

Evaluating the Effect of Positive Childhood Experiences on the Risk of Psychiatric Disorders in Early Adulthood

Jennifer Murphy, M.Sc.,¹ Colm Healy, Ph.D.,^{2,3,4,5} David Mongan, M.B.B.Ch., Ph.D.,¹ Mary Clarke, M.D., F.R.C.Psych.,⁶ Ian Kelleher, Ph.D.,^{2,3,4,5} Agnes Higgins, B.N.S., Ph.D.,⁷ Brian O'Donoghue, Ph.D.,^{2,8} Ciaran Shannon, D.Clin.Psych.,⁹ Ciaran Mulholland, Ph.D.,¹⁰ Mary Cannon, M.B.B.Ch., Ph.D.,^{1,11} David R. Cotter, M.B.B.Ch., Ph.D.,^{1,11}

Objective: While the negative impacts of traumatic childhood experiences are well established, less is known about whether positive childhood experiences (PCEs) contribute to long-term mental health. The aim of this study was to estimate the effect of PCEs on the risk of psychiatric disorders in early adulthood.

Methods: Participants included 3,499 children from the Avon Longitudinal Study of Parents and Children. Eligible participants were nonrandomly exposed to PCEs (e.g., "school enjoyment" or "feeling safe in neighborhood") between ages 0 and 17, measured as a score ranging from 0 to 10. Inverse probability weighting (IPW) was used to account for the likelihood of PCE exposure conditional on confounders. The effect of PCE score on risk of psychiatric disorders at age 24, using IPW- and confounder-adjusted estimates, is reported. Subgroup analysis of individual disorders was subsequently conducted.

Results: In unweighted analyses, each one-unit increase in the PCE score was associated with a 12% decrease in the odds of psychiatric disorder (odds ratio=0.88, 95% CI=0.82, 0.95). In the IPW- and confounder-adjusted model, this effect was retained (odds ratio=0.89, 95% CI=0.82, 0.95). Robust associations between PCEs and lower odds of depressive disorder (odds ratio=0.84, 95% CI=0.76, 0.93) and generalized anxiety disorder (odds ratio=0.91, 95% CI=0.84, 0.99) were found. The findings for PCE score and psychotic disorder were inconclusive.

Conclusions: The findings indicate that PCEs are associated with reduced odds of meeting criteria for psychiatric disorders in early adulthood, particularly depression. Further research should explore PCEs as a potential preventive strategy that might reduce the burden of psychiatric disorders in early adulthood.

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Trauma-exposed individuals have a higher risk of psychiatric disorders than nonexposed individuals (1, 2), although not all develop adverse mental health outcomes (3). Resilience theory provides a strengths-based framework for understanding these divergent developmental trajectories (4). Zimmerman (4) refers to promotive factors or positive childhood experiences (PCEs), which interfere with developmental trajectories and help to buffer adversity and support healthy adult outcomes (5). PCEs have been described as independent factors that may enhance health and well-being over time (6, 7), and there has been an increased focus in understanding how they, and not just traumatic exposures, influence developmental and health outcomes.

The Health Outcomes from Positive Experiences (HOPE) framework identifies specific positive experiences, which can inform intervention strategies aimed at building children's resilience against adversity (8). PCEs, including high-quality relationships between parent, teacher, and

child, feeling safe in the neighborhood, and stimulating home-learning environments, are important for optimal development (8). PCEs are not simply reflective of an absence of trauma or adversity (6, 7). A child can simultaneously experience support (e.g., good relationship with parents) and trauma (e.g., emotional trauma from another caregiver) within the same environment. Moreover, PCEs and trauma are not on a continuum, but may reflect interacting systems operating through distinct resilience and risk pathways (9). While trauma exposure can heighten fear systems, increasing susceptibility to anxiety (10), PCEs promote emotional security and feelings of self-worth (11) to protect against negative feelings, including low mood.

The literature is gradually expanding, with studies demonstrating a link between PCEs and improved mental health outcomes (12). PCEs were associated with improved mental well-being and decreased anxiety and depression symptoms in children (13–15) and older adults (3). Young people with

high PCE exposure had lower psychological stress compared to peers with low PCE exposure and low adverse childhood experience exposure (16). There is also recent evidence of reduced risk of suicidal ideation and behavioral problems in adolescents with frequent positive experiences in childhood (17). Additionally, PCEs showed protective associations with adult outcomes, even at high levels of trauma exposure (3), which strengthens the conceptualization of PCEs as distinct from the absence of adversity. However, many of these studies used retrospectively reported PCEs, which can be subject to biases relating to the motivation of reporters or memory biases (e.g., 3, 15). Comparatively less attention has also been given to other forms of psychopathology, such as psychotic disorder.

