period for each patient was from the index date until the exit date. Exit date is defined as the earliest of the following dates:

study end date, last date of data collection from a given general practice, date patient transferred from general practice, date of death or date the outcome of interest occurred.

Co-variates

Co-variates considered in our modelling were selected due to their independent relationship with the development of mental ill health.[29] These included: age, gender and Townsend deprivation score[30] which were captured at baseline. The Townsend score is a measure of material deprivation within a locality, incorporating information on unemployment, household overcrowding and car/home ownership;[30] a higher score indicates a greater level of socioeconomic deprivation.

Data analysis

STATA version 15.1 MP/4 software (Statacorp 2017) was used to conduct all analyses.

Categorical baseline data were described using proportions, continuous data were described using means or median with standard deviations or inter quartile range. Missing data are highlighted in relevant baseline characteristic tables. Where there were missing data in our covariates, they were treated as a separate missing category and included in the final analysis.

To describe the presence of mental ill health at baseline, we used logistic regression to estimate unadjusted odds ratio (OR) and adjusted OR (aOR), following adjustment for key covariates (age, gender, Townsend deprivation score).

In order to calculate an incidence rate ((IR) per 1 000 person years) for each of the outcomes of interest, patients with pre-existing illness (defined as a mental ill health code or prescription used to treat mental ill health) were excluded to ensure the IR reflected outcomes which occurred following cohort entry. Poisson regression offsetting for person years of follow-up was then used to calculate an incidence rate ratio (IRR) for each outcome of interest during the study period. Following adjustment for the co-variates, we calculated and present an adjusted IRR (aIRR). ORs and IRRs are presented with 95% confidence intervals with statistical significance set at $p < 0.05$.

An initial sensitivity analysis was conducted to explore if findings differed when only looking at officially confirmed maltreatment codes. A second sensitivity analysis was conducted, isolating incident only cases (where the exposure occurred during the study period) compared to their respective controls. A third sensitivity analysis was conducted to examine if the outcomes differed when the groups were disaggregated (rather than adjusted for) by gender. Additionally, in order to examine the impact of gender on the findings, an interaction term between gender and the exposure were added to the logistic and Poisson regression models.

Patient and public involvement

No patients were actively involved in setting the research question, outcome measures nor involved in the design of the study. Patients were not involved in interpretation or write up of the results, nor are there plans for the results to be disseminated to the patient community affected by this research.

Ethical Approval

Anonymised data were used throughout the study provided by the data provider to the University of Birmingham. Studies using The Health Improvement Network (THIN) database have had initial ethical approval from the NHS South-East Multicentre Research Ethics Committee, subject to prior independent scientific review. The Scientific Review Committee (IQVIA) approved the study protocol (SRC Reference Number: SRC18THIN034) prior to its undertaking.

RESULTS

Of the total database cohort of 11 831 850 patients, we identified 217 758 patients who had any recorded childhood maltreatment. These patients were matched to 423 410 unexposed controls (no recorded exposure) who met the matching criteria. The median follow-up period was shorter in the exposed group (1·8 years) compared to the unexposed (3·2 years). Patients in the exposed cohort were more likely to be transferred out of the practice (45·7% vs. 27·7%) and therefore had a shorter follow-up in comparison to the unexposed group. Mean age at cohort entry (12 years) and distribution of gender (47.3% male) were similar between the groups as a result of matching. The mean age of recorded exposure to childhood maltreatment in the exposed group was 7 years. There was missing data for body mass index, drinking status and smoking status. However, where recorded, smoking was twice as common at baseline in the exposed group (13·1%) compared to the unexposed group (6·7%). A greater proportion of participants in the exposed group were in the most socio-economically deprived Townsend quintile (22.9%) compared to unexposed group (15.5%). Further details are noted in table 1.

