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The association between exposure to domestic abuse in women and the development of syndromes indicating central nervous system sensitization: A retrospective cohort study using UK primary care records

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Abstract

Background: Domestic abuse is a global public health issue. The association between the development of central sensitivity syndromes (CSS) and previous exposure to domestic abuse has been poorly understood particularly within European populations.

Methods: A retrospective cohort study using the 'The Health Improvement Network,' (UK primary care medical records) between 1st January 1995–31st December 2018. 22,604 adult women exposed to domestic abuse were age matched to 44,671 unexposed women. The average age at cohort entry was 36 years and the median follow-up was 2.5 years. The outcomes of interest were the development of a variety of syndromes which demonstrate central nervous system sensitization. Fibromyalgia, chronic fatigue syndrome and temporomandibular joint disorder outcomes have been reported previously. Outcomes were adjusted for the presence of mental ill health.

Results: During the study period, women exposed to domestic abuse experienced an increased risk of developing chronic lower back pain (adjusted incidence rate ratio [aIRR] 2.28; 95% CI 1.85–2.80), chronic headaches (aIRR 3.15; 95% CI 1.07–9.23), irritable bowel syndrome (aIRR 1.41; 95% CI 1.25–1.60) and restless legs syndrome (aIRR 1.89; 95% CI 1.44–2.48). However, no positive association was seen with the development of interstitial cystitis (aIRR 0.52; 95% CI 0.14–1.93), vulvodynia (aIRR 0.42; 95% CI 0.14–1.25) and myofascial pain syndrome (aIRR 1.01; 95% CI 0.28–3.61).

Conclusion: This study demonstrates the need to consider a past history of domestic abuse in patients presenting with CSS; and also consider preventative approaches in mitigating the risk of developing CSS following exposure to domestic abuse.

Significance: Domestic abuse is a global public health issue, with a poorly understood relationship with the development of complex pain syndromes. Using a large

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UK primary care database, we were able to conduct the first global cohort study to explore this further. We found a strong pain morbidity burden associated with domestic abuse, suggesting the need for urgent public health intervention to not only prevent domestic abuse but also the associated negative pain consequences.

1 | INTRODUCTION

Domestic abuse ('controlling, coercive, threatening behaviour, violence or abuse between those >16 who are, or have been, intimate partners or family members') (HM Government, 2016) is a global public health problem thought to affect up to one in three women (World Health Organization, 2018). Globally, 6.7 million disability-adjusted life years are thought to be attributable to intimate partner violence, a form of domestic abuse. The burden of morbidity and mortality as a result of associated injury, psychological illness or non-communicable disease with domestic abuse and traumatic experiences in the household is substantial (Bacchus et al., 2018; Chandan, Bandyopadhyay et al., 2020; Chandan, Keerthy, et al., 2020; Chandan, Okoth, et al., 2020; Chandan, Thomas, Bradbury-Jones, Taylor, et al., 2019; Chandan, Thomas, et al., 2020; Chandan, Thomas, Gokhale, et al., 2019).

Exposure to stressful events related to domestic abuse may be associated with changes in the hypothalamic-pituitary-adrenal (HPA) axis, daily cortisol regulation and ultimately lead to altered inflammatory processes (Griffin et al., 2005; Heath et al., 2013; Pico-Alfonso et al., 2004). In addition, exposure to domestic abuse has been associated with the development of poor mental health outcomes and a tendency to adopt harmful lifestyle choices as coping mechanisms (Chandan, Thomas, Bradbury-Jones, Russell, et al., 2019; Crane et al., 2013). A cumulation of these bio-psycho-social outcomes of domestic abuse have been thought to play a role in the development of associated physical and psychological morbidity. Emerging evidence suggests the association between exposure to domestic abuse and the development of pain disorders as a result of injury (Petrisor et al., 2013). However, the association of domestic abuse with chronic pain disorders where there is no clear injury explaining their cause is not well understood (Chandan, Thomas, Bradbury-Jones, Taylor, et al., 2019).