Randomized control trials (RCTs) are typically the gold standard for studying the efficacy of an intervention (18). However, running a PCE-related RCT would be challenging. Therefore, we chose to use an emulated target trial (ETT) framework, which offers a more robust approach than conventional observational analyses. This framework aims to control for measured confounders and make two groups of interest as exchangeable as possible by using statistical methods to emulate randomization and improve the accuracy of estimated associations (19). A target trial is not the “ideal” RCT, but one that can be reasonably emulated with the available observational data (19). When compared, studies using a target trial framework have been found to reach conclusions similar to those of RCTs (20).

While a focus on trauma is important for developing and improving services and supports, a focus on PCEs moves to a more strengths-based and balanced view of children’s lives. Thus, guided by principles of the ETT framework, we aimed to explore the relationship between exposure to PCEs and meeting criteria for psychiatric outcomes at age 24, including psychotic disorder, generalized anxiety disorder (GAD), and moderate/severe depressive disorder. To our knowledge, this is the first study to look at psychotic disorder with respect to PCE exposure. We hypothesized that higher PCE exposure would be associated with reduced risk of meeting criteria for psychiatric disorders at age 24, as well as moderate/severe depression, psychotic disorder, and GAD specifically. These associations are expected to remain after adjustment for childhood trauma exposure.

METHODS

The main research question was to estimate the effect of exposure to PCEs between the ages of 0 and 17 years on the risk of meeting criteria for at least one of three psychiatric disorders at age 24: moderate/severe depression, psychotic disorder, and GAD. Previous studies have also used these outcomes (e.g., 21). The present study was reported in line with the Transparent Reporting of Observational Studies Emulating a Target Trial (TARGET) guidelines (22). An ETT framework was used to guide the study design and analysis (19).

Target Trial Specification

In the hypothetical trial, children would be randomized at birth to receive various numbers of PCEs throughout childhood (0–17 years). The outcome would include adult measures of psychiatric disorders, including psychotic disorder, GAD, and depressive disorder, at age 24, assessed by clinical interview. Those who developed the disorder during the intervention period would be excluded from the study. We would estimate an intention-to-treat effect by comparing assignment to having grown up with or without PCE exposure on adult psychiatric outcomes by age 24 using logistic regression. This estimate would compare the odds of adult psychiatric disorders among those exposed and unexposed to PCEs.

Emulated Target Trial

Following an ETT framework, we used data from the Avon Longitudinal Study of Parents and Children (ALSPAC), which is a general-population birth cohort based in Avon county in England (23–25). Study data were collected and managed using REDCap tools (26). For further details, see the online supplement. Individuals were included in the analysis if they met the eligibility criteria for the target trial (see Table S1 in the online supplement).

Psychiatric Outcomes at Age 24

Psychiatric disorders. Outcomes were based on measurement considerations and prior research (e.g., 21, 27) with a focus on disorders measured using validated assessment tools at the age-24 ALSPAC clinic which helps to preserve temporality, rather than self-reported lifetime diagnoses (e.g., bipolar disorder). As done previously (e.g., 27), individual psychiatric outcomes were combined, creating one primary outcome measure of meeting criteria for at least one of three psychiatric disorders (psychotic disorder, GAD, or moderate/severe depressive disorder) at age 24. To avoid issues with temporality, 331 individuals were excluded prior to analysis due to meeting criteria for psychotic disorder, GAD, or moderate/severe depressive disorder by age 17, resulting in a study sample of 3,499 participants.

Psychotic disorder. ALSPAC participants completed the semi-structured Psychosis-Like Symptoms Interview (PLIKSi) (28). In line with previous studies (21, 29), psychotic disorder was defined as having at least one definite psychotic experience not attributable to sleep or fever that recurred at least once per month over the previous 6 months and was associated with severe distress or marked impairment of social or occupational functioning, or led the participant to seek help from a professional source.

Generalized anxiety disorder. Participants completed a self-administered computerized version of the Clinical Interview Schedule–Revised (CIS-R) (30), which is used to measure the presence and severity of common psychiatric disorders. The tool was used to assess whether participants met criteria for GAD based on *ICD-10* criteria (31), as done previously (21).

Moderate/severe depressive disorder. The CIS-R also included questions about depressive symptoms. Similarly, the tool was used to assess whether participants met criteria for moderate/severe depressive disorder based on *ICD-10* criteria (31), as done previously (21). For further details, see the online supplement.

Exposure: Positive Childhood Experiences

The HOPE framework and prior research (32) guided our measurement of PCEs (see the online supplement) (8, 32, 33). Ten PCEs were constructed from a total of 37 questions from ALSPAC clinics and surveys (32), which were asked of the parent or study child from infancy to age 17 (see Table S2 in the online supplement). The majority of questions were reported by the study child, and some reported by the study child's mother.

