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## Pediatrics Adverse Childhood Experiences and Related Life Events Screener (PEARLS) and Health in a Safety-net Practice

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### Abstract

**Background:** Adverse Childhood Experiences (ACEs) are associated with behavioral, mental, and clinical outcomes in children. Tools that are easy to incorporate into pediatric practice, effectively screen for adversities, and identify children at high risk for poor outcomes are lacking.

**Objective:** To examine the relationship between caregiver-reported child ACEs and related life events with health outcomes.

**Participants and Setting:** Participants (0–11 years) were recruited from the University of California San Francisco Benioff's Children Hospital Oakland Primary Care Clinic. There were 367 participants randomized.

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Declarations of interest: none

**Methods:** Participants were randomized 1:1:1 to item-level (item response), aggregate-level (total number of exposures), or no screening for ACEs (control arm) with the PEdiatric ACEs and Related Life Event Screener (PEARLS). We assessed 10 ACE categories capturing abuse, neglect, and household challenges, as well as 7 additional categories. Multivariable regression models were conducted.

**Results:** Participants reported a median of 2 (IQR 1–5) adversities with 76% (n=279) reporting at least one adversity; participants in the aggregate-level screening arm, on average, disclosed 1 additional adversity compared to item-level screening (p=0.01). Higher PEARLS scores were associated with poorer perceived child general health (adjusted  $B = -0.94$ , 95%CI:  $-1.26, -0.62$ ) and Global Executive Functioning (adjusted  $B = 1.99$ , 95%CI:  $1.51, 2.46$ ), and greater odds of stomachaches (aOR 1.14; 95%CI:  $1.04-1.25$ ) and asthma (aOR 1.08; 95%CI  $1.00, 1.17$ ). Associations did not differ by screening arm.

**Conclusion:** In a high-risk pediatric population, ACEs and other childhood adversities remain an independent predictor of poor health. Increased efforts to screen and address early-life adversity are necessary.

### Keywords

Adverse Childhood Experiences; screening; childhood adversities; pediatric practice

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### Introduction

Three in five U.S. adults report at least one Adverse Childhood Experience (ACE) (Merrick et al., 2018, 2019). ACEs are ten categories of adversities representing three domains: Abuse, Neglect, and Household Challenges experienced by age 18. ACEs are an important public health concern that have been repeatedly linked to poor health (Merrick et al., 2019). In the landmark ACE Study (Felitti et al., 1998), report of 4 ACEs was associated with at least two times greater risk for chronic respiratory disease, heart disease, and cancer – drawing attention to cumulative adversity as an important risk factor for negative long-term outcomes.

Numerous studies have replicated these findings (Gilbert et al., 2015; Hughes et al., 2017; Merrick et al., 2019) and have furthered our understanding of ACEs and health by demonstrating that the association between ACEs and health begins as early as infancy, and even prenatally (Flaherty et al., 2013; Oh, Jerman, Silvério Marques, et al., 2018; Racine et al., 2018). The toxic stress response, which includes neuro-endocrine-immune and genetic regulatory alterations has been an important putative mechanism of how cumulative exposures to early adversities increase risk of morbidity and mortality throughout the life course (Berens et al., 2017; Seeman et al., 1997; Shonkoff et al., 2012). Indeed, ACEs are associated with important, proximal outcomes that occur during childhood, including academic achievement (McKelvey et al., 2018b) behavioral challenges (Burke et al., 2011; McKelvey et al., 2018b; Wilson et al., 2015), mental health (ADHD) (Hunt et al., 2017; Jimenez et al., 2017), and physical health (recurrent infections, obesity, and respiratory) (Burke et al., 2011; McKelvey et al., 2019; Oh, Jerman, Silvério Marques, et al., 2018; Wing et al., 2015).

Increasingly, leading health policy and practice institutions are recommending screening for childhood adversity to facilitate early detection and intervention for ACEs (Merrick et al., 2019; Summary | Vibrant and Healthy Kids: Aligning Science, Practice, and Policy to Advance Health Equity | The National Academies Press, n.d.). Moreover, research has demonstrated that bolstering resilience and linkage to services can mitigate the negative effects of ACEs on health (Bethell et al., 2014; Merrick et al., 2019). ACEs screening also offers a unique opportunity for health care providers to deliver anticipatory guidance and, when done with a trauma-sensitive, person-centered approach, begins an open-dialogue on the impact of ACEs and stress on health. In this role, pediatricians can serve a potential change-agents to support families' needs and parenting goals regardless of ACE level. (Brown et al., 2017; Conn et al., 2018) Yet, a study of American Academy of Pediatrics members demonstrated that only a third of primary care providers screened for some ACEs and only 4% screened regularly for all ACEs, despite the majority agreeing ACEs are an important contributor to health and screening is within the scope of practice (Kerker et al., 2016).

One significant barrier to screening is that, until recently, there were no comprehensive, prospective ACEs screening tool for use in pediatric clinical settings. Prior studies (Oh, Jerman, Purewal Boparai, et al., 2018) focused on ACEs screening have been largely limited to youth in already in high-risk settings (Kisiel et al., 2009; McKelvey et al., 2017a) or involved longer formats either through extensive questionnaires (Kisiel et al., 2009; Marie-Mitchell et al., n.d.) or use a semi-structured interview format (Angold et al., 2000; McKelvey et al., 2017a). In addition, some measures do not explicitly ask about reportable offenses (including physical and sexual abuse, and neglect), but rather proxies (Dubowitz et al., 2011; McKelvey et al., 2017a); focus on older children or teens (Bernstein et al., 2003; Flowers et al., 2000); and/or were not performed within the context of primary care (Bernstein et al., 2003; Flowers et al., 2000; Kisiel et al., 2009; McKelvey et al., 2017a). Most closely aligned with the current measure are the Whole Child Assessment (WCA) (Marie-Mitchell et al., n.d.) and the Pediatric ACEs Algorithm (Scholer et al., 2010); both prospectively screen for child-ACEs within primary care, but are largely limited to interpersonal risk factors. With growing evidence that social risk factors activate similar pathways to ACEs (Berens et al., 2017; Seeman et al., 1997; Shonkoff et al., 2012), a screening tool that explicitly includes these measures stands to have a large potential impact, especially when screening within health systems that deliver a significant amount of care to high-risk, vulnerable populations (safety-net systems). Moreover, neither instrument has been evaluated for associations with health outcomes and relies on an item-level response screening method which may result in under-reporting when compared to aggregate-level screening tools (Bethell, Carle, et al., 2017; Gillespie et al., 2017). These studies support acceptability by families for screening and feasibility of screening in different settings, including primary care, but largely leave out the question about best practice for screening and whether screening improves detection of children at-risk for poor health outcomes.

Through an iterative process, we developed the PEdiatric ACEs and Related Life Event Screener (PEARLS) tool (Koita et al., 2018). The PEARLS tool assesses for both Adverse Childhood Experiences (ACEs) and related life events thought to be risk factors for toxic stress (collectively referred to as “adversities”). In the present study, we seek to:

(1) document the frequency and distribution of adversities using the PEARLS tool in a safety-net pediatric setting, and (2) evaluate the association between adversities identified by PEARLS with key pediatric biomedical, mental and behavioral outcomes.