There were 18 502 patients (8·5%) in the exposed group who had a diagnosis of mental ill health at cohort entry compared to 15 314 (3·6%) in the unexposed group. Following adjustment for co-variates this translated to an aOR of 3·07 (95% CI 3·00-3·15). The increased risk was most notable in the exposed group for a pre-existing diagnosis of depression (aOR 3·33; 95% CI 3·23-3·44) and SMI (aOR 5·80; 95% CI 5·26-6·39). 8 572 exposed patients (3·9%) had a prescription for mental ill health treatment in the year preceding their study entry compared to 13 031 (3·1%) in the unexposed group (aOR 1·27; 95% CI 1·23-1·31). Further results can be seen in table 2 and figure 1.

During the study period there were 11 665 (5·9%) new diagnoses of mental ill health in the exposed cohort relating to an IR of 16·8 per 1 000 person years compared to 8·3 per 1 000 person years (15 301 (3·7%) new recorded diagnoses) in the unexposed cohort. This

translated to an increased aIRR of 2·14 (95% CI 2·08-2·19). The results were similar when exploring incident prescriptions. The exposed cohort included 30 911 (IR 46·5 per 1 000 person years) patients (14.8%) who received a new prescription for any type of mental ill health compared to 36 390 patients (8.9%) in the unexposed group (IR 20·5 per 1 000 person years) resulting in an increased aIRR of 2·44 (95% CI 2·40-2·48). When exploring by all types of mental ill health and prescription, the exposed group had a significantly increased risk of both diagnosis and prescription (anxiety: 1·71 (95% CI 1·65-1·77), depression: 2·31 (95% CI 2·24-2·38), SMI: 3·90 (95% CI 3·45-4·31), anxiolytic: 2·12 (95% CI 2·06-2·19), anti-depressant: 2·66 (95% CI 2·62-2·71), anti-psychotic: 2·08 (95% CI 2·03-2·14)). These results can be seen in table 3 and figure 2.

We identified within the total cohort that 36 607 (16·8% of total exposed cohort) patients had confirmatory codes relating to childhood maltreatment. These patients were matched to 73 034 (17·2% of total unexposed cohort) unexposed patients (characteristics are described in appendix p56). Notably, this cohort had a significantly higher average age (19 years) at study entry compared to the main cohort. When the treatment group contained only the officially confirmed maltreatment coded patients, we noted a considerable increase in the effect sizes of all measured outcomes. Of particular note, this cohort had a higher prevalence of mental illness at study entry, with 7 730 (21·1% of the exposed group) having any type of mental ill health compared to 5 742 (7·9% in the unexposed group) translating into an aOR of 3·91; 95% CI 3·75-4·08. Additionally, during follow-up the effect size of the composite mental ill health diagnosis (aIRR 2·67; 95% CI 2·54-2·80) and incident prescriptions (aIRR 3·02 (2·93-3·12) increased compared to the cohort that consisted of both confirmed and indicative diagnosis of childhood maltreatment. The most noticeable specific increase was the incidence of initiation of anti-depressant prescriptions (aIRR 3·48; 95% CI 3·37-3·59). Further details can be found in appendix p57.

Of the total exposed cohort 84 687 (38·9% of total exposed cohort) patients had a child maltreatment code entered during the study period (incident cohort), and were matched to 159 171 (37·6% of total unexposed cohort) unexposed cohort (characteristics described in appendix p59). The mean age of both groups was 7 years. In this exposed group, the odds ratio of having mental ill health (aOR 2·64; 95% CI 2·38-2·92) or a prescription for a mental ill health related drug (aOR 3·61; 95% CI 3·25-4·01) was greater at baseline compared to the unexposed group. During the study period, 2 672 new diagnoses of a mental ill health (IR 8·8 per 1 000 person years) were identified in the exposed group (3.1%) compared to 3 207 diagnoses (2.0%; IR 4·7 per 1 000 person years) in the unexposed group (aIRR 1·91; 95% CI 1·81-2·01). This effect was similar for new prescriptions of medications used to treat mental ill health (aIRR 1·87; 95% CI 1·80-1·94). Further details can be found in appendix p60.