The 10 PCEs were 1) high-quality parent relationship with study child, 2) high-quality teacher relationship with study child, 3) high peer/social support for study child, 4) feeling safe in the neighborhood/high neighborhood livability, 5) high neighborhood social capital, 6) structured and stable living environment, 7) positive home learning environment for study child, 8) high number of activities outside the home for study child, 9) high-frequency contact between study child and family and friends, and 10) high school enjoyment. Table S3 in the online supplement presents the sample distribution of the 10 PCEs.

A total PCE score was derived from adding the 10 PCE questions and assigning a score of 0 to that PCE if the child had not experienced it and 1 if the child had experienced it, so that the final variable reflected a total PCE score ranging from 0 to 10. The total PCE score reflects the overall breadth of positive experiences across childhood, rather than focusing on any single domain in isolation, which is in line with the HOPE framework (8) and prior research (e.g., 15, 33, 34). Our aim was to capture the combined influence of growing up in a more positive environment.

Confounders

Confounders were selected based on previous research, available data, and their likely association with PCEs and the psychiatric disorders (see the online supplement). The included confounders were sex, low birthweight (z-standardized), maternal age at birth, maternal history of psychiatric disorder, maternal smoking during pregnancy, parental education level, child ethnicity, familial socioeconomic status (SES), and home ownership status. We included a child ethnicity-by-familial SES interaction term to improve covariate balance after weighting, resulting in a better-specified model (see Figure S2 in the online supplement).

Post hoc sensitivity analyses involved adjusting for additional covariates, including an adverse childhood experiences score and polygenic risk scores (PRSs). For further details, see the online supplement.

Statistical Analysis

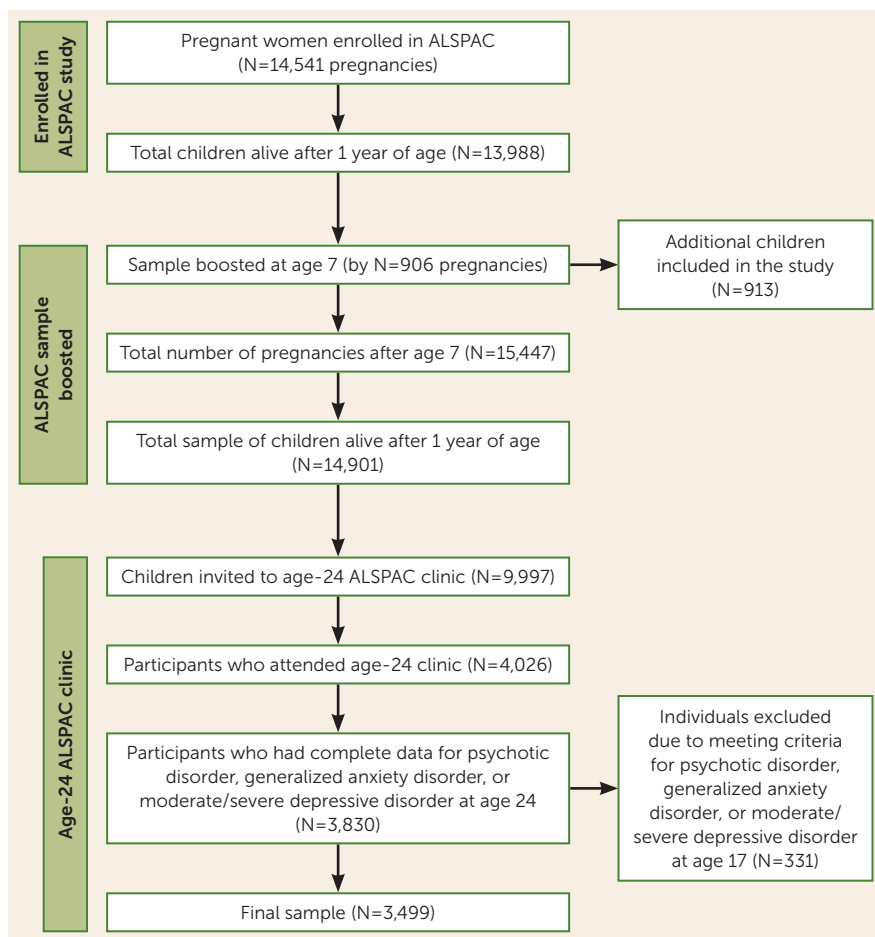
Descriptive statistics. Key participant sociodemographic characteristics were examined for individuals who met or did not meet criteria for a psychiatric disorder, using chi-square or Wilcoxon rank sum tests as appropriate. Frequencies and percentages, and median and interquartile ranges (IQR), are reported for the categorical data, and mean values and standard deviations are presented for continuous data.