## Methods

### Participants and Study Design

The Pediatric ACEs and Resiliency Study is a randomized control study (NCT04182906) designed to 1) validate a prospective pediatric screen for ACEs and related life events (i.e. the PEARLS tool), 2) examine the association between stress-related biomarkers and adversities identified with PEARLS, and 3) pilot interventions to prevent and mitigate the toxic stress response in pediatric settings. Here on out, the use of the acronym PEARLS refers solely to the screening tool developed through the Pediatric ACEs and Resiliency Study. Eligible participants were between the ages of 3 months to 11 years, not in foster care, English and/or Spanish speaking, and had a primary caregiver 18 years who spoke English and/or Spanish. Siblings were excluded from participation. All participants provided written informed consent and, where appropriate, oral assent. The study was approved by the BCHO institutional review board.

### Pediatric ACEs and Resiliency Study Overview

**Provider-level training:** Health care providers of the patients and caregiver enrolled received training on ACEs and health and on how to deliver anticipatory guidance with a trauma-informed lens. This occurred through a series of didactic and interactive sessions that started with 1:1 training and group sessions (topics ranged from understanding their own ACEs, mindfulness, referrals and resources) with study investigators and followed by monthly presentations, including staff meeting and grand rounds, over a 12-month period.

**Pediatric ACEs and Resiliency Study:** Participation in the larger study included four study visits for survey completion (time points 1–4), biospecimen collection including blood, nasal and buccal swabs, and stool (time points 2–4), and, dependent upon PEARLS score and randomization, participation in a social or psychosocial intervention (between time points 2–3). Participants were compensated up to \$300 for their time participating in the entire study (12 months). From March 2017-October 2018, we approached 1443 families presenting for well-child checks at the University of California San Francisco Benioff's Children Hospital Oakland (BCHO) Primary Care Clinic. 796 families declined participation, 92 were ineligible, and 555 families were enrolled. Eligible caregivers and participants were randomized via a random number generator (randomization blocks of 12) and programmed by the study analyst to automatically display to the research coordinator via RedCap to one of the three screening formats in a 1:1:1 allocation ratio (n=188 no screening, n=185 Item-level response screening, and n=182 Aggregate-level response screening; Figure 1). Research coordinators were not blinded to assignments due to the nature of the screener and how questions are asked. However, study investigators and those performing analyses were blinded to assignment. Screening included 1) an item-level response PEARLS screen: caregivers disclose specific adversities their child has experienced; or, 2) an aggregate-level response PEARLS screen: caregivers report the total number of adversities their child has

experienced. Screened participants also received anticipatory guidance from their primary care provider.

**Present Study:** As one of our primary aims was to examine the association of baseline health outcomes with the PEARLS tool and whether these associations differed by screening arm (due to reporting differences), we limited the present analysis to those randomized to Item-level or Aggregate-level screening formats (n=367), i.e. those with available PEARLS data, and measures that occurred at baseline (time point 1) or one-month follow-up (time point 2), which we considered in tandem. Trained, bilingual research staff administered the PEARLS tool and comprehensive questionnaires at the primary care clinic in a private room, collecting sociodemographic, psychosocial stress, and health data. Caregivers completed the PEARLS tool in approximately 4.20 minutes (IQR 2.97, 5.82) and 5.56 minutes (IQR 4.11, 7.95) for item-level response and aggregate-level response screening formats, respectively based on RedCap timestamps. The full study assessments took approximately 45–90 minutes depending on study timepoint. Healthcare utilization and disease diagnosis codes were obtained from the Electronic Health Record (EHR) for the 12-months *prior* to enrollment.

### Exposure and Outcome Assessment

*ACEs and Related Life Events* were measured using the PEdiatric ACEs and Related Life Event Screener (PEARLS), a face-valid pediatric ACEs screen developed with patient families and providers for use in clinical practice (Koita et al., 2018). The 17-item screen includes the ten original ACEs categories (Felitti et al., 1998), plus Related Life Events including exposure to discrimination, food insecurity, housing instability, community violence, physical illness/disability of a caregiver, death of a caregiver, and forced separation from caregiver. The Related Life Event questions were informed by other studies and thought to operate, at least in part, through the toxic stress mechanism (Koita et al., 2018; Shonkoff et al., 2012). Item responses were summed, and responses were analyzed as a continuous variable (total PEARLS Score, possible range 0 to 17). We also examined associations with the ten original ACEs items (10-item), here on referred to as ACEs, and the Related Life Event items (7-item). To better compare to previous findings with health outcomes (Felitti et al., 1998; Merrick et al., 2019), we categorized the ten ACE responses as “no ACEs,” “1–3 ACEs,” and “ 4 ACEs.”

*General health* was measured via: (1) the Patient-Reported Outcomes Measurement Information System (PROMIS) Global 10-item questionnaire that assessed physical, mental, and social health, pain, fatigue, and perceived quality of life (Ader, 2007). Continuous raw scores were converted into T-scores and norm-referenced; (2) Reported missed school days due to health collected numerically for 1–9 days or 10 missed school days; and (3) Healthcare utilization EHR-based measures for the 12 months preceding recruitment included emergency room visits and hospitalizations (any visit vs. none).

**Mental Health.**—Attention Deficit Hyperactivity Disorder (ADHD) diagnosis was based on ICD-10 codes with current disease defined as at least one corresponding ICD-10 code in the 12 months prior to recruitment. Behavioral health was assessed using the Behavior

Rating Inventory of Executive Function (BRIEF 2/P versions administered to appropriate age group) tool (Sherman et al., 2010), reporting on Global Executive Composite scale t-score, in which scores  $\geq 65$  are considered clinically significant.

**Physical Health Measures:** The International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire, validated and standardized for international use (Asher et al., 1995), was used to obtain history of asthma, allergic rhinitis, or atopic dermatitis. Height and weight were obtained from clinical exam, and sex- and age-specific BMI z-scores and percentiles were calculated using 2000 Centers for Disease Control and Prevention growth charts ( $\geq 95$ th percentile classified as obese) (Kuczmarski et al., 2000). Report on headaches/dizziness and stomachaches in the previous 12 months were obtained as self-report (yes/no). ICD-10 codes from EHR records were retrieved to create binary measures of the presence of: (1) Acute Infections (upper and lower respiratory infection, sinusitis, bronchiolitis, pneumonia, influenza and other viral infections, scarlet fever, otitis media, conjunctivitis, and urinary tract infections); and (2) Somatic Symptoms (headache, nausea, abdominal pain, epigastric pain, colic, constipation, and migraine) in the 12 months prior to recruitment.

*Socio-demographic covariates* were identified a priori based on existing literature on childhood adversities and health outcomes and collected from the questionnaire (Halfon et al., 2017; Slopen et al., 2016). Race/ethnicity was categorized as Non-Hispanic White, Non-Hispanic Black, Hispanic, or other; caregiver's educational level was categorized as some high school or less, high school graduate, some college, college or greater; family income was dichotomized as  $< \$25,000$  vs  $\geq \$25,000$  annually based on the sample distribution and approximation of federal poverty level for a family of four (the mean number of reported children per household was 4).