Our third sensitivity analysis was to examine outcomes by gender. Both male and female patients experienced a higher odds ratio of having mental ill health at cohort entry if they had experienced childhood maltreatment (male: aOR 3·18 (3·03-3·32); female: aOR 3·02 (2·93-3·11)), as well as a subsequently higher risk of developing mental illness following exposure to childhood maltreatment (male: aIRR 2·21 (2·11-2·30); female: aIRR 2·11 (2·04-2·17)). Although the IR of developing any mental ill health was higher in the total female cohort (exposed and unexposed population), the effects of childhood maltreatment was similar between male and female patients who had experienced childhood maltreatment in

comparison to their controls. When we added an interaction term to allow the effect size to vary by sex within a single model, following adjustment, we noted no statistical difference (p<0.05) in the diagnosis of mental ill health between male and female exposed patients. However, we identified significant differences for the following outcomes: all mental ill health prescriptions, anti-depressants and anti-psychotics at baseline; initiation of anti-psychotics and anti-depressants during the study period. Further details can be seen from appendix p61.

DISCUSSION

To our knowledge, this is the first attempt to synthesise data exploring the relationship between childhood maltreatment and the development of mental ill health in a UK retrospective cohort derived from medical records. Our study demonstrates that exposure to childhood maltreatment is associated with double the risk of developing a diagnosed mental ill health and more than doubles the requirement for prescription medications used to treat mental ill health during the short median follow-up of 2·7 years in this study. Patients who present with maltreatment had a higher odds ratio of having mental ill health at baseline. When analysing officially confirmed maltreatment cases only, this risk increased significantly with a tripling of risk in requiring prescription medications. The risk also persists when analysing only patients who experienced childhood maltreatment during the study period.

Our results support findings from the meta-analyses documented with cohorts largely derived from North America.[7,11] Our overall findings demonstrated similarly positive effect sizes of an aIRR of 2·13 (2·07-2·18) and 1·73 (1·68-1·78) for depression and anxiety respectively. However, as our study was conducted in the UK, our results may not be directly comparable, and there are also differences in the methods we have utilised to isolate exposures and outcomes. Interestingly, our third sensitivity analysis demonstrated little difference in effect size between the risk of being given a diagnosis of a mental ill health following childhood maltreatment in the male and female exposed groups which agrees with known literature.[31] However, we did find differences in the risk of new initiation of mental ill health prescriptions which has previously been untested between male and female exposed patients.

The findings are important in a UK setting where there is a professional and moral obligation to report suspected child maltreatment.[32]. The burden of mental ill health on disability adjusted life years within the UK is substantial.[33] A major UK survey conducted by the National Health Service (NHS) demonstrated that an eighth of 5 to 19-year olds had at least one mental disorder, with the prevalence increasing by age.[34] Adult mental ill health is increasing over time within the UK;[35] it is imperative to understand the contribution of childhood maltreatment to this burden. The NSPCC reported that one in four 18-24 year olds stated they had experienced some form of severe maltreatment in their childhood.[36] From our study, this could translate into a considerable proportion of adults developing mental ill health in the future. Therefore, there is an important public health message to focus not only on approaches that prevent or detect childhood maltreatment but also to explore methods of prevention and detection of mental ill health in those who have experienced childhood maltreatment. Building resilience in children, families, local services

and communities of those at risk might be a way of improving mental health outcomes.[37,38] A broad public health approach is needed that addresses multiple facets on an individual's life (such as: reducing school time absence; diversion from the youth justice system and improving the rates of children in education, training and employment)[39,40] as is community action which will indirectly affect the child (including asset based, social network and support based approaches).[38]