Analysis. Logistic regression was used to estimate the unadjusted association between exposure to PCEs and meeting criteria for psychiatric disorders at age 24. Stabilized inverse probability weighting (IPW) was then used to adjust for confounding (19). Due to the count nature of the PCE score, we used Poisson regression models of the exposure, and the full conditional probability distribution was modeled. The denominator was the estimated conditional mean of the exposure given their pretreatment covariates, and the numerator of the weight was the unconditional mean of the exposure without confounders (35). The resulting stabilized IPWs were applied in a weighted logistic regression model, additionally adjusted for confounders to estimate the effect of exposure to PCEs on the risk of meeting criteria for psychiatric disorders at age 24. Predicted values for each counterfactual scenario (all individuals assigned the lowest observed PCE score [0] and all individuals assigned the highest observed PCE score [10]) were estimated from the logistic regression model. Robust standard errors were used, and reported metrics include odds ratios with 95% confidence intervals. Formal assessment of nonlinearity and presentation of predicted absolute risks are discussed in the online supplement. The child ethnicity-by-familial SES interaction term was not included as a confounder when exploring the relationship between PCE exposure and psychotic disorder due to lack of statistical power.

To assess the robustness of the observed association to unmeasured confounding, we calculated the e-value, which reflects the minimum strength of association that an unmeasured confounder would need to have with both the exposure and outcome to fully explain away a specific exposure-outcome association, conditional on the measured confounders (36).

In the primary analyses, missing data for PCEs and confounders were imputed using multiple imputation with chained equations (see Table S3 in the online supplement) (37). Sixteen auxiliary variables were included in the imputation model, with the exposure and confounding variables (see the online supplement). Twenty imputed datasets were created. All analyses were conducted using the imputed sample. Multiple imputation has previously been used with an ETT framework (38).

Additional sensitivity analyses. We additionally adjusted for the number of traumas experienced between ages 0 and 17, alongside the confounders included in the IPWs (27). Restricted cubic splines with three knots were used to account

FIGURE 1. Flow chart of ALSPAC participants^a

^aALSPAC, Avon Longitudinal Study of Parents and Children.

for potential nonlinear associations between trauma exposure and psychiatric outcomes (39). Trauma exposure was derived from 121 parent- and self-reported items assessing the following trauma types: physical, sexual, and emotional abuse, emotional neglect, domestic violence, and bullying (40).

Sensitivity analyses included the use of a binary PCE variable and complete case analysis (CCA) to assess the impact of PCE score specification and missing data. Post hoc sensitivity analyses additionally adjusted for adverse childhood experience scores and PRSs, included participants reporting psychiatric outcomes at age 17, and compared child (0–11 years) and adolescent (12–17 years) PCE scores. For further details as well as sex-stratified analyses, see the online supplement.

RESULTS

Sample Characteristics

The study sample included 3,499 participants who attended the age-24 ALSPAC clinic and completed psychiatric assessments (Figure 1). Outcome frequencies were psychotic disorder (N=33), GAD (N=278), and moderate/severe depression (N=217). Those meeting psychiatric criteria were more likely to be female, had higher trauma exposure and differ-

ent PCE scores relative to those who did not meet psychiatric criteria, and were more likely to have mothers who smoked during the first trimester of pregnancy (Table 1). The median PCE score was 3 (IQR=2) (for the distribution, see Table S3 in the online supplement).

Stabilized IPWs

Table S4 in the online supplement shows the mean and average range of stabilized IPWs across imputations. Figure S2 in the online supplement plots the covariate balance for PCEs in unweighted and weighted participants.

Positive Childhood Experiences and Psychiatric Disorders

In unadjusted analyses, PCEs were significantly associated with reduced odds of meeting criteria for a psychiatric disorder at age 24 (odds ratio [OR]=0.88, 95% CI=0.82, 0.95, $p=0.001$) (model 1, Table 2). Specifically, each one-unit increase in the PCE score was associated with a 12% decrease in the odds of these psychiatric outcomes. In the IPW- and confounder-adjusted model, this relationship remained (OR=0.89, 95% CI=0.82, 0.95, $p=0.001$) (model 2, Table 2).

Subgroup Analysis

Moderate/severe depressive disorder at age 24. In unadjusted analyses, total PCE score was significantly associated with reduced odds of meeting criteria for moderate/severe depressive disorder at age 24 (OR=0.84, 95% CI=0.76, 0.93, $p=0.001$) (model 1, Table 2). In the IPW- and confounder-adjusted model, this effect remained (OR=0.84, 95% CI=0.76, 0.94, $p=0.001$) (model 2, Table 2).

Psychotic disorder at age 24. In terms of the relationship between psychotic disorder, the findings were inconclusive. Specifically, in the unadjusted analyses, total PCE score was not significantly associated with reduced odds of meeting criteria for psychotic disorder at age 24 (OR=0.81, 95% CI=0.63, 1.04, $p=0.09$) (model 1, Table 2). This relationship did not substantially change in the IPW- and confounder-adjusted model (OR=0.82, 95% CI=0.66, 1.03, $p=0.09$) (model 2, Table 2). However, these analyses could be imprecisely estimated due to the small number of cases with psychotic disorder (N=33).