### Statistical Analysis

Negative binomial regressions were used to evaluate the association between socio-demographic covariates and PEARLS score by screening arm (item-level vs. aggregate-level response) and in a pooled analysis (item-level plus aggregate-level response). Chi-squared tests were used to examine the probability of reporting ACEs among individuals reporting at least one Related Life Event. Multivariable logistic and linear regressions were used to examine the relationship between reported adversities and health outcomes by screening arm. As indicated, adversities were examined as an ACEs, Related Life Events, total PEARLS Score, and ACE category (none, 1–3, 4). Separate models were run with each health outcome as the dependent variable. Lastly, we tested for an interaction between adversities reported (ACEs, Related Life Events, total PEARLS Score, and ACE category) and screening format to examine for significant health outcome associations across the different screening formats.

We performed multiple imputation with iterative chained equations to impute missing socio-demographic covariate data (Groenwold et al., 2012; Jakobsen et al., 2017; Sullivan et al., 2018). Thirty imputed datasets were generated, and we obtained averaged results from the

repeated analyses. Participants missing outcome data (i.e. general health, mental health, and physical health measures) were excluded from the analyses.

For sensitivity analysis, we compared the averaged results from the multiple imputation to the complete case analysis. Statistical significance was set at  $P < .05$ . All analyses were performed with R 3.3.2, STATA version 14, and SPSS 26.

## Results

The population was predominantly non-Hispanic Black and low-income, with a mean age of 5.9 years (Table 1). 76% of the population reported 1 or more adversity with a median report of 2 (IQR 1–5) adversities. The prevalence and type of adversities are shown in Figure 2. Older age was associated with higher PEARLS Score (IRR 1.09; 95%CI: 1.06, 1.13). Non-Hispanic White and/or high-income participants had lower reports of adversities compared to non-Hispanic Black and/or low-income participants (IRR 0.48; 95%CI: 0.26, 0.89 and IRR 0.71; 95%CI: 0.53, 0.96, respectively) (Table 2). Measure of internal consistency, assessed with the KR-20, a special case of Cronbach's alpha, was determined to be adequate to high (PEARLS score .81 and .82; ACEs: .75 and .74;) and moderate for Additional Life Events: .61 and .61 for item-level and originally aggregate-level screening respectively). Those who completed the aggregate-level PEARLS tool reported 1 additional adversity compared to families administered the item-level PEARLS tool (median 3 vs. 2,  $p=0.01$ , Table 3). Across the two screening arms, 54 experiences of physical and sexual abuse and neglect were reported by caregivers. Each of these families met with the provider and/or mental health clinician and were assessed for safety. Four Child Protective Service Reports were generated, three of these cases had been previously reported, and one de novo case was made. For persons reporting any single Related Life Event, the probability of exposure to two or more ACE categories ranged from 58.7–81.1% (median: 79.7%), Table 4.

### General Health Outcomes

Increased adversities were associated with lower caregiver ratings of child's general health as assessed by PROMIS (mean t-scores 50, SD 8.65): ACEs (adjusted  $B -1.35$ ; 95%CI:  $-1.82, -0.88$ ), Related Life Events (adjusted  $B -1.63$ ; 95%CI:  $-2.39, -0.88$ ), PEARLS Score (adjusted  $B -0.94$ ; 95%CI:  $-1.26, -0.62$ ) (Table 5). Participants with 1–3 ACEs and 4 ACEs had lower PROMIS t-scores compared with participants with no ACEs reported (adjusted  $B -3.74$ ; 95%CI:  $-5.82, -1.67$ ; adjusted  $B -8.17$ ; 95%CI:  $-10.85, -5.48$ , respectively). Adversities were also associated with increased odds of missing school due to health reasons, with a near significant association for ACEs (aOR 1.15; 95%CI: 0.99, 1.33), and significant associations for Related Life Events (aOR 1.26; 95%CI: 1.01, 1.57) and PEARLS Score (aOR 1.11; 95%CI: 1.01, 1.23). No associations were observed between adversities with ED-visits or hospitalizations, with the exception of a negative association with ACEs when categorized. No differences were associated by screening arm for general health outcomes.



## Mental Health Outcomes

Greater adversities were highly associated with clinically poorer Global Executive Functioning (seen by t-scores of  $\geq 65$  on the BRIEF 2/P Global Executive Composite Scale). This pattern was consistent across the: ACEs (aOR 1.74; 95%CI: 1.42, 2.14), Related Life Events (aOR 1.66; 95%CI: 1.29, 2.15), and PEARLS Score (aOR 1.49; 95%CI: 1.26, 1.66; Table 6). There was a large and graded increase in the odds of executive functioning concerns associated with the ACEs categories. While only 5.3% of children with no reported ACEs reached the clinical threshold for Global Executive Functioning concerns, this number rose to 23.4% of children with 1–3 reported ACEs, and to 50% of children with  $\geq 4$  ACEs reaching the clinical threshold. There was evidence of effect modification by screening arm: the aggregate-level screening arm had higher odds of executive functioning concerns compared to the item-level screening arm (aOR 3.17; 95%CI: 1.82, 5.52 vs. aOR 1.46; 95%CI: 1.13, 1.87,  $p_{\text{int}}=0.02$ ). Associations with greater odds of ICD-10 documented ADHD were marginal for ACEs (aOR 1.15; 95%CI: 0.99, 1.33,  $p=0.07$ ) and PEARLS Score (aOR 1.09; 95%CI: 0.98, 1.20,  $p=0.10$ ); and for participants with  $\geq 4$  ACEs (aOR 2.16; 95%CI: 0.85, 5.44,  $p=0.10$ ) compared to children with no reported ACEs.

## Physical Health Outcomes

We found positive associations between adversities and all atopic conditions identified by ISAAC (Table 7). A near significant association was observed between asthma and the ACEs (aOR 1.12; 95%CI: 1.00, 1.26), Related Life Events (aOR 1.14; 95%CI: 0.95, 1.37), and PEARLS Score (aOR 1.08; 95%CI: 1.00, 1.17). We saw similar associations between adversities measured by PEARLS and allergic rhinitis and eczema (Table 7). When categorized by the ten ACEs, compared with participants with no ACEs, those with 1–3 and  $\geq 4$  ACEs had an increased odds of asthma (aOR 2.20; 95%CI: 1.22, 3.97; aOR 2.36; 95%CI: 1.17, 4.80, respectively), rhinitis (aOR 2.36; 95%CI: 1.35, 4.13; aOR 2.40; 95%CI: 1.22, 4.74, respectively), and eczema (aOR 2.19; 95%CI: 1.32, 3.65; aOR 2.75; 95%CI: 1.44, 5.23, respectively). There was evidence of effect modification by screening arm for asthma ( $p_{\text{int}} = 0.05$ ) with a significant association observed in the item-level screening arm with ACEs, Related Life Events, and PEARLS Score, but not within the aggregate-level screening arm, with the exception of a significant association with asthma among those that reported 1–3 ACEs in the aggregate-level screening arm.