The use of electronic health records for epidemiological research largely relies upon the accuracy of documenting by the healthcare professionals contributing to the dataset. A limitation of using such records is that no study has validated the Read codes relating to childhood maltreatment and mental ill health in UK primary care,[41] however, work has been done to try and improve maltreatment-related coding in primary care.[26] We selected the Read codes relating to outcomes with the assistance of individuals trained in psychiatry, and to mitigate any misclassification risk, we also conducted the analysis pertaining to prescription data which is coded accurately. On the other hand, as childhood maltreatment coding has not been validated, and given a likely a hidden burden of abuse, some members of the unexposed group might have been exposed to maltreatment. Therefore, it is possible our findings are an underestimate of the true effect size. Considering the possibility of improved coding during the study period, there was an absence of evidence in our data to suggest this affected the effect size witnessed in our main results (appendix p66). Alternatively, signs of maltreatment might have been overlooked in some families, especially where education and class may have misled those who might have identified it. Although there is an association between poverty and maltreatment,[42] there remains a leaning towards over-surveillance of the poor. Future research should consider patient and public involvement to shape study design and inform interpretation of the results.

Another important consideration is the possibility that if maltreatment against a child was recorded by their healthcare practitioner, it could mean that the maltreatment was particularly severe; however, as we used non-granular codes we were unable to assess this. It is also possible that the most severe cases are unable to report their concerns owing to concealment of the abuse or because of fear of telling another individual. To mitigate this, we utilised the maltreatment related code lists to identify other factors relating to maltreatment that could identify children who may be at risk of direct maltreatment to ensure they are captured. Our sensitivity analysis showed that officially confirmed childhood maltreatment led to increased effect sizes. One of the limitations in this study was the inability to conduct further subgroup analysis by type of abuse.

We observed the median follow-up time in the exposed group was shorter due to a higher proportion of patients transferring to a different general practice. Despite the shorter follow-up period, there was evidence of increased risk for mental ill health in the exposed patients. Given that the effects of child maltreatment may present to primary care much later in life, there is a possibility that the results may have under-estimated the effects of childhood maltreatment. Even though we were able to account for the impact of recorded socio-economic deprivation, an NHS England review[43] of barriers to primary care access highlighted that vulnerable populations such as travellers, migrants and the homeless may

still struggle to register with a GP practice. Therefore, it is likely that our analysis was unable to capture the experiences of this population.

In conclusion, our study showed increased risk of developing mental ill health following child maltreatment. Public health approaches, including preventing and detecting childhood maltreatment and its associated negative consequences, are needed to prevent mental ill health.

Contributors

This study contributed to the PhD thesis for the main author JSC. JSC, TT, KG, JT, SB and KN were responsible for initial conception of the study. JSC, KG and TT were responsible for data extraction, analysis and first draft of the manuscript. The final manuscript was authorised by all the authors with JT providing expert knowledge on childhood maltreatment and SB with KN providing methodological expertise.

Funding

There is no funding to declare in this study.

Declaration of Interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

FIGURE LEGENDS

Figure 1: The odds ratio for having mental ill health at study entry in those exposed in comparison to those unexposed to childhood maltreatment

Figure 2: The risk of developing mental ill health in those exposed and unexposed to childhood maltreatment

REFERENCES

1   World Health Organization. Violence Info – Child maltreatment. 2017.http://apps.who.int/violence-info/child-maltreatment/ (accessed 29 Jul2019).
2   World Health Organization (WHO). Child Maltreatment. 2017 doi:10.4135/9781412963978.n22.

3   Hughes K, Bellis MA, Hardcastle KA *et al.* The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *Lancet Public Heal* 2017; **2**: e356–e366.

4   Nanni V, Uher R, Danese A. Childhood Maltreatment Predicts Unfavorable Course of Illness and Treatment Outcome in Depression: A Meta-Analysis. *Am J Psychiatry* 2012; **169**: 141–151.

5   Maniglio R. Child sexual abuse in the etiology of depression: A systematic review of reviews. *Depress Anxiety* 2010; **27**: 631–642.

6   Maniglio R. Child Sexual Abuse in the Etiology of Anxiety Disorders. *Trauma, Violence, Abus* 2013; **14**: 96–112.

7   Li M, D'Arcy C, Meng X. Maltreatment in childhood substantially increases the risk of adult depression and anxiety in prospective cohort studies: systematic review, meta-analysis, and proportional attributable fractions. *Psychol Med* 2016; **46**: 717–730.