Generalized anxiety disorder at age 24. In unadjusted analyses, total PCE score was significantly associated with reduced odds of meeting criteria for GAD at age 24 (OR=0.91,

TABLE 1. Characteristics of the sample^a

Characteristic	No psychiatric disorder (N=3,091)		Psychiatric disorder (N=408)		p	Missing data	
	N	%	N	%		N	%
Sex					<0.001	<5	<5
Male	1,251	40.47	113	27.70			
Female	1,840	59.53	295	72.30			
Socioeconomic status					0.11	740	21.15
High	2,140	69.23	258	63.24			
Low	312	10.09	49	12.01			
Child ethnicity					0.6	402	11.49
White	2,633	85.18	341	83.58			
Non-White	107	3.46	16	3.92			
Maternal history of psychiatric disorder					0.36	<5	<5
No	2,921	94.50	381	93.38			
Yes	170	5.50	27	6.62			
Maternal age at birth of study child					0.13	263	7.52
<15–24 years	353	11.42	60	14.71			
25–34 years	2,110	68.26	263	64.46			
≥35 years	399	12.91	51	12.50			
Maternal education					0.9	366	10.46
Less than O-levels	458	16.53	61	16.80			
O-level or higher	2,312	83.47	302	83.20			
Paternal education					0.5	419	11.97
Less than O-levels	611	22.41	85	24.01			
O-level or higher	2,115	7.59	269	75.99			
Home ownership status					0.05	582	7.52
Own home/mortgage	314	12.11	52	16.00			
Rent or other	2,278	87.89	273	84.00			
Maternal smoking during pregnancy					<0.001	323	9.23
No	2,415	85.91	287	78.63			
Yes	396	14.09	78	21.37			
Number of childhood trauma exposures							
0 trauma	1,255	43.85	136	36.76			
1 trauma	872	30.47	98	26.49			
2 traumas	422	30.47	76	20.54			
3 traumas	220	7.69	41	11.08			
4 or more traumas	93	3.25	19	5.14			
Number of PCEs							
0	313	10.13	65	15.93			
1	379	12.26	56	13.73			
2	568	18.28	88	21.32			
3	669	21.64	76	18.63			
4	590	19.09	65	15.93			
5	344	11.13	42	10.29			
6	162	5.24	10	<5			
7	57	<5	5	<5			
8	<5	<5	<5	<5			
9	<5	<5	<5	<5			
10	<5	<5	<5	<5			
	Median	SD	Median	SD	p	N	%
Median total number of traumas experienced	3	2	2	3	0.002	<5	<5
Median total PCE score	1	2	1	2	<0.001	267	7.63
	Mean	SD	Mean	SD	p	N	%
Birth weight (kg)	3.42	0.53	3.42	0.53	0.83	298	8.52

^a Note that <5 may include zero. IQR, interquartile range; PCE, positive childhood experience.

95% CI=0.84, 0.99, p=0.027) (model 1, Table 2). In the IPW- and confounder-adjusted model, this relationship did not substantially change (OR=0.91, 95% CI=0.84, 0.99, p=0.031) (model 2, Table 2).

E-Value Checks

It was estimated that unmeasured confounding would require an effect size (odds ratio) range of 1.43–1.74 of the exposure-outcome relationship to remove the effect of PCE

TABLE 2. Unadjusted and IPW- and confounder-adjusted associations of the effect of PCE score on risk of psychiatric disorders at age 24, including subgroup analysis of individual disorders^a

Psychiatric outcome	Odds ratio	95% CI	p
Any psychiatric disorder at age 24			
Model 1: Unadjusted model	0.88	0.82, 0.95	0.001
Model 2: IPW- and confounder-adjusted model	0.89	0.82, 0.95	0.001
Subgroup analysis			
Moderate/severe depressive disorder at age 24			
Model 1: Unadjusted model	0.84	0.76, 0.93	0.001
Model 2: IPW- and confounder-adjusted model	0.84	0.76, 0.94	0.001
Psychotic disorder at age 24			
Model 1: Unadjusted model	0.81	0.63, 1.04	0.090
Model 2: IPW- and confounder-adjusted model ^b	0.82	0.66, 1.03	0.090
Generalized anxiety disorder at age 24			
Model 1: Unadjusted model	0.91	0.84, 0.99	0.027
Model 2: IPW- and confounder-adjusted model	0.91	0.84, 0.99	0.031

^a IPW, inverse probability weighting.^b Analysis does not include ethnicity-by-socioeconomic status interaction term as a confounder.

on each outcome (see Figures S3–S6 in the online supplement).

Sensitivity Analyses

Sensitivity analyses. After adjusting for the number of childhood trauma exposures, total PCE score remained associated with lower odds of meeting criteria for psychiatric disorder overall (IPW- and confounder-adjusted OR=0.88, 95% CI=0.80, 0.96, $p=0.004$), specifically depressive disorder (IPW- and confounder-adjusted OR=0.82, 95% CI=0.73, 0.93, $p=0.002$). Associations with GAD were weaker ($p=0.056$). Findings for psychotic disorder remained inconclusive (see Table S6 in the online supplement).