As our understanding of pain has improved, it has been hypothesized that patients experiencing common chronic pain disorders may experience sensitization of the central nervous system (Nijs et al., 2011, 2019). The accepted umbrella term for these conditions is central sensitivity syndromes, and they include fibromyalgia; chronic fatigue syndrome; temporomandibular joint disorders; chronic lower back pain; interstitial cystitis; vulvodynia; chronic headaches; myofascial pain syndrome; irritable bowel syndrome and restless legs syndrome (Moshiree et al., 2006; Nijs et al., 2011). These conditions are characterized by chronic upregulation of peripheral

nociception which can lead to allodynia and hyperalgesia (Latremoliere & Woolf, 2009; Woolf, 2011). The cause of central sensitization is not clear, however, it is thought that dysregulation of the HPA axis may be an aetiological component, and therefore this suggests domestic abuse may play a role in the development of CSS (Eller-Smith et al., 2018).

The evidence base associating domestic abuse and CSS is scarce, and where present is limited by study design (case-control or cross-sectional), low participant numbers or self-reported exposure and outcomes (Becker-Dreps et al., 2010; Campbell et al., 2002; Perona et al., 2005; Peters et al., 2007; Vives-Cases et al., 2011; Wuest et al., 2008). There have yet to be any studies exploring an association between domestic abuse with the development of chronic headaches, myofascial pain syndrome, vulvodynia or restless legs syndrome. Although not specific to domestic abuse, recent studies examining other traumatic exposures and psycho-social co-morbidities with the development of central sensitization clearly identifies a plausible relationship which requires more investigation due to the largely cross-sectional nature of existing evidence (McKernan, Johnson, Crofford, et al., 2019; McKernan, Johnson, Reynolds, et al., 2019; McKernan et al., 2018). An approach which overcomes many of the limitations highlighted above, previously adopted by our team, was to use a population-based dataset to explore the association of domestic abuse with CSS: fibromyalgia, chronic fatigue syndrome and temporomandibular joint disorders using an extract of data which ended in 2017 (Chandan, Thomas, Bradbury-Jones, Taylor, et al., 2019; Chandan, Thomas, Raza, et al., 2019).

However, cohort evidence is still needed to explore the association with other types of CSS. Therefore, we have conducted the first retrospective cohort study using 'The Health Improvement Network' (THIN) dataset to explore the association of domestic abuse exposure in women with the subsequent development of chronic lower back pain, interstitial cystitis, vulvodynia, chronic headaches, myofascial pain syndrome, irritable bowel syndrome and restless legs syndrome.

2 | METHODS

2.1 | Study design and data source

A population based retrospective open (allowing for patients to enter and exit the study at different time points) cohort

study using THIN was conducted. The study period was between 1st January 1995 and 31st December 2018.

During the study period, the dataset consisted of medical records taken from 787 UK general practices and deemed to be representative of the UK population (Blak et al., 2011). Symptoms, examinations, and diagnoses in THIN are recorded using a hierarchical clinical coding system called Read codes (Booth, 1994). General practices were eligible for inclusion 12 months following their installment of electronic practice records or from the practice's acceptable mortality recording date (Maguire et al., 2009). During the study period, this left 9,588,734 patients eligible to contribute. Data extraction was facilitated using the Data Extraction for Epidemiological Research (DExtER) tool (Gokhale et al., 2020).

2.2 | Exposure and outcome definition

Each adult (>18 years) woman exposed to domestic abuse (the presence of Read code relating to domestic abuse exposure in their medical record) was age matched (± one year) with up to two unexposed (no domestic abuse code) women. Both the exposed and unexposed group were followed up to assess the risk of developing a CSS: chronic lower back pain, interstitial cystitis, vulvodynia, chronic headaches, myofascial pain syndrome, irritable bowel syndrome or restless legs syndrome.

Exposure code selection relating to domestic abuse has been described in our previous work (Chandan, Thomas, Bradbury-Jones, Russell, et al., 2019). There are currently no validated code lists for CSS outcomes, however, as the musculoskeletal and chronic pain burden of GP consultations is extensive (Phillips, 2009). Code lists were created with the assistance of co-authors with expertise in primary care and Read code selection. To ensure we are including conditions relating to CNS sensitization we have not included non-specific/acute pain codes (e.g. acute back pain).