Adversities were significantly associated with caregiver-report of stomachaches for ACEs and PEARLS score (aORs 1.25; 95%CI: 1.09, 1.43; and aOR 1.14; 95%CI: 1.04, 1.25, respectively) and marginally associated with Related Life Events (aOR 1.18; 95%CI: 0.96, 1.47) (Table 7). Across screening arms, Related Life Events were significantly associated with an increased odds of stomachaches among the item-level screening arm (aOR 1.65; 95%CI: 1.16, 2.34) but not the aggregate-level arm (aOR 0.97; 95%CI: 0.72, 1.31) ( $p_{\text{int}}=0.04$ ). Similarly, increased ACEs, Related Life Events, and PEARLS Score were observed to be associated with headaches and dizziness in the item-level arm but not in the aggregate-level arm ( $p_{\text{int}}=0.05$ ). Lastly we found an increased odds for infections in the item-level arm and decreased odds in the aggregate-level arm for ACEs ( $p_{\text{int}}=0.04$ ), related life events ( $p_{\text{int}}=0.04$ ), and PEARLS score ( $p_{\text{int}}=0.02$ ).

Participants with missing data were more likely to be of ‘other’ race/ethnicity (data not shown); otherwise, they did not differ from those with complete data. The pattern of results from the complete case and multiple imputation analyses was virtually identical.

## Discussion

In the present study, we report the net effect of complex adverse exposures during childhood. Our study contributes to the extant body of literature by documenting the relative associations between ACEs with health outcomes in childhood. We also assessed whether other common social determinants are comparable in their risks to child health as the traditional ACEs through the addition of the Related Life Events section of the PEARLS tool. We screen for lifetime exposures to ACEs and Related Life Events to understand the cumulative risk as prior studies demonstrate that early-life exposure affects middle and late childhood outcomes, even if distally experienced. Unlike other child-ACEs screening tools for primary care, the PEARLS tool specifically asks about food insecurity and housing instability, two factors associated with poverty. Additionally, PEARLS screens for discrimination and exposure to community violence, two other social adversities associated with poor health. Therefore, our findings should be considered in the context of a growing literature around pediatric prospective social risk screening (e.g., current food insecurity or housing instability), which has been demonstrated to be associated with child and caregiver health as well as facilitating response and resource linkage (Gold et al., 2019; Gottlieb et al., 2016). In addition, we found that report of these Related Life Events was highly associated with the odds of reporting one of the original ACEs, highlighting that these cumulative lifetime exposures often co-occur. Thus, PEARLS can work in concert with social risk screening and potentially accentuate resource connections and assistance for families.

In this diverse, low socioeconomic population, we observed that adversities were highly prevalent; in comparison to other studies, the prevalence of adversities in our population is almost one-and-a-half times higher (68.4% vs. 46.3%, reporting at least one adversity) (Bethell, Davis, et al., 2017). Despite the high prevalence of adversity, we were able to demonstrate concurrent validity in that the PEARLS was effective at identifying children at high risk for a number of clinically significant outcomes. Most striking, reported adversities were consistently associated with poorer global executive functioning with 50% of children with 4 ACEs experiencing clinically relevant problems with executive functioning. And, while the disclosure rate for PEARLS was higher in the aggregate-level screening arm, the strengths of the associations between ACEs and the selected health outcomes did not differ in clinically meaningful ways.

A notable finding is the lack of statistically significant associations between childhood adversities and certain health outcomes. Particularly, the finding that 50% of children with 4 ACEs demonstrate clinically measurable impairment of global executive functioning but do not demonstrate an association with ADHD. Prior studies have demonstrated a strong association between early life adversities (i.e. ACEs before 5 years of age) and mental health outcomes, including ADHD diagnosis, in middle childhood (Hunt et al., 2017; McKelvey et al., 2018b). As the median age of our study population was 5.8 years, and ADHD is more often diagnosed later in childhood, it is not surprising that we did not observe this

association in the present study. While we did not observe this association with ADHD, we did observe a strong association between high PEARLS score (regardless of screening method and subset of PEARLS score) and poor global executive dysfunction as measured by the BRIEF-P/2, which may be an early indicator of children at risk of developing ADHD later in childhood (Hawkey et al., 2018).

Other possible avenues for the lack of an observed association between childhood adversities health outcomes –specifically for obesity, ADHD and other EHR-derived outcomes which have been previously demonstrated to be significantly related to childhood adversities (Burke et al., 2011; Hunt et al., 2017; McKelvey et al., 2018a, 2019; Oh, Jerman, Silvério Marques, et al., 2018), may be attributable to: cross-sectional nature of study; small sample size; young age of the study population, i.e. not enough time elapsed to see health effects; use of EHR-data; and under-reporting of adversities by caregivers as we were collecting information on particularly sensitive items, such as physical and sexual abuse that require mandated reporting.

A longitudinal study would provide an opportunity to examine for a latency period (i.e., period of time between demonstrating behavioral/symptoms of trauma and developing mental and physical health outcomes), the cumulative impact of adversities, and how the timing and period of adversity exposure changes disease risk. McKelvey et al. demonstrated the five patterns of adversity exposure in early childhood (ages 0–3 years) associated with development, with more proximal exposures having the greatest predictive value in cognitive, language, and physical developmental milestones (McKelvey et al., 2017b). Further work in understanding these patterns of adversity exposures for pediatric outcomes in mid- and late-childhood are needed.

Other limitations of the present study include: the timing of certain measurements, specifically the use of EHR data which was collected for the 12 months prior to recruitment, however, the PEARLS tool asks about lifetime prevalence of ACEs and related life events and not for a specific time-point after recruitment; potential differences by age and gender due to power limitations, and in those who did not agree to participate (volunteer bias) and selection bias. Lastly, this study took place in an urban, primary care center where the majority of patients (>95%) are on state-sponsored Medicaid limiting the generalizability of the study results. This population is disproportionately burdened by socio-environmental adversities, some captured by the PEARLS tool, and our findings may reflect these cumulative and interactive effects.

Even in this low-socioeconomic, diverse patient population, we saw great variability in childhood adversity exposure and demonstrate significant associations with poor health outcomes. Moreover, our results replicate findings in other studies (Halfon et al., 2017; Slopen et al., 2016), suggesting childhood adversities are an independent predictor of poor health.

**Conclusion:**

Adverse Childhood Experiences and Related Life Events are important contributors to poor health in children. The PEARLS tool is an effective screener for pediatric, primary care that identifies children at high risk for important pediatric health outcomes.

