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Childhood adversity increases risk of psychotic experiences in patients with substance use disorder

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ABSTRACT

Introduction: Adverse childhood experiences (ACEs) increase the risk of psychotic experiences (PE), but little is known about heterogeneities of this association in different developmental stages, dimensions, or whether they are affected by substance use disorder (SUD). This study examines the association between different types of ACEs at various developmental stages and lifetime PE in patients with SUD in Chile.
Methods: We included 399 consenting adults in outpatient or residential SUD treatment programs. Sociodemographic data and information about PE and ACEs were obtained by trained clinical psychologists.
Results: Patients reporting PE experienced more ACEs compared to patients without PE (4.2 versus 3.4). They also experienced more complex adversities (41.8% versus 25.1%), had more psychiatric comorbidities (85% versus 70.4%), and reported using more substances (mean 4.5 versus 3.9). Adjusted association between ACEs and PE showed the highest OR for arrests (1.88), sexual abuse (1.81), alcohol abuse by parents (1.48), school exclusion (1.39), foster or residential care (18.3).
Conclusion: Early exposure to ACEs is a risk factor for later PE among patients with SUD. Type of ACE and the period when they occurred is important, suggesting the existence of critical periods where the individual is more susceptible to adverse environmental stimuli.

1. Introduction

Approximately 5–10% of the general population experience perceptual abnormalities or unusual thought content (McGrath et al., 2015). Most psychotic experiences (PE) are found in non-diagnosed individuals, but they cluster within general measures of nonpsychotic psychopathology (Kelleher and Cannon, 2016; McGrath et al., 2016). They also render the behavioral expression of distributed risk for psychotic disorders (Kaymaz and van Os, 2010). PE may represent transdiagnostic clinical markers of psychopathology severity, as they predict poorer socio-occupational and neurocognitive functioning, psychopathology, and a higher risk for suicidal behavior (Kelleher and Cannon, 2016).

Exposure to Adverse Childhood Experiences (ACEs), such as violence, abuse, neglect, separation from caregivers, and poverty, are associated with altered patterns of emotional, cognitive, and social development (Hughes et al., 2017; McLaughlin et al., 2019). Children experiencing ACEs have a two-fold increase in the risk of developing a mental disorder, and the odds increase dramatically as exposure to adversity increases (Bielas et al., 2016; Kessler and Üstün, 2004; McLaughlin et al., 2019; Vásquez Núñez, 2020). ACEs have also been associated with an elevated risk of later PE (Mackie et al., 2011;

Abbreviations: ACE, adverse childhood experience; PE, psychotic experience; SUD, substance use disorder.

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McGrath et al., 2017; McLaughlin et al., 2019; Morgan and Gayer-Anderson, 2016; Trotta et al., 2015; Varese et al., 2012) and psychotic disorders (Morgan et al., 2020; Thompson et al., 2014; van Nierop et al., 2016). While the evidence for both of these associations is strong, little is known about whether they vary at different developmental stages (McGrath et al., 2017) or by type of ACEs (McLaughlin et al., 2019; Morgan et al., 2020).

Different ACEs reflect distinctive environmental experiences, influencing early cognitive, emotional, and neurological development (Bellis et al., 2014; Hughes et al., 2017; Kessler et al., 2010; McLaughlin et al., 2014; McLaughlin and Sheridan, 2016; Sheridan and McLaughlin, 2014). Conceptual models to study the consequences of ACEs are still a matter of debate (Kalmakis and Chandler, 2014 McLaughlin et al., 2014; McLaughlin and Sheridan, 2016). Nonetheless, previous research has differentiated between experiences of harm, deprivation, and complex experiences involving both (McLaughlin et al., 2014). Most of these adversities are not experienced separately, and the consequences of co-occurring or repeated exposure over time are additive (Bernardi et al., 2018; George, 2013; Harris and Schorpp, 2018; McLaughlin and Sheridan, 2016). Overall, there is evidence of a dose-response relation between adversities and later PE (Kelleher et al., 2013; McGrath et al., 2017; Morgan and Gayer-Anderson, 2016; Varese et al., 2012). Cumulative risk is one of the most frequent approaches when studying the relationship between ACEs and mental health. It considers the number of distinct ACEs and uses risk scores as outcome predictors. Nevertheless, cumulative risk has been criticized because it assumes that their effects are quantitatively and qualitatively similar and do not consider ACEs' type, severity, and chronicity, which are usually considered when a dimensional approach is used (Evans et al., 2013).