8   Jaworska-Andryszewska P, Rybakowski JK. Childhood trauma in mood disorders: Neurobiological mechanisms and implications for treatment. *Pharmacol Reports* 2019; **71**: 112–120.

9   Chen LP, Murad MH, Paras ML, Colbenson KM, Sattler AL, Goranson EN *et al.* Sexual Abuse and Lifetime Diagnosis of Psychiatric Disorders: Systematic Review and Meta-analysis. *Mayo Clin Proc* 2010; **85**: 618–629.

10   Sedgwick P. What is recall bias? *BMJ* 2012; **344**: e3519–e3519.

11   Gallo EAG, Munhoz TN, Loret de Mola C, Murray J. Gender differences in the effects of childhood maltreatment on adult depression and anxiety: A systematic review and meta-analysis. *Child Abuse Negl* 2018; **79**: 107–114.

12   Munro ER, Manful E. Safeguarding children : a comparison of England ' s data with that of Australia , Norway and the United States. 2012.https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/183946/DFE-RR198.pdf (accessed 2 Aug2019).

13   Pirkola S, Isometsä E, Aro H, Kestilä L, Hämäläinen J, Veijola J *et al.* Childhood adversities as risk factors for adult mental disorders. *Soc Psychiatry Psychiatr Epidemiol* 2005; **40**: 769–777.

14   Björkenstam E, Hjern A, Mittendorfer-Rutz E, Vinnerljung B, Hallqvist J, Ljung R. Multi-exposure and clustering of adverse childhood experiences, socioeconomic differences and psychotropic medication in young adults. *PLoS One* 2013; **8**: e53551.

15   Björkenstam E, Vinnerljung B, Hjern A. Impact of childhood adversities on depression in early adulthood: A longitudinal cohort study of 478,141 individuals in Sweden. *J Affect Disord* 2017; **223**: 95–100.

16   Dahl SK, Larsen JT, Petersen L *et al.* Early adversity and risk for moderate to severe unipolar depressive disorder in adolescence and adulthood: A register-based study of 978,647 individuals. *J Affect Disord* 2017; **214**: 122–129.

17   Lereya ST, Copeland WE, Costello EJ, Wolke D. Adult mental health consequences of peer bullying and maltreatment in childhood: two cohorts in two countries. *The Lancet Psychiatry* 2015; **2**: 524–531.

18   Agnew-Blais J, Danese A. Childhood maltreatment and unfavourable clinical outcomes in bipolar disorder: a systematic review and meta-analysis. *The lancet Psychiatry* 2016; **3**: 342–9.

19   Blak BT, Thompson M, Dattani H, Bourke A. Generalisability of The Health Improvement Network (THIN) database: demographics, chronic disease prevalence

and mortality rates. *Inform Prim Care* 2011; **19**: 251–5.

20 Booth N. What are the Read Codes? *Health Libr Rev* 1994; **11**: 177–82.

21 Maguire A, Blak BT, Thompson M. The importance of defining periods of complete mortality reporting for research using automated data from primary care. *Pharmacoepidemiol Drug Saf* 2009; **18**: 76–83.

22 NHS Digital. Quality and Outcomes Framework (QOF) business rules v42 2019-2020 baseline release - NHS Digital. 2019.https://digital.nhs.uk/data-and-information/data-collections-and-data-sets/data-collections/quality-and-outcomes-framework-qof/quality-and-outcome-framework-qof-business-rules/quality-and-outcomes-framework-qof-business-rules-v42-2019-2020-baseline-releas (accessed 31 Jul2019).

23 Mcmanus S, Bebbington P, Jenkins R, Brugha T. Mental health and wellbeing in England: Adult Psychiatric Morbidity Survey 2014. *Apms 2014* 2016; : 1–405.

24 Martin-Merino E, Ruigomez A, Wallander M-A, Johansson S, Garcia-Rodriguez LA. Prevalence, incidence, morbidity and treatment patterns in a cohort of patients diagnosed with anxiety in UK primary care. *Fam Pract* 2010; **27**: 9–16.