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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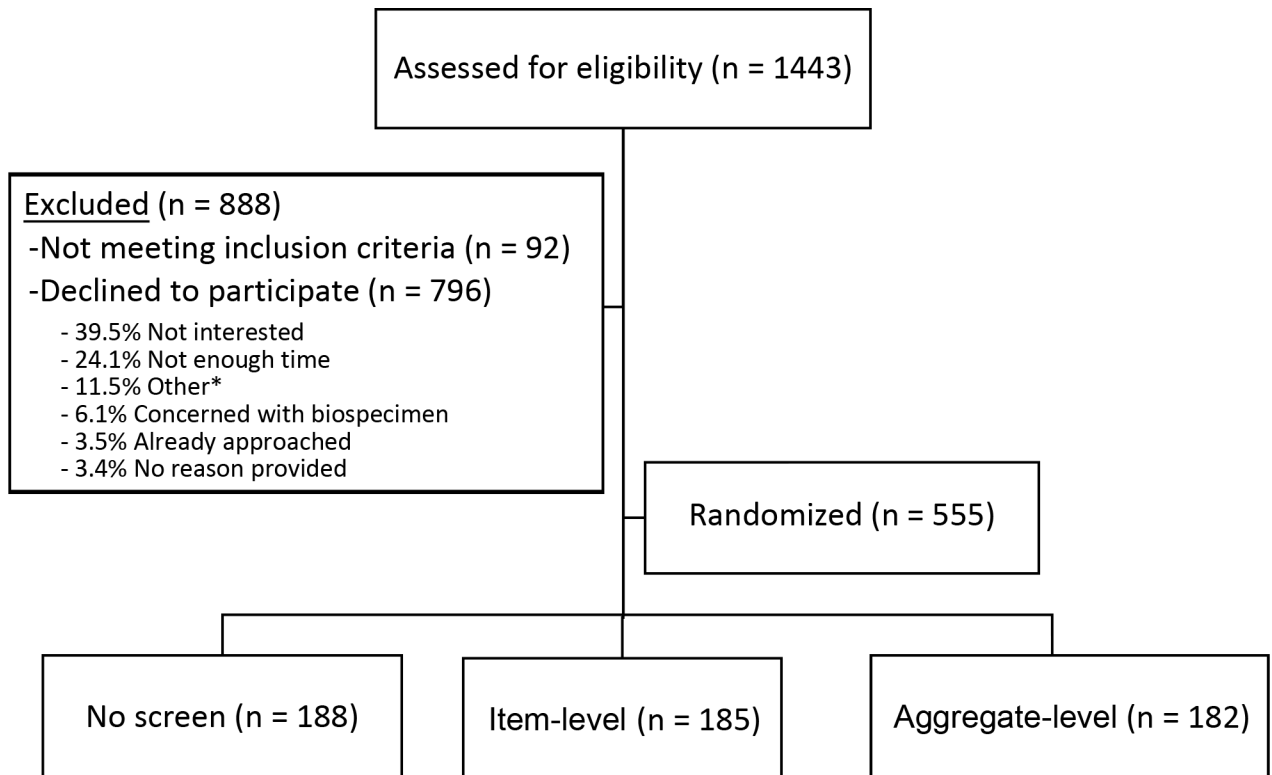
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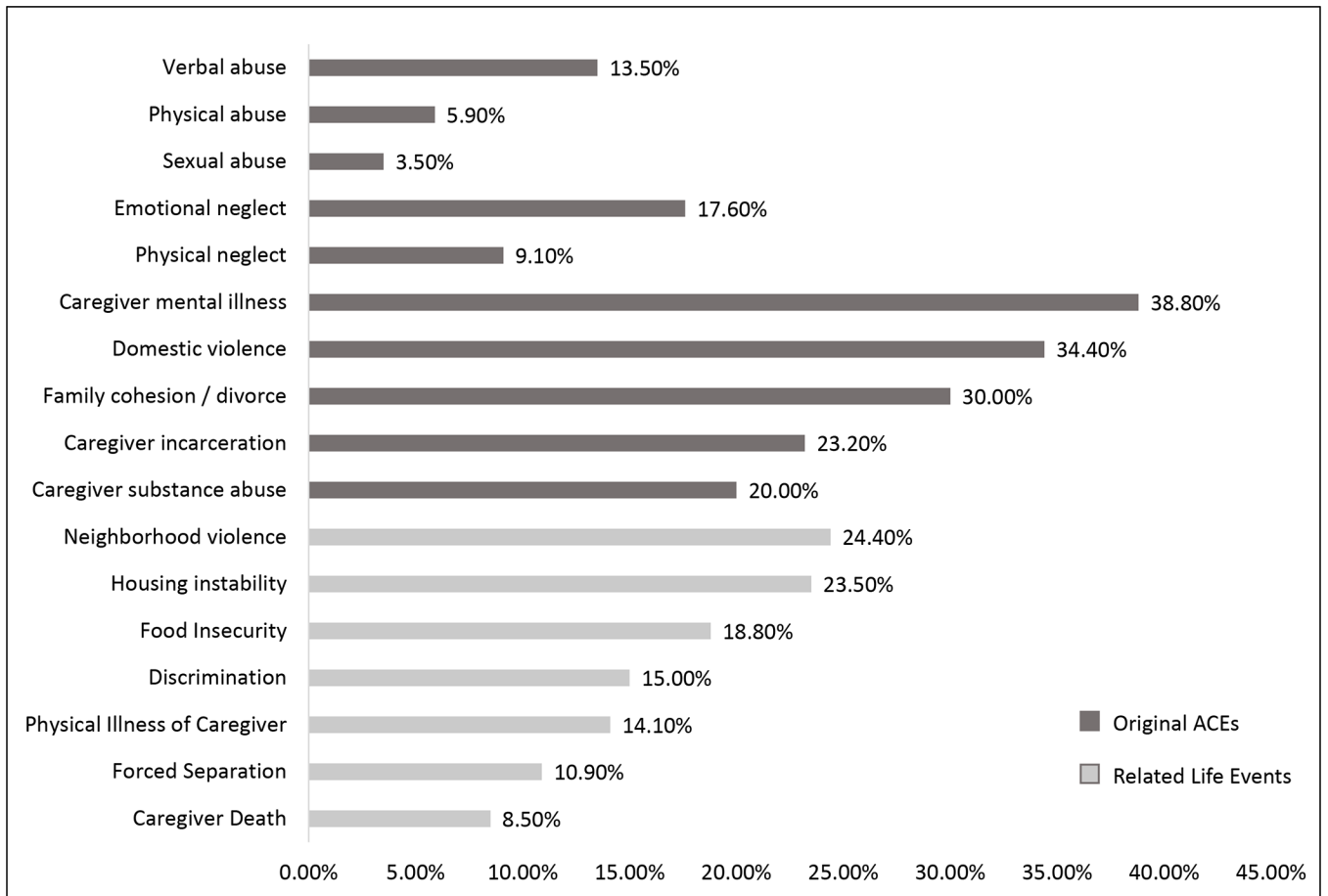
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\*Other includes not primary caregiver (n=27), did not want to consent without spouse (n=20), sibling in study (n=17), child declined (n=16), transportation (n=13), more time to think about study (n=12) moving from area/ traveling (n=6), not feeling well (n=3)

**Figure 1.**  
Consort Diagram for the Pediatrics ACEs Screening and Resilience Study.





**Figure 2.** Distribution of Adverse Childhood Experiences and Related Life Events in PEARLS. Individual responses were obtained from caregivers completing the item-response PEARLS tool and from caregivers who subsequently identified the items their child experienced from the total-response PEARLS tool (n=340, 7.4%). Responses were summarized and displayed here.