Exposure to adversity in critical periods can significantly influence neurodevelopment (Elder, 1998; Fox et al., 2010; Luby et al., 2013; Miguel et al., 2019; Noble et al., 2015; Schalinski et al., 2016). For example, McGrath et al. (2017) found a larger effect of sexual abuse during childhood and later development of PE (four to twelve years old, OR 8.5, 95% CI: 3.6–20.2) when compared to adolescence (thirteen to nineteen years old, OR 1.8, 95% CI: 1.0–3.1). In contrast, Morgan et al. (2020) showed larger effects of sexual abuse on later development of psychotic disorders when suffered during adolescence (twelve to sixteen years old, OR 6.39, 95% CI: 1.68–24.29) compared to childhood (zero to eleven years old, OR 2.42, 95% CI: 1.21–4.82).

There is no closure on the association between substance use and PE, as substance use increases the risk of suffering from PE, but PE may also drive substance use (Arendt et al., 2005;Degenhardt et al., 2018; DeVylder et al., 2018). Degenhardt et al. (2018) found that lifetime tobacco use, alcohol use, and extra-medical prescription drug use are associated with an increased odds of subsequent onset of PEs. On the other hand, individuals with a history of PEs have a higher risk of subsequent tobacco, alcohol, and cannabis use (Degenhardt et al., 2018). The association between substance use and PE is often bidirectional (Degenhardt et al., 2018; McGrath et al., 2016). Also, there is growing evidence that patients with substance use disorder constitute a high-risk group for developing psychotic illness (Ghose, 2018), but little is known about its etiology or mechanisms (Hjorthøj et al., 2020). Individuals with PE have more cognitive and motor dysfunction (Blanchard et al., 2010; Kelleher et al., 2013; Roddy et al., 2012), less social support (Saha et al., 2012), higher perception of social stigma (Lien et al., 2015), and suffer to a greater extent of health problems (Moreno et al., 2013).

In sum, research shows that ACEs increase the risk for PE. However, little is known about heterogeneities of this association in different developmental stages, by ACE dimensionality, or whether they are affected by substance use. Furthermore, most existing research has been conducted in western, high-income countries, limiting the generalizability of findings (Henrich et al., 2010). The present study addresses these gaps by examining the association between different types of ACEs at various developmental stages and lifetime PE in patients with substance use disorder in Chile. We used a novel life-course dataset of patients attending substance abuse treatment centers in a country with persistent inequalities and violence (Cociña et al., 2017). This article may contribute to increasing our understanding of how social determinants shape mental health in underrepresented environments (Crossley et al., 2019). It may also help focus attention on populations at higher risk for PE and provide essential input for understanding, prioritizing, and designing more effective public health preventive interventions.

2. Methods

2.1. Study design and participants

We conducted a prospective three-wave cohort study in the Metropolitan Region in Chile. The study included all consenting adults entering outpatient and residential substance abuse treatment programs. Patients with more than three months of treatment attendance were excluded, and most people had been in treatment for less than a month. 612 patients participated in the baseline interview (July to November 2018) and were followed for 18 months. We gathered information on PE only in the third wave of the study (January to April 2020, $n = 399$). This study examines participants in this third wave. Data were collected by trained clinical psychologists. The sample was not randomly selected as people with substance use disorder represent a hard-to-reach population and are thus underrepresented in clinical and population studies (Tourangeau, 2014).

The ethical review committee from Pontificia Universidad Católica de Chile (protocol 171,211,011) approved this study. All participants provided written, informed consent to participate and for aggregate and anonymous reporting of the clinical findings.

2.2. Variables

2.2.1. Lifetime psychotic experiences

PE were measured using the Spanish version of the Composite International Diagnostic Interview (CIDI) V7.1 (Kessler and Üstün, 2004), validated in Spanish (Montoya Gonzalez et al., 2016) (Supplementary Material, Table S1). We excluded answers regarding PE during sleep-related states or acute substance intoxication. Participants were asked about six types of PE: two related to hallucinatory experiences (visual and auditory) and four related to delusional experiences: two bizarre delusional items (thought insertion and or withdrawal and mind control and or passivity) and two paranoid delusional items (ideas of reference and plot to harm and or being followed) (Supplementary Material). Participants provide yes/no responses. We defined PE as reporting at least one lifetime PE.