Read code lists relating to exposure terms and outcomes are provided (Appendix S1).

2.3 | Follow-up period

The index date for those in the exposed group was the date of the first Read code relating to domestic abuse exposure (incident cases) or when they became eligible to enter the study for those with a previous history of exposure (prevalent cases). To mitigate immortality time bias (Lévesque et al., 2010), 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.

2.4 | Co-variates

Co-variates considered in our modelling were selected due to their independent relationship with CSS development: age, gender, depression, anxiety, serious mental ill health (Chandan, Thomas, Bradbury-Jones, Russell, et al., 2019) and Townsend deprivation score (Townsend et al., 1988) which were captured at baseline. In addition, data on body mass index (BMI), alcohol drinking status and smoking status are reported. Psychological covariates (depression, anxiety and serious mental illness) were identified following review of General practitioner recorded (Read codes) diagnoses of the relevant conditions. The code list selection process of these covariates has been previously reported (Chandan, Thomas, Gokhale, et al., 2019) and notably steps included the reviews from general practitioners and a public health clinician with a psychiatry background in selection of the final code lists. Although there has been no prior published validation of these code lists, depression and SMI are thought to be well coded as they form part of the Quality Outcomes Framework, (NHS Digital, 2019) (performance indicators linked to general practice payments in the UK). Additionally, anxiety is thought 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 (Martin-Merino et al., 2010; Mcmanus et al., 2016).

2.5 | Statistical analysis

Categorical baseline data were described using proportions, continuous data were described using means or median with standard deviations or inter quartile range. Where there were missing data in our covariates, it was treated as a separate missing category.

In order to calculate an incidence rate (IR) per 100,000 person years for each of the outcomes of interest, patients with pre-existing illness (defined as a CSS code) were excluded to ensure the IR reflected incident outcomes. 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). IRRs are presented with 95% confidence intervals (CI) with statistical significance set at $p < .05$.

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

FIGURE 1 The risk of developing a central sensitivity syndrome in women exposed and unexposed to domestic abuse
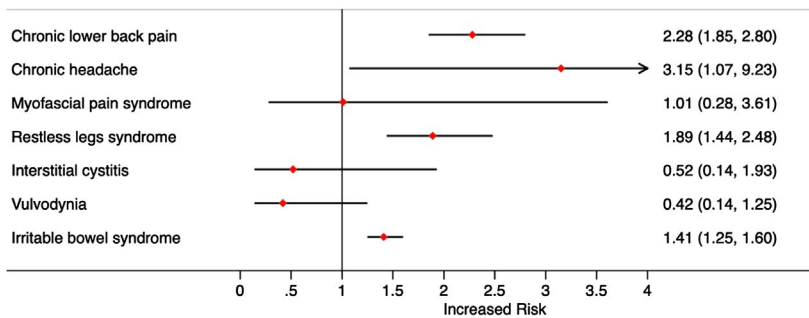
Despite previously published literature presenting mental illness as potential confounders (Chandan, Thomas, Bradbury-Jones, Russell, et al., 2019) it is also possible they may act as mediators in this relationship. Although it was outside of the remit of this study to conduct a mediation analysis, a sensitivity analysis was also conducted whereby depression, anxiety and serious mental ill health were not included *in* the regression model to give an indication as to the impact of including these covariates as control factors.

2.6 | Patient and public involvement

No patients were actively involved in setting the research question, outcome measures, study design, results interpretation of write-up of the results. There are plans for the results to be disseminated to the patient community affected by this research through domestic abuse charities and social media channels.

3 | RESULTS

3.1 | Baseline characteristics

Of the total eligible patients in the dataset, 22,604 (0.2%) adult women were identified as exposed to domestic abuse who were matched to 44,671 (0.5%) unexposed women. The average age in the cohort was 36 years and follow-up was longer in the unexposed group (2.7 years compared to 2.0 years) due to exposed women transferring practice more frequently than the unexposed group. The exposed group had a greater prevalence of current smokers and CSS morbidity at baseline, in addition to a greater proportion of those in lower socioeconomic classes compared to the unexposed group. Further details are shown in Table 1 which has been reported as per the STROBE guideline without inferential measures presented (Vandenbroucke et al., 2007).