25 NICE. BNF: British National Formulary - NICE. 2019.https://bnf.nice.org.uk/ (accessed 20 May2019).

26 McGovern AP, Woodman J, Allister J *et al.* A simple clinical coding strategy to improve recording of child maltreatment concerns: an audit study. *J Innov Heal informatics* 2015; **22**: 227–34.

27 Woodman J, Freemantle N, Allister J, de Lusignan S, Gilbert R, Petersen I. Variation in recorded child maltreatment concerns in UK primary care records: a cohort study using The Health Improvement Network (THIN) database. *PLoS One* 2012; **7**: e49808.

28 Lévesque LE, Hanley JA, Kezouh A, Suissa S. Problem of immortal time bias in cohort studies: example using statins for preventing progression of diabetes. *BMJ* 2010; **340**: b5087.

29 Baker C. Mental health statistics for England: orevelance, services and funding. *House Commons Libr* 2018; : 1–31.

30 Townsend P, Phillimore P, Beattie A. Health and deprivation: inequality and the North. 1988. *London Croom Helm Google Sch* 1988.

31 Gallo EAG, Munhoz TN, Loret de Mola C, Murray J. Gender differences in the effects of childhood maltreatment on adult depression and anxiety: A systematic review and meta-analysis. *Child Abuse Negl* 2018; **79**: 107–114.

32 Gavazzi J. Child Abuse Reporting Guidelines: Ethical and Legal Issues. 2015.https://www.slideshare.net/psychbuilder/child-abuse-reporting-guidelines-ethical-and-legal-issues (accessed 31 Jul2019).

33 Steel N, Ford JA, Newton JN *et al.* Changes in health in the countries of the UK and 150 English Local Authority areas 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet (London, England)* 2018; **392**: 1647–1661.

34 NHS Digital. Mental Health of Children and Young People in England, 2017 [PAS] - NHS Digital. 2017.https://digital.nhs.uk/data-and-information/publications/statistical/mental-health-of-children-and-young-people-in-england/2017/2017 (accessed 7 Apr2019).

35 Office for national statistics. Counts and percentages of adults with a mental illness, by occupation, age, sex and ethnicity, between May and July 2012 to 2017 - Office for National Statistics. 2018.https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/

mentalhealth/adhocs/008200countsandpercentagesofadultswithamentalillnessbyocc
upationagesexandethnicitybetweenmayandjuly2012to2017 (accessed 7 Apr2019).

36   Radford L, Corral S, Bradley C, Fisher H, Bassett C, Howat N *et al.* Child abuse and
     neglect in the UK today. .

37   Friedli L. Mental health, resilience and inequalities.
     2009http://www.euro.who.int/pubrequest (accessed 7 Apr2019).

38   Public Health England, NHS England. A guide to community-centred approaches for
     health and wellbeing - FULL REPORT. 2015www.facebook.com/PublicHealthEngland
     (accessed 29 Jul2019).

39   Association for Young People's Health. A public health approach to promoting young
     people ' s resilience. 2016www.youngpeopleshealth.org.uk (accessed 7 Apr2019).

40   Early Intervention Foundation. Search | EIF Guidebook.
     2019.https://guidebook.eif.org.uk/search?filters_type=search&eif_outcomes%5B%5
     D=supporting-childrens-mental-health-and-
     wellbeing&eif_outcomes%5B%5D=preventing-child-maltreatment&search= (accessed
     29 Jul2019).

41   McBrien KA, Souri S, Symonds NE *et al.* Identification of validated case definitions for
     medical conditions used in primary care electronic medical record databases: a
     systematic review. *J Am Med Informatics Assoc* 2018; **25**: 1567–1578.

42   Bywaters P, Bunting L, Davidson G, Hanratty J. The relationship between poverty,
     child abuse and neglect: an evidence review. 2016; : 74.

43   NHS England. Improving access for all: reducing inequalities.
     2017https://www.england.nhs.uk/wp-content/uploads/2017/07/inequalities-
     resource-sep-2018.pdf (accessed 29 Jul2019).