**Table 1.**

Baseline Characteristics of Study Population by ACEs Screening Arm from PEARLS

Characteristic	Item-level ACEs Screen	Aggregate-level ACEs Screen	p-value
	N (%) Total N = 185	N (%) Total N = 182	
Age, mean (SD)	5.91 (3.57)	5.83 (3.46)	0.82
Sex			0.97
Male	100 (54.1)	98 (53.8)	
Female	85 (45.9)	84 (46.2)	
Race			0.13
Non-Hispanic White	8 (4.3)	7 (3.8)	
Hispanic	31 (16.8)	36 (19.8)	
Non-Hispanic Black	96 (51.9)	108 (59.3)	
Other	50 (27.0)	31 (17.0)	
Caregiver Education <sup>a</sup>			0.34
Some high school or less	19 (10.3)	12 (6.6)	
High school	39 (21.1)	51 (28.0)	
Some college	68 (36.8)	63 (34.6)	
College	55 (29.7)	55 (30.2)	
Income <sup>a</sup>			0.40
25,000 or less	80 (43.2)	73 (40.1)	
Greater than 25,000	44 (23.8)	50 (27.5)	
PROMIS t-score, mean (SD)	50.4 (9.1)	50.6 (8.2)	0.83
Missing	46 (24.9)	49 (26.9)	
Missed School Days Due to Health			0.58
Less than 10 days	93 (50.3)	93 (51.1)	
10 days or more	27 (14.6)	23 (12.6)	
Missing	65 (35.1)	66 (36.3)	0.95
ED visit in the past year			
No	100 (54.1)	99 (54.4)	
Yes	85 (45.9)	83 (45.6)	
Hospitalization in the past year			0.18
No	180 (97.3)	172 (94.5)	
Yes	5 (2.7)	10 (5.5)	
ADHD			0.31
No	166 (89.7)	157 (86.3)	
Yes	19 (10.3)	25 (13.7)	
BRIEF-P Global Executive Composite T score, mean (SD)	54.9 (12.1)	55.8 (12.8)	0.63
Missing	84 (45.4)	82 (45.1)	
Stomach Aches			0.13
No	156 (84.3)	145 (79.7)	
Yes	21 (11.4)	31 (17.0)	

Characteristic	Item-level ACEs Screen	Aggregate-level ACEs Screen	p-value
	N (%) Total N = 185	N (%) Total N = 182	
Missing	8 (4.3)	6 (3.3)	
Headaches/Dizziness			0.41
No	155 (83.8)	159 (87.4)	
Yes	22 (11.9)	17 (9.3)	
Missing	8 (4.3)	6 (3.3)	
Asthma			0.10
No	108 (58.4)	92 (50.5)	
Yes	69 (37.3)	84 (46.2)	
Missing	8 (4.3)	6 (3.3)	
Rhinitis			0.56
No	99 (53.5)	93 (51.1)	
Yes	78 (42.2)	83 (45.6)	
Missing	8 (4.3)	6 (3.3)	
Eczema			0.24
No	99 (53.5)	88 (48.4)	
Yes	77 (41.6)	88 (48.4)	
Missing	9 (4.9)	6 (3.3)	
Obesity			0.36
No	142 (76.8)	133 (73.1)	
Yes	42 (22.7)	49 (26.9)	
Missing	1 (0.5)	0 (0.0)	
Infections			0.09
No	101 (54.6)	83 (45.6)	
Yes	84 (45.4)	99 (54.4)	
Somatic symptoms			0.45
No	150 (81.1)	153 (84.1)	
Yes	35 (18.9)	29 (15.9)	

<sup>a</sup>Numbers do not add to 100% because of missing data: 5 for caregiver education (1.4%); 120 for income (32.7%)

**Table 2.**

Association between demographic factors with PEARLS

	Adversities Identified with PEARLS IRR (95% CI)		
	ACEs	Related Life Events	Total PEARLS Score
Age	<b>1.07 (1.04, 1.11)</b>	<b>1.11 (1.07, 1.15)</b>	<b>1.09 (1.06, 1.13)</b>
Sex			
Male	Ref	Ref	Ref
Female	0.91 (0.72, 1.15)	0.96 (0.75, 1.22)	0.93 (0.74, 1.16)
Race			
Non-Hispanic Black	Ref	Ref	Ref
Non-Hispanic White	0.58 (0.30, 1.10)	<b>0.31 (0.13, 0.76)</b>	<b>0.48 (0.26, 0.89)</b>
Hispanic	1.00 (0.74, 1.35)	0.95 (0.69, 1.31)	0.98 (0.73, 1.31)
Other	0.77 (0.57, 1.03)	0.79 (0.58, 1.09)	0.78 (0.59, 1.03)
Caregiver Education			
College	Ref	Ref	Ref
Some college	1.16 (0.88, 1.53)	1.19 (0.88, 1.61)	1.17 (0.89, 1.53)
High school	0.78 (0.56, 1.07)	0.96 (0.68, 1.36)	0.84 (0.62, 1.14)
Some high school or less	1.07 (0.69, 1.66)	1.24 (0.78, 1.98)	1.13 (0.74, 1.72)
Income			
25,000 or less	Ref	Ref	Ref
Greater than 25,000	0.90 (0.69, 1.19)	<b>0.71 (0.53, 0.96)</b>	0.83 (0.64, 1.08)

**Table 3.**

ACEs by ACEs Screening Arm from PEARLS

ACEs	Item-level ACEs Screen Total N = 185	Aggregate-level ACEs Screen Total N = 182	p-value
Original ACEs, median (IQR)	1 (0–3)	2 (0–4)	0.01
Original ACEs			0.21
0 ACEs, N (%)	65 (35.1)	51 (28.0)	
1–3 ACEs, N (%)	85 (45.9)	85 (46.7)	
4 or more ACEs, N (%)	35 (18.9)	46 (25.3)	
Related Life Events, median (IQR)	1 (0–2)	1 (0–2)	0.04
Total PEARLS score, median (IQR)	2 (0–5)	3 (1–5)	0.01

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**Table 4.**

Probability of Original ACEs and Related Life Events\* (n=340)

Related Life Event	n(%)	Probability of 1 Original ACE	Probability of 2 Original ACEs
Neighborhood violence	83 (24.4)	90.4	73.5
Food Insecurity	64 (18.8)	95.3	79.7
Discrimination	51 (15.0)	92.2	80.4
Housing instability	80 (23.5)	93.7	79.9
Physical Illness of Caregiver	48 (14.1)	91.7	79.2
Forced Separation	37 (10.9)	94.6	81.1
Caregiver Death	29 (8.5)	75.9	58.7
	Median	92.2	79.7
	Range	75.9 – 95.3	58.7 – 81.1

\* Individual responses were obtained from caregivers completing the item-response PEARLS tool and from caregivers who subsequently identified the items their child experienced from the total-response PEARLS tool.