Analyses using a binary PCE variable (low [≤ 3] vs. high [≥ 4]) produced similar results. Summary statistics for stabilized IPWs are shown in Table S7 in the online supplement. Covariate balance before and after weighting is presented in Figure S6 in the online supplement. Total PCE score was associated with reduced odds of meeting criteria for psychiatric disorder (IPW- and confounder-adjusted OR=0.74, 95% CI=0.59, 0.94, $p=0.012$; see Table S8 in the online supplement). Corresponding e-values and adjusted estimates are reported in Tables S9 and S10, respectively, in the online supplement.

CCA findings were also consistent with the main findings. Summary statistics for stabilized IPWs are shown in Table S11 in the online supplement, and covariate balance is presented in Figure S7 in the online supplement. Total PCE score was associated with reduced odds of meeting criteria for psychiatric disorder overall (IPW- and confounder-adjusted OR=0.78, 95% CI=0.68, 0.90, $p=0.001$), specifically moderate/severe depressive disorder (IPW- and confounder-adjusted OR=0.64, 95% CI=0.53, 0.77, $p<0.001$; see Table S12 in the online supplement). Associations with GAD were not significant, likely due to reduced statistical power. Corresponding e-values are shown in Table S13 in the online supplement, and estimates adjusted for childhood trauma exposures in Table S14 in the online supplement.

Analyses for psychotic disorder were not conducted due to the small sample size ($N=9$).

Post hoc sensitivity analyses. Post hoc analyses adjusting for an adversity score continued to show significant associations between total PCE score and lower odds of meeting criteria for psychiatric disorder overall, specifically depressive disorder, while associations with GAD and psychotic disorder were nonsignificant (see Table S15 in the online supplement).

Further analyses adjusting for PRSs yielded findings consistent with the main analyses. Summary statistics for stabilized IPWs are presented in Table S16 in the online supplement, and estimates for all associations are shown in Table S17 in the online supplement.

For example, total PCE score was associated with reduced odds of meeting criteria for psychiatric disorder in the PRS-adjusted analyses (IPW- and confounder-adjusted OR=0.76, 95% CI=0.65, 0.88, $p<0.001$). Corresponding e-values are shown in Table S18 in the online supplement, and covariate balance is presented in Figure S8 in the online supplement.

Including participants with psychiatric outcomes at age 17 ($N=3,830$) did not substantially alter the findings. Summary statistics for stabilized IPWs are presented in Table S19 in the online supplement, estimates are shown in Table S20 in the online supplement, corresponding e-values are shown in Table S21 in the online supplement, and covariate balance is presented in Figure S9 in the online supplement.

Analyses using child (0–11 years) and adolescent (12–17 years) PCE scores also broadly reflected the main findings. Summary statistics for stabilized IPWs are presented in Table S22 in the online supplement. Child PCE score was not significantly associated with meeting criteria for psychiatric disorder. However, it was associated with reduced odds of meeting criteria for psychotic disorder (IPW- and confounder-adjusted OR=0.74, 95% CI=0.59, 0.94, $p=0.015$) (see Table S23 in the online supplement). Associations for adolescent PCE score were consistent with the main analyses (see Table S23 in the online supplement). Corresponding e-values are reported in Table S24 in the online supplement, and covariate balance is presented in Figure S10 in the online supplement.

Sex-stratified post hoc exploratory analyses were conducted. Tables S25 and S27 in the online supplement provide summary statistics for stabilized IPWs. When stratified by male, the findings were not significant (see Table S26 in the online supplement). When stratified by female, the unadjusted and IPW- and confounder-adjusted models for the effect of PCE score on risk of meeting criteria for psychiatric disorder were significant (see Table S28 in the online supplement).

supplement). Figures S11 and S13 in the online supplement show the corresponding e-value statistics, and Figures S12 and S14 in the online supplement show the covariate balance before and after IPW.

DISCUSSION

To our knowledge, this study is the first to use an ETT framework as an approach to investigate the relationship between PCE exposure and psychiatric outcomes. In line with our hypothesis, PCE exposure was associated with reduced odds of meeting criteria for a psychiatric disorder, which remained significant after adjustment for trauma. PCE score was associated with reduced odds of meeting criteria for moderate/severe depressive disorder and GAD. Contrary to our hypothesis, the relationship between PCE exposure and psychotic disorder was inconclusive.