2.2.2. Childhood adversity

A total of twelve types of childhood adversity were measured and categorized within three dimensions following the model proposed by McLaughlin and Sheridan (2014, 2016). We included six privative experiences: (1) one or both parents with alcohol use disorder, (2) one or both parents with substance use disorder, (3) one or both parents abandoned household, (4) being raised by people other than their parents, (5) one or both parents incarcerated, and (6) dropped out of school; three harmful or threatening experiences: (1) being physically abused, (2) being a victim of sexual abuse, and (3) witnessing intrafamilial violence; and three complex experiences: (1) homelessness, (2) lived in foster or residential care, and (3) being arrested by the police. Participants were asked to specify the period in which they were exposed to each ACE: childhood (0–12 years) or adolescence (13–17 years). We used lifetime (0–17), childhood, and adolescence for the analyses.

2.2.3. Lifetime substance use

We systematically assessed the use of alcohol, cannabis, cocaine, cocaine by-products, amphetamine, amphetamine by-products, and

other stimulants, non-prescribed benzodiazepines, inhalants, opioids, hallucinogens, and ketamine. To account for substance burden, we constructed a lifetime substance use continuous variable by summing all the substances patients declared ever using, ranging from one to thirteen.

2.2.4. Psychiatric comorbidity

Information about lifetime (1) depression, (2) panic disorder, (3) anxiety disorder, and (4) post-traumatic stress syndrome was assessed using the Spanish version of the Mini-International Neuropsychiatric Interview (MINI). MINI is a short structured diagnostic interview for DSM-IV and ICD-10 psychiatric disorders (Sheehan et al., 1998). We used the validated version in Spanish (Bobes, 1998).

2.2.5. Social network quality index

In each study wave, participants were asked 'Would you say your relationship with (family member) is excellent, good, neither good nor bad, bad, very bad?', where excellent was coded as 5 and very bad as 1. A total of five types of family members were included: (1) father, (2) mother, (3) offspring, (4) siblings, (5) partner or spouse. If a participant declared not having a family member, a zero was coded for that relative. For each wave, we constructed a social network quality index averaging the sum of these responses, ranging from 0 to 25, where less score can be interpreted as having a more deficient social network (Valenzuela et al., 2020).

Sociodemographic characteristics were collected from all participants, including gender, age, and education (defined as incomplete high school, complete high school, and technical or college).

2.3. Statistical analysis

2.3.1. Descriptive and association analyses

Between-group comparisons were made using a chi-square test for categorical variables and a *t*-test for continuous variables. We used univariate and multivariate logistic regressions to analyze the association between PE and (1) the lifetime relationship for each ACE type and dimension, (2) the critical period (childhood or adolescence) for ACE type and dimension, (3) the lifetime number of ACEs.

2.3.2. Multiple imputations

We conducted multiple imputations to handle missing values. Analysis of complete cases (i.e., a subset with no missing data in any variable included in the analysis) may result in biased estimates and reduced statistical power and precision (von Hippel and Lynch, 2013; Zhao and Long, 2016). Therefore, we assumed missingness at random (MAR), implying that missing data depends on observable characteristics of participants and not on unobserved data. The missing values were imputed with multiple imputations by chain equations (MICE). MICE is a robust method for dealing with missing data (Zhao and Long, 2016). As the maximum fraction of missing information was 15%, we conducted imputations with $m = 20$ (White et al., 2011). We checked the robustness of our results comparing models with and without imputation of missing values.

All analyses were conducted in Stata version 16 (StataCorp, 2019).

3. Results

The study sample included 399 patients, with 220 (55.1%) reporting at least one psychotic experience throughout their lifetime. Table 1 shows descriptive statistics by PE for sociodemographic and control variables. The mean age in the study sample was 39 years old, 32.3% were female, and 38.9% did not complete high school. Patients reporting PE had more psychiatric comorbidities, including depression, panic disorder, and anxiety disorder. Patients with PE reported using a higher number of substances during their lifetime (mean 4.5 versus 3.9 in patients without PE, *p*-value<0.001). In addition, hallucinations were the psychotic experience most frequently recalled (41%). Fig. S1, Supplementary Material, shows the distribution of PE reported in the sample. About half (44.9%) participants in the sample reported no PE. Table 2 shows descriptive statistics for adverse Childhood Experiences (ACEs) by dimension, period of exposure, and PE. Patients reporting PE experienced more complex adversities (41.8% versus 25.1% in patients without PE, *p*-value<0.001). In addition, they experienced more ACEs (4.2 versus 3.4 in patients without PE, *p*-value<0.001).