**Table 5.**

Association between ACEs and Related Life Events and General Health Outcomes

	Pooled Mean difference (95% CI)	Item-level Mean difference (95% CI)	Aggregate-level Mean difference (95% CI)	p-interaction
<b>PROMIS</b>				
<b>Original ACEs</b>				
Categorical				
0	Ref	Ref	Ref	0.18
1-3	-3.74 (-5.82, -1.67)	-5.70 (-8.70, -2.71)	-1.73 (-4.72, 1.26)	
4+	-8.17 (-10.85, -5.48)	-10.56 (-14.47, -6.66)	-6.05 (-9.90, -2.21)	
Continuous	-1.35 (-1.82, -0.88)	-1.68 (-2.37, -1.00)	-1.09 (-1.75, -0.44)	0.28
<b>Related Life Events</b>				
Continuous	-1.63 (-2.39, -0.88)	-2.47 (-3.57, -1.36)	-1.16 (-2.24, -0.07)	0.16
<b>Total PEARLS Score</b>				
Continuous	-0.94 (-1.26, -0.62)	-1.24 (-1.70, -0.78)	-0.75 (-1.20, -0.29)	0.20
Missed school days due to health (10 or more vs. < 10 days)				
<b>Original ACEs</b>				
Categorical				
0	Ref	Ref	Ref	0.62
1-3	0.84 (0.38, 1.87)	0.62 (0.30, 1.91)	1.11 (0.31, 3.95)	
4+	1.63 (0.66, 4.00)	1.28 (0.35, 4.64)	2.01 (0.50, 8.07)	
Continuous	1.15 (0.99, 1.33)	1.13 (0.91, 1.40)	1.14 (0.93, 1.41)	0.87
<b>Related Life Events</b>				
Continuous	<b>1.26 (1.01, 1.57)</b>	<b>1.54 (1.08, 2.11)</b>	1.04 (0.72, 1.51)	0.12
<b>Total PEARLS Score</b>				
Continuous	<b>1.11 (1.01, 1.23)</b>	<b>1.15 (0.99, 1.34)</b>	1.07 (0.93, 1.24)	0.51
<b>ED visit</b>				
	Pooled OR (95% CI)	Item-level OR (95% CI)	Aggregate-level OR (95% CI)	p-interaction
<b>Original ACEs</b>				
Categorical				
				0.84

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0	Ref	Ref	Ref	0.96
1-3	0.53 (0.27, 1.06)	0.73 (0.35, 1.51)	0.73 (0.35, 1.51)	
4+	0.73 (0.29, 1.86)	0.77 (0.33, 1.79)	0.77 (0.33, 1.79)	
Continuous	0.93 (0.80, 1.10)	0.95 (0.83, 1.10)	0.95 (0.83, 1.10)	0.96
<b>Related Life Events</b>				
Continuous	1.12 (0.87, 1.43)	0.99 (0.79, 1.25)	0.99 (0.79, 1.25)	0.81
<b>Total PEARLS Score</b>				
Continuous	0.99 (0.89, 1.11)	0.98 (0.89, 1.08)	0.98 (0.89, 1.08)	0.98
<b>Hospitalization</b>				
<b>Original ACEs</b>				
Categorical				
0	Ref	Ref	Ref	0.56
1-3	0.96 (0.28, 3.26)	0.19 (0.01, 2.56)	1.92 (0.34, 10.75)	
4+	0.75 (0.16, 3.60)	0.59 (0.03, 10.72)	1.12 (0.14, 9.14)	
Continuous	1.01 (0.78, 1.32)	0.92 (0.54, 1.59)	1.04 (0.77, 1.41)	0.77
<b>Related Life Events</b>				
Continuous	0.81 (0.50, 1.29)	0.38 (0.09, 1.89)	0.90 (0.53, 1.53)	0.42
<b>Total PEARLS Score</b>				
Continuous	0.97 (0.81, 1.17)	0.85 (0.55, 1.33)	1.00 (0.81, 1.24)	0.61

Models are adjusted for child's age, sex, race/ethnicity, caregiver's educational level, and family income. Pooled models were additionally adjusted for screening arm



**Table 6.** Association between ACEs and Related Life Events and Behavioral-Mental Health Outcomes

	Pooled OR (95% CI)	Item-level OR (95% CI)	A aggregate-level OR (95% CI)	p-interaction
<b>ADHD</b>				
<b>Original ACEs</b>				
Categorical				0.88
0	Ref	Ref	Ref	
1-3	0.95 (0.39, 2.29)	1.74 (0.48, 6.27)	0.56 (0.14, 2.26)	
4+	2.16 (0.86, 5.44)	3.22 (0.72, 14.41)	1.85 (0.45, 7.61)	
Continuous	1.15 (0.99, 1.33)	1.10 (0.87, 1.40)	1.21 (0.95, 1.53)	0.36
<b>Related Life Events</b>				
Continuous	1.12 (0.88, 1.41)	1.07 (0.74, 1.54)	1.16 (0.79, 1.70)	0.54
<b>Total PEARLS Score</b>				
Continuous	1.09 (0.98, 1.20)	1.06 (0.90, 1.25)	1.12 (0.95, 1.32)	0.40
<b>BRIEF Global Executive Composite Scale t-score (&lt; 65 vs. ≥ 65 clinical threshold)</b>				
<b>Original ACEs</b>				
Categorical				0.19
0	Ref	Ref	Ref	
1-3	5.58 (1.52, 20.42)	5.10 (0.95, 27.55)	6.30 (0.70, 56.51)	
4+	18.26 (4.60, 72.53)	10.63 (1.82, 62.23)	57.43 (4.99, 660.73)	
Continuous	1.74 (1.42, 2.14)	1.46 (1.13, 1.87)	3.17 (1.82, 5.52)	0.02
<b>Related Life Events</b>				
Continuous	1.66 (1.29, 2.15)	2.10 (1.37, 3.22)	1.63 (1.10, 2.42)	0.99
<b>Total PEARLS Score</b>				
Continuous	1.49 (1.26, 1.66)	1.39 (1.16, 1.67)	1.85 (1.37, 2.51)	0.11

Models are adjusted for child's age, sex, race/ethnicity, caregiver's educational level, and family income. Pooled models were additionally adjusted for screening arm