3.2 | Cohort findings

During our study period we identified that exposure to domestic abuse was associated with the development of chronic lower back pain (aIRR 2.28; 95% CI 1.85–2.80), chronic headaches (aIRR 3.15; 95% CI 1.07–9.23), irritable bowel syndrome (aIRR 1.41; 95% CI 1.25–1.60) and restless legs syndrome (aIRR 1.89; 95% CI 1.44–2.48). It is important to state that chronic lower back pain (exposed IR 307.70; unexposed IR 112.51 per 100,000 py), irritable bowel syndrome (exposed IR 750.67; unexposed IR 487.12 per 100,000 py) and restless legs syndrome (exposed IR 162.06; unexposed IR 69.59 per 100,000 py) were relatively common occurring outcomes in the dataset, whereas there were only nine incident cases of chronic headache in the exposed group (IR 12.80 per 100,000 py) and six in the unexposed group (3.67 per 100,000 py) during the study period.

There was no statistically significant association noted with the development of interstitial cystitis (aIRR 0.52; 95% CI 0.14–1.93), vulvodynia (aIRR 0.42; 95% CI 0.14–1.25) and myofascial pain syndrome (aIRR 1.01; 95% CI 0.28–3.61). However, the occurrence of these events was also low during the study period. Further details are in Table 2 and Figure 1.

4 | DISCUSSION

The key findings from our study demonstrate that exposure to domestic abuse in women leads to an increased risk of developing irritable bowel syndrome, restless legs syndrome, chronic headaches and more than a tripling of the risk of developing chronic lower back pain. Whereas, domestic abuse was not clearly associated with the development of interstitial cystitis, vulvodynia and myofascial pain syndrome. However, it must be noted that the number of outcomes during the study period for non-significant findings and the significant finding chronic headaches were low.

TABLE 1 Baseline characteristics of women exposed and unexposed to domestic abuse

Baseline characteristics (standard deviation, interquartile range or percentage)	Domestic abuse	
	Exposed group	**Unexposed group**
Number of patients	22,604	44,671
Median follow-up period (person years)	2.0 (IQR 0.8–4.2)	2.7 (IQR 1.2–5.1)
Age at cohort entry (years)	36.1 (*SD* 12.5)	35.7 (*SD* 12.3)
Age when abuse occurred (years)	33.4 (*SD* 12.0)	-
Body mass index		
<25kg/m^2	8,475 (37.5%)	19,352 (43.3%)
25−30kg/m^2	4,054 (17.9%)	9,606 (21.5%)
>30kg/m^2	3,451 (15.3%)	8,370 (18.7%)
Not available	6,624 (29.3%)	7,343 (16.4%)
Smoking status		
Current smoker	9,039 (40.0%)	9,912 (22.2%)
Non-current smoker	10,534 (46.6%)	33,322 (74.6%)
Not available	3,031 (13.4%)	1,437 (3.2%)
Drinking status		
Non-drinker	5,877 (26.0%)	9,657 (21.6%)
Drinker	10,076 (44.6%)	25,657 (57.4%)
Not available	6,651 (29.4%)	9,357 (21.0%)
Townsend index		
(Least deprived) 1	2008 (8.9%)	7,361 (16.5%)
2	2,469 (10.9%)	7,033 (15.7%)
3	3,758 (16.6%)	8,276 (18.5%)
4	5,032 (22.3%)	8,340 (18.7%)
5	5,049 (22.3%)	6,823 (15.3%)
Not available	4,288 (19.0%)	6,838 (15.3%)
Mental ill health at baseline		
Depression	8,679 (38.4%)	7,808 (17.5%)
Anxiety	4,246 (18.8%)	4,388 (9.8%)
Serious mental illness	581 (2.6%)	418 (0.9%)
Central sensitivity syndrome at baseline		
Chronic lower back pain	285 (1.3%)	327 (0.7%)
Interstitial cystitis	20 (0.1%)	23 (0.1%)
Vulvodynia (female)	9 (0.0%)	11 (0.0%)