Table 1
Sociodemographic and control variables of the sample by psychotic experiences.

	Total	Psychotic experiences (PE)		*p*-value [a]
	Total N = 399	No (44.9%)	Yes (55.1%)	
	Mean (SD)			
Age (years at inclusion)	39.2 (10.6)	39.7 (10.7)	38.8 (10.6)	0.42
Lifetime substance use (substances used)	4.2 (1.9)	3.9 (1.8)	4.5 (2)	0.01
Social network quality index [b]	13.9 (4.3)	14.2 (4.6)	13.6 (4.1)	0.17
	Percentage			
Woman (=1; man=0)	32.3	31.3	33.2	0.69
Educational level				
Incomplete high school	38.9	37.4	40	0.74
Complete high school	32.4	32.4	32.3	
Higher education	28.6	30.2	27.3	
Psychiatric comorbidity	78.5	70.4	85	0.00
Lifetime substance use (% Yes)	32.3	31.3	33.2	0.69
Alcohol	94.5	93.9	95.0	0.61
Cannabis	77.9	73.7	81.3	0.07
Cocaine or cocaine paste	87.2	86.0	88.2	0.52
Other stimulants	13.8	11.7	15.5	0.28
Benzodiazepines	40.8	32.6	47.5	0.00
Inhalants	13.4	7.3	18.4	0.00
Synthetic hallucinogens	8.4	7.9	8.8	0.75
Natural hallucinogens	8.7	6.8	10.2	0.23
Opioids	1.5	1.7	1.4	0.82
Ketamine	2.0	2.8	1.4	0.31
Lifetime psychiatric comorbidities (%)				
Depression	69.2	60.9	75.9	0.00
Panic disorder	35.1	29.6	39.6	0.03
Anxiety disorder	49.6	42.5	55.5	0.01
Post-traumatic stress syndrome	18.8	15.1	21.8	0.08
Lifetime psychotic experiences (%)				
Hallucinations	41.4	–	–	–
Bizarre delusions	19.3	–	–	–
Paranoid delusions	22.8	–	–	–

$N = 399$.
[a] Statistical significance was calculated without considering missing data.
[b] Missing: 15 (5.9%).

We first examined the cumulative effect of ACEs. Table 3 shows a general model of the association between the number of ACEs and PE. The number of ACEs during the lifetime (0–17 years of age) were associated with a higher risk of presenting PE (OR 1.10, 95% CI: 1.00–1.21, *p*-value<0.05). The results also suggest that the predicted probability of PE increases about 10% for each lifetime ACE (Fig. S2, Supplementary Material). Psychiatric comobidity was consistently associated with higher odds of PE during the lifetime (OR 2.07, 95% CI: 1.24 – 3.47, *p*-value<0.01) and in childhood (OR: 2.13; *p*-value<0.01) and adolescence (OR: 2.12; *p*-value<0.01). Lifetime substance use was also associated higher odds of PE (OR 1.13, 95% CI: 1.00 – 1.27, *p*-value<0.05). Likewise, each additional substance consumed throughout life increased the odds of PE by approximately 15%.

We next examined the association between the three main dimensions of ACEs (privative, harmful, complex) and PE in a single model, to understand how much of the association found in Table 3

Table 2
Adverse Childhood Experiences (ACEs) by dimension, period of exposure and psychotic experiences.