**Table 7.** Association between ACEs and Related Life Events and Physical Health Outcomes

	Pooled OR (95% CI)	Item-level OR (95% CI)	Aggregate-level OR (95% CI)	p-interaction
<b>Stomachaches</b>				
<b>Original ACEs</b>				
Categorical	Ref	Ref	Ref	0.17
0				
1-3	<b>3.06 (1.24, 7.57)</b>	<b>5.60 (1.09, 28.76)</b>	2.17 (0.69, 6.85)	
4+	<b>5.65 (2.18, 15.09)</b>	<b>18.24 (2.87, 115.79)</b>	3.12 (0.92, 10.57)	
Continuous	<b>1.25 (1.09, 1.43)</b>	<b>1.45 (1.14, 1.84)</b>	1.17 (0.98, 1.40)	0.26
<b>Related Life Events</b>				
Continuous	1.18 (0.96, 1.47)	<b>1.65 (1.16, 2.34)</b>	0.97 (0.72, 1.31)	0.04
<b>Total PEARLS Score</b>				
Continuous	<b>1.14 (1.04, 1.25)</b>	<b>1.33 (1.12, 1.57)</b>	1.07 (0.95, 1.20)	0.08
<b>Headaches/dizziness</b>				
<b>Original ACEs</b>				
Categorical	Ref	Ref	Ref	0.05
0				
1-3	1.44 (0.56, 3.71)	2.68 (0.61, 11.75)	0.63 (0.17, 2.37)	
4+	2.32 (0.85, 6.34)	<b>8.28 (1.69, 40.68)</b>	0.74 (0.18, 3.13)	
Continuous	1.11 (0.95, 1.29)	<b>1.28 (1.02, 1.61)</b>	0.98 (0.77, 1.23)	0.14
<b>Related Life Events</b>				
Continuous	1.24 (0.98, 1.58)	<b>1.51 (1.07, 2.13)</b>	1.01 (0.69, 1.46)	0.14
<b>Total PEARLS Score</b>				
Continuous	1.09 (0.98, 1.21)	<b>1.22 (1.04, 1.43)</b>	0.99 (0.85, 1.16)	0.09
<b>Asthma</b>				
<b>Original ACEs</b>				
Categorical	Ref	Ref	Ref	0.05
0				
1-3	<b>2.20 (1.22, 3.97)</b>	1.48 (0.62, 3.50)	<b>3.40 (1.44, 8.02)</b>	

	Pooled OR (95% CI)	Item-level OR (95% CI)	Aggregate-level OR (95% CI)	p-interaction
4+	<b>2.36 (1.17, 4.80)</b>	<b>3.80 (1.22, 11.84)</b>	2.23 (0.84, 5.94)	
Continuous	<b>1.12 (1.00, 1.26)</b>	<b>1.20 (1.00, 1.44)</b>	1.12 (0.95, 1.31)	0.75
<b>Related Life Events</b>				
Continuous	1.14 (0.95, 1.37)	<b>1.36 (1.00, 1.84)</b>	1.10 (0.85, 1.42)	0.39
<b>Total PEARLS Score</b>				
Continuous	<b>1.08 (1.00, 1.17)</b>	<b>1.16 (1.02, 1.32)</b>	1.07 (0.96, 1.20)	0.52
<b>Rhinitis</b>				
<b>Original ACEs</b>				
Categorical				
0	Ref	Ref	Ref	0.91
1–3	<b>2.36 (1.35, 4.13)</b>	<b>2.22 (1.04, 4.73)</b>	<b>2.47 (1.05, 5.82)</b>	
4+	<b>2.40 (1.22, 4.74)</b>	2.23 (0.82, 6.07)	2.57 (0.95, 6.90)	
Continuous	<b>1.12 (1.00, 1.25)</b>	1.13 (0.96, 1.34)	1.10 (0.94, 1.29)	0.51
<b>Related Life Events</b>				
Continuous	1.01 (0.85, 1.21)	1.10 (0.85, 1.44)	0.95 (0.74, 1.23)	0.35
<b>Total PEARLS Score</b>				
Continuous	1.06 (0.98, 1.14)	1.08 (0.96, 1.22)	1.04 (0.93, 1.15)	0.37
<b>Eczema</b>				
<b>Original ACEs</b>				
Categorical				
0	Ref	Ref	Ref	0.23
1–3	<b>2.19 (1.32, 3.65)</b>	1.53 (0.75, 3.12)	<b>3.50 (1.60, 7.68)</b>	
4+	<b>2.75 (1.44, 5.23)</b>	<b>2.83 (1.07, 7.48)</b>	<b>3.14 (1.25, 7.88)</b>	
Continuous	<b>1.16 (1.04, 1.29)</b>	1.16 (0.99, 1.37)	1.16 (0.99, 1.34)	0.86
<b>Related Life Events</b>				
Continuous	<b>1.24 (1.04, 1.47)</b>	<b>1.48 (1.12, 1.95)</b>	1.09 (0.86, 1.37)	0.09
<b>Total PEARLS Score</b>				
Continuous	<b>1.11 (1.03, 1.20)</b>	<b>1.16 (1.03, 1.30)</b>	1.08 (0.98, 1.20)	0.35
<b>Obesity</b>				

	Pooled OR (95% CI)	Item-level OR (95% CI)	Aggregate-level OR (95% CI)	p-interaction
<b>Original ACEs</b>				
Categorical				0.17
0	Ref	Ref	Ref	
1-3	1.74 (0.96, 3.16)	<b>2.94 (1.14, 7.55)</b>	1.02 (0.46, 2.31)	
4+	1.45 (0.70, 2.98)	2.69 (0.82, 8.76)	0.82 (0.31, 2.12)	
Continuous	1.02 (0.91, 1.15)	1.10 (0.92, 1.33)	0.96 (0.82, 1.12)	0.22
<b>Related Life Events</b>				
Continuous	1.02 (0.85, 1.22)	1.24 (0.94, 1.62)	0.87 (0.67, 1.13)	0.07
<b>Total PEARLS Score</b>				
Continuous	1.01 (0.93, 1.10)	1.09 (0.96, 1.24)	0.96 (0.86, 1.07)	0.11
<b>Infections</b>				
<b>Original ACEs</b>				
Categorical				0.10
0	Ref	Ref	Ref	
1-3	0.85 (0.52, 1.40)	0.91 (0.46, 1.81)	0.75 (0.35, 1.60)	
4+	0.89 (0.48, 1.64)	1.53 (0.60, 3.87)	0.52 (0.22, 1.24)	
Continuous	0.92 (0.83, 1.02)	1.03 (0.88, 1.20)	<b>0.83 (0.72, 0.96)</b>	0.04
<b>Related Life Events</b>				
Continuous	1.00 (0.85, 1.18)	1.17 (0.92, 1.50)	0.85 (0.67, 1.08)	0.04
<b>Total PEARLS Score</b>				
Continuous	0.96 (0.90, 1.03)	1.05 (0.94, 1.17)	<b>0.89 (0.80, 0.99)</b>	0.02
<b>Somatic symptoms</b>				
<b>Original ACEs</b>				
Categorical				0.45
0	Ref	Ref	Ref	
1-3	1.91 (0.98, 3.71)	1.91 (0.77, 4.73)	1.74 (0.64, 4.78)	
4+	0.99 (0.41, 2.35)	1.13 (0.33, 3.90)	0.79 (0.22, 2.78)	
Continuous	0.97 (0.84, 1.11)	1.05 (0.87, 1.28)	0.88 (0.72, 1.07)	0.15
<b>Related Life Events</b>				
Continuous	1.17 (0.96, 1.43)	1.30 (0.98, 1.72)	1.04 (0.77, 1.41)	0.28

	<b>Pooled OR (95% CI)</b>	<b>Item-level OR (95% CI)</b>	<b>Aggregate-level OR (95% CI)</b>	<b>p-interaction</b>
<b>Total PEARLS Score</b>				
Continuous	1.02 (0.93, 1.11)	1.08 (0.95, 1.23)	0.95 (0.82, 1.09)	0.14

Models are adjusted for child's age, sex, race/ethnicity, caregiver's educational level, and family income. Pooled models were additionally adjusted for screening arm