Our findings suggest that PCEs may be promotive factors for mental health in early adulthood (4). Our results support findings from previous research that showed associations between PCEs and reduced psychiatric outcomes in mid-life (27) and lower odds of depression (3, 14). Moreover, our findings extend this growing body of PCE literature, first by using an ETT framework as an approach to demonstrate the persistent effects of childhood PCEs through to early adulthood. Second, existing research has predominantly investigated the impact of PCEs on outcomes in childhood/adolescence (17, 34) or middle adulthood (27). Lee et al. (41) explored mental health outcomes in a sample 18–97 years of age. While valuable, other critical windows are somewhat underexplored, including early adulthood. There is limited research that shows reduced symptoms of anxiety and depression and substance use outcomes within the 18- to 25-year age range, but PCEs are retrospectively reported (16, 42) or only measured between the ages of 10–13 years (7). Early adulthood represents a key developmental period: young adults are navigating major life transitions, including higher education or full-time work (43). It is also a period of heightened instability, as young people face the trials of relationships and frequent job changes (43). As elevated stress exposure during this phase may interact with early-life exposures to influence physiological regulation and long-term health risk, emerging adulthood constitutes an important target for research. Collectively, the findings may support an “expanded” multiple-hit model (44, 45) in which outcomes are impacted by the interplay between cumulative environmental risk and protective experiences (44).

The evidence of a relationship between PCEs and psychotic disorder was inconclusive, which may be due in part to the relatively low prevalence of psychotic disorder in the sample. We hypothesize that in a larger sample, the effects shown by PCEs on the odds of meeting criteria for depressive disorder in this study may be evident for people with psychotic disorder. Frequent reports of pathophysiological, genetic (46), and inflammatory (47) overlap between psychotic and depressive disorder suggest a mutual relationship of risk between the

two disorders (46). Additionally, while the sample was small, post hoc sensitivity analyses showed that child PCE score was associated with reduced odds of psychotic disorder in early adulthood. Future studies with larger prospective datasets should consider this approach.

Furthermore, a previous study showed that PCEs were most protective for individuals with fewer adversities (27). In our study, higher PCE scores were still associated with lower odds of meeting psychiatric disorder criteria, after adjusting for trauma, suggesting that PCEs promote general resilience rather than specifically buffering trauma (11). This association also remained following trauma adjustment for moderate/severe depressive disorder but was attenuated for GAD. This could be due to lower prevalence of GAD, or perhaps PCEs and trauma influence different resilience and risk pathways (9, 10). Moreover, the PCE indicators in this study have not been formally validated, and the findings should be interpreted in light of this measurement limitation.

Several strengths of this study are noteworthy. First, a longitudinal birth cohort was used, which provided a large overall sample size with repeated measures of PCEs. However, the ALSPAC participants are mostly White, which may limit generalizability. Second, the PCEs were prospectively reported, which reduces recall bias (48). In addition to self-reported data by the study children, parental reports of PCEs were used. This multi-informant approach to PCEs can be considered a strength of the study. However, parental reports could also overreport PCEs experienced by the child due to social-desirability effects (49). Additionally, given the associations observed with depression/anxiety, at-risk individuals may have reported their circumstances more negatively. Third, the PCEs were identified in line with previous research (8, 32) and were defined using an “ever exposed” approach consistent with previous research (32, 33). The decision to use a total PCE score was motivated by several considerations. First, our measure from 0–17 years is conceptually aligned with a life-course perspective in which the accumulation of stressors (or positive events), rather than any single exposure or specific timing, may be most relevant for later outcomes (50). Second, PCE scores have been widely used in prior research (e.g., 3, 34), allowing our findings to be situated within a broader evidence base. Third, stratifying the PCE exposures by specific developmental stages, duration, or intensity would increase model complexity and reduce statistical power.

However, this approach has limitations, as the PCE score does not capture the type, frequency, intensity, chronicity, or timing of exposures, and the long exposure window may increase the likelihood of the exposure, independent of underlying risk. Also, substantial developmental changes take place across childhood and adolescence, and PCE measures should be validated for sensitivity to these changes. Post hoc analyses using separate child and adolescent PCE scores showed that adolescent PCE findings reflected the main analyses, while child PCE score was significantly associated with psychotic

disorder. These findings provide some reassurance that associations were not driven solely by a single developmental stage, although the inability to account fully for the timing, duration, and variability of PCEs across youth remains a limitation.

Additionally, a limitation of using a total PCE score is that it assumes that each PCE contributes equally to mental health outcomes and may mask differences in the relative importance of specific experiences. Although cumulative measures are useful for capturing overall exposure to protective experiences, future studies should investigate whether particular PCE domains have stronger or more specific associations with mental health outcomes.

Moreover, this approach does not align with a strict ETT framework, in which treatment assignment and follow-up would be anchored to a clearly defined time zero and exposures would be explicitly time-varying (19). Our aim was that the ETT approach would strengthen the transparency and interpretability of the research, as the analysis is structured around a clearly defined question and specified time frame, rather than as a design that could be perfectly implemented given the available data.