(Continues)

TABLE 1 (Continued)

Baseline characteristics (standard deviation, interquartile range or percentage)	Domestic abuse	
	Exposed group	**Unexposed group**
Chronic headache	9 (0.0%)	16 (0.0%)
Myofascial pain syndrome	8 (0.0%)	10 (0.0%)
Irritable bowel syndrome	2,184 (9.7%)	3,691 (8.3%)
Restless leg syndrome	91 (0.4%)	168 (0.4%)

As this was the first study to assess outcomes of CSS using UK definitions of domestic abuse, it is not easily possible to compare our incidence rates with other international study findings. Particularly for myofascial pain syndrome, chronic headaches, vulvodynia and restless legs syndrome these findings are novel. The prevalence of domestic abuse exposure has previously been shown to be high in a cohort of women who experience irritable bowel syndrome (Perona et al., 2005), and our findings are in concurrence with a previous population-based study including women from Nicaragua which showed an increased odds ratio (OR) of having exposure to domestic abuse in women who present with irritable bowel syndrome (Becker-Dreps et al., 2010). However, that study only included 151 cases of irritable bowel syndrome (physical abuse; OR 2.08; 95% CI 1.35–3.21: sexual abuse: OR 2.85; 95% CI 1.45–5.59) and recall of domestic abuse without consideration of temporality. Another cross-sectional study in Spain demonstrated an increased odds ratio (OR 2.34; 95% CI 1.53–3.57) of having experienced domestic abuse in women who present with chronic back pain, but only explored the violent form of domestic abuse. The only study exploring the relationship between interstitial cystitis and domestic abuse identified that within a cohort of 76 women with interstitial cystitis, a high proportion (49%) had experienced domestic abuse, but little further insight was available in this relationship. Therefore, the findings of our study greatly build on previous work in this field.

Our study demonstrates the need to consider a past history of domestic abuse in patients presenting with CSS; and also consider preventative approaches mitigating the risk of developing CSS following exposure to domestic abuse.

The use of UK primary care records for epidemiological research relies upon the accuracy of documenting by the healthcare professionals contributing to the dataset. A limitation of the study is the exposure and outcome Read codes have not yet been validated against clinical notes (McBrien et al., 2018). Previous work conducted using the THIN

TABLE 2 The risk of developing a central sensitivity syndrome in women exposed and unexposed to domestic abuse

	Chronic headache		Myofascial pain syndrome		Irritable bowel syndrome		Restless leg syndrome	
	Exposed	Unexposed	Exposed	Exposed	Unexposed	Unexposed	Exposed	Unexposed
Number of patients	22,595	44,655	22,596	44,661	20,420	40,980	22,513	44,503
Numbers of outcomes	9	6	<5	7	464	719	113	113
Person-years	70,293	163,318	70,321	163,318	61,812	147,603	69,727	162,382
Incidence rate (per 100,000 person years)	12.80	3.67	5.69	4.29	750.67	487.12	162.06	69.59
Incidence rate ratio (95% confidence intervals)[a]	3.49 (1.24–9.79)		1.33 (0.39–4.53)		1.54 (1.37–1.73)		2.33 (1.79–3.02)	
p value	0.018		0.652		<0.001		<0.001	
Adjusted incidence rate ratio (95% confidence intervals)[b]	3.15 (1.07–9.23)		1.01 (0.28–3.61)		1.41 (1.25–1.60)		1.89 (1.44–2.48)	
p value	0.037		0.990		<0.001		<0.001	
Sensitivity analysis[c]	3.57 (1.26–10.10)		1.10 (0.32–3.82)		1.58 (1.41–1.78)		2.23 (1.72–2.91)	
p value	0.016		0.877		<0.001		<0.001	