Additionally, three PCEs tended to be low scoring in the sample (high peer/social support for study child, high neighborhood social capital, and high school enjoyment). While we cannot infer causality, parental reports may not reflect accurate school experience. Additionally, peer relationships can change, and therefore our measure may only capture young people with stable friendships. While the PCEs used in the study were largely derived from previous research (32), and we aimed to identify the variables that most closely aligned with those conceptual definitions, the PCE indicators were not formally validated, and some measures may vary in their degree of conceptual alignment. Future research should aim to use prospective cohorts and use validated PCE measures, or validate derived PCE measures in longitudinal cohorts where direct assessments of PCEs are unavailable.

This study is also the first, to our knowledge, to include psychotic disorder as an outcome, although the small sample size hinders interpretation of the findings. Furthermore, the criteria for GAD and depressive disorder were self-reported and defined according to the CIS-R. While case definitions in the CIS-R used by ALSPAC are comparable to primary care data (51), future research should consider using both clinical and self-reported measures for mental health outcomes.

This study is also the first, to our knowledge, to use an ETT as an approach to investigate the relationship between exposure to PCEs and early adult psychiatric outcomes (52). E-values indicated that an unmeasured confounder would need to be associated with both exposure and outcome by a risk ratio of approximately 1.46–1.88 to fully explain the observed associations. While primary models adjusted for as many covariates as possible, and post hoc analyses additionally included adverse childhood experience scores and PRSs, which strengthened confidence in the findings, the modest e-values suggest that residual confounding cannot be excluded. For

example, early family environment factors (e.g., parenting style) may influence both PCE exposure and later psychiatric risk but are difficult to fully measure. Therefore, no matter how well the ETT framework is attempted (53), the findings should be interpreted with some caution.

In the primary analyses, missing data for PCEs and confounders were imputed using multiple imputation (37). While sensitivity analyses were conducted using CCA, this design reduces the sample size, potentially impacting the generalizability of the findings (54). However, the consistency of results in the primary analyses and CCA provides some reassurance regarding the robustness of the findings.

We excluded individuals who met criteria for psychiatric disorders during the exposure period (0–17 years) to preserve temporal order, but this may have introduced survivorship or selection bias (55), where those with fewer PCEs are more likely to develop the outcome earlier, and so their exclusion could lead to an underestimation of the true association. Additionally, it is logical to assume that those who presented earlier are a more vulnerable or at-risk group. Post hoc analyses including these participants in the ETT design produced similar estimates to the main analyses, suggesting that the results are unlikely to be substantially driven by this bias, although it cannot be fully ruled out. Future studies should consider alternative baseline definitions.

In summary, this study is the first to use an ETT approach to investigate the relationship between exposure to PCEs and psychiatric outcomes in early adulthood. The findings indicate that PCE exposure reduced the odds of meeting criteria for a psychiatric disorder and moderate/severe depressive disorder, and these associations persisted after childhood trauma adjustment. Well-powered studies are warranted to fully explore the relationship between PCEs and other disorders, including psychotic disorder, in early adulthood.

AUTHOR AND ARTICLE INFORMATION

¹Department of Psychiatry, RCSI University of Medicine and Health Sciences, Dublin. ²School of Medicine, University College Dublin, Belfield, Dublin. ³Institute for Neuroscience and Cardiovascular Research, University of Edinburgh, Edinburgh. ⁴Faculty of Medicine, University of Oulu, Oulu, Finland. ⁵Saint John of God Hospitaller Services Group, Stillorgan, Dublin. ⁶DETECT Early Intervention for Psychosis Service, Blackrock, Co. Dublin. ⁷School of Nursing and Midwifery, Trinity College Dublin, Dublin. ⁸Department of Psychiatry, St. Vincent's University Hospital, Elm Park, Dublin. ⁹Northern Health and Social Care Trust (STEP team and IMPACT Research Centre), Antrim, UK. ¹⁰Centre for Medical Education, School of Medicine, Queen's University Belfast, Belfast. ¹¹FutureNeuro Research Ireland Centre, Royal College of Surgeons in Ireland, Dublin.

Send correspondence to Ms. Murphy (jennifermurphy22@rcsi.com).

Ms. Murphy  <https://orcid.org/0000-0002-2480-7656>

Dr. Healy  <https://orcid.org/0000-0001-7974-1861>

Dr. Mongan  <https://orcid.org/0000-0001-7931-9636>

Prof. Kelleher  <https://orcid.org/0000-0003-1484-651X>

Prof. Higgins  <https://orcid.org/0000-0002-0631-1884>

Prof. O'Donoghue  <https://orcid.org/0000-0001-6240-6952>

Dr. Shannon  <https://orcid.org/0000-0001-6407-4840>

Dr. Mulholland  <https://orcid.org/0000-0002-8707-2562>

Prof. Cannon  <https://orcid.org/0000-0002-0910-299X>

Prof. Cotter  <https://orcid.org/0000-0003-4308-0648>

Drs. Healy, Mongan, Cannon, and Cotter are co-senior authors.

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