	Chronic lower back pain		Interstitial cystitis		Vulvodynia	
	Exposed	Unexposed	Exposed	Unexposed	Exposed	Unexposed
Number of patients	22,319	44,344	22,584	44,648	22,595	44,660
Numbers of outcomes	212	182	<5	11	<5	21
Person-years	68,898	161,764	70,290	163,250	70,332	163,296
Incidence rate (per 100,000 person years)	307.70	112.51	4.27	6.74	5.69	12.86
Incidence rate ratio (95% confidence intervals)[a]	2.73 (2.24–3.33)		0.63 (0.18–2.27)		0.44 (0.15–1.29)	
p value	<0.001		0.483		0.135	
Adjusted incidence rate ratio (95% confidence intervals)[b]	2.28 (1.85–2.80)		0.52 (0.14–1.93)		0.42 (0.14–1.25)	
p value	<0.001		0.327		0.118	
Sensitivity analysis[c]	2.51 (2.05–3.07)		0.71 (0.20–2.60)		0.52 (0.18–1.54)	
p value	<0.001		0.610		0.238	

[a]Unadjusted incidence rate ratio.

[b]Adjusted Incidence rate ratio: adjusted for age, gender, depression, anxiety, serious mental ill health and Townsend deprivation score at baseline.

[c]Sensitivity analysis: adjusted for age, gender and Townsend deprivation score at baseline.

database exploring the incidence and prevalence of domestic abuse in a primary care cohort suggests that substantial under-recording when compared to self-reported national survey estimates (Chandan, 2020; Chandan, Gokhale, et al., 2020; Chandan, Taylor, et al., 2020; Jeyaraman & Chandan, 2020; Office For National Statistics, 2016). Although, it is difficult to assess the representativeness of the sample when there is such a level of under-recording,

when compared to national statistics there are similar patterns in the age and deprivation of domestic abuse survivors (Chandan, Gokhale, et al., 2020). Under-recording of the exposure is likely to lead to misclassification bias where the unexposed group may be incorrectly coded as unexposed when they are in fact exposed. Therefore, it is possible our findings are an underestimate of the true effect size. Alternatively, it is possible that the cases recorded by

healthcare practitioners are the most severe which we are unable to discern in this study. Equally, it is clear that our results show a likely under-recording of CSS in the primary care population. In total across the study period 8,334 women (12.4%) had a recorded CSS of any type, which when compared to nationally accepted prevalence statistics of sub-types of CSS such as IBS (National Institute of Health & Care Excellence, 2015) indicates under-recording in this dataset. Although there is no published literature suggesting a surveillance bias in those exposed to domestic abuse, this may still be possible and in fact could lead to more women being identified to having a diagnosis of CSS, suggesting our effect sizes may in fact be an over-estimate. Additionally, although it is anticipated that recording of mental health conditions is expected to be relatively representative of the burden of disease in the general population, there is also a possibility of under-recording as there is still no formal validation of these clinical code lists.

Lastly, although in the main analysis we have accounted for mental illness and other important confounders as potential confounders, in this study we have been unable to explore the causal pathway for this relationship. This may mean that there is a possibility that some of the covariates selected such as mental illness may in fact be mediators in the relationship pathway rather than moderators. Although, we were unable to conduct a mediation analysis in this study, we have presented a sensitivity analysis (seen in Table 2) which demonstrated that when removing mental illness from the adjustment covariates there was no substantial change or variation in the nature of the effect size when examining the outcomes. Future research should be directed to establish the nature of the pathway between domestic abuse and CSS, as an increased understanding of the role of differing mediators and moderators may provide insight in the development and delivery of interventions aiming to prevent morbidity subsequent to domestic abuse exposure.

In conclusion, our study showed an increased risk of many types of CSS following exposure to domestic abuse. Primary prevention approaches targeting domestic abuse as well as secondary preventative approaches should be developed (or continued where provision exists) to minimize the associated burden of CSS.

ETHICAL APPROVAL

Anonymized 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.

AUTHOR CONTRIBUTIONS

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

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 organization for the submitted work, no financial relationships with any organizations 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.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.