	Lifetime (0 to 17 years old)				Childhood (0 to 12 years old)				Adolescence (13 to 17 years old)			
	Total	Psychotic experiences		*p*-value [a]	Total	Psychotic experiences		*p*-value [a]	Total	Psychotic experiences		*p*-value [a]
		No (44.9%)	Yes (55.1%)			No (44.9%)	Yes (55.1%)			No (44.9%)	Yes (55.1%)	
Number of ACEs	3.9	3.4	4.2	0.00	2.5	2.3	2.6	0.07	2.3	2	2.5	0.01
Dimension of ACE		Percentage										
Privative	86.5	84.4	88.2	0.27	70.4	70.4	70.5	0.55	70.9	65.4	75.7	0.03
Any parent with alcohol problem	56.4	51.4	60.5	0.10	48.6	46.4	50.5	0.40	37.6	34.6	40	0.30
Any parent with drug use problem	17.3	15.6	18.6	0.25	13.8	13.4	14.1	0.25	12	11.2	12.7	0.22
Any parent left home	44.6	44.1	45	0.12	32.6	34.6	30.9	0.02	15.5	14	16.8	0.01
Raised by people that were not their parents	39.9	34.1	44.4	0.03	30.3	25.1	34.5	0.11	22.3	19.6	24.5	0.44
Any parent incarceration	9.5	8.9	10	0.35	6.8	7.3	6.4	0.36	2.3	1.7	2.7	0.28
School exclusion	47.1	41.9	51.4	0.10	7	6.1	7.7	0.55	40.1	35.8	43.6	0.17
Harmful	67.4	63.7	70.5	0.15	58.9	53.1	63.6	0.03	40.4	38.5	41.8	0.51
Physical maltreatment	47.4	44.7	49.5	0.2	39.1	35.2	42.3	0.12	25.1	22.3	27.3	0.17
Sexual abuse	24.1	18.4	28.6	0.06	16.8	11.7	20.9	0.05	6.5	6.7	6.4	0.95
Intrafamilial violence	52.9	52	53.6	0.33	43.9	40.8	46.4	0.28	28.8	26.8	30.5	0.43
Complex	34.3	25.1	41.8	0.00	5.5	3.9	6.8	0.29	31.3	23.5	37.7	0.05
Homelessness	10	7.8	11.8	0.42	1.3	0.6	1.8	0.49	9	7.3	10.5	0.49
Foster or Residential Care	9	5.6	11.8	0.06	4.5	3.4	5.5	0.26	5.3	3.9	6.4	0.24
Arrested	27.8	19.6	34.5	0.00	0.8	0.6	0.9	0.67	26.8	19	33.2	0.00
Number of ACEs												
0	7.8	10.1	5.9	0.31	20.6	23.5	18.2	0.64	17.8	23.5	13.2	0.05
1	10.8	12.8	9.1		16.5	16.2	16.8		22.6	22.9	22.3	
2	14.3	13.4	15		17.8	17.9	17.7		18.6	18.4	18.6	
3	13.3	14	12.7		18.1	18.4	17.7		15.5	11.7	18.6	
4 or more	53.9	49.7	57.3		27.1	24	29.5		25.6	23.5	27.3	

$N = 399$.
[a] Statistical significance was calculated without considering missing data.

Table 3
Bivariate and multivariate associations between number of childhood adversities and psychotic experiences.

	Lifetime (0–17 years)		Childhood (0–12)		Adolescence (13–17)	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Woman		1.00		1.02		1.05
		(0.63–1.57)		(0.65–1.62)		(0.67–1.65)
Age		1.00		1.00		1.00
		(0.98–1.02)		(0.98–1.02)		(0.98–1.02)
Complete high school		1.01		0.91		0.97
		(0.61–1.67)		(0.56–1.48)		(0.59–1.58)
Higher education		0.91		0.82		0.88
		(0.54–1.52)		(0.50–1.37)		(0.53–1.47)
Lifetime substance use		1.13**		1.14**		1.13**
		(1.00–1.27)		(1.02–1.27)		(1.02–1.27)
Psychiatric comorbidity		2.07***		2.13***		2.12***
		(1.24–3.47)		(1.27–3.56)		(1.27–3.54)
Social network quality index		0.98		0.97		0.98
		(0.93–1.03)		(0.92–1.02)		(0.93–1.03)
Number of ACEs	1.14***	1.10**	1.10*	1.06	1.17***	1.12*
	(1.05–1.25)	(1.00–1.21)	(0.99–1.21)	(0.95–1.17)	(1.04–1.30)	(0.99–1.26)
Constant	0.73	0.42	0.98	0.59	0.87	0.44
	(0.50–1.07)	(0.09–1.93)	(0.72–1.34)	(0.14–2.56)	(0.63–1.19)	(0.10–2.01)
Observations	399	399	399	399	399	399

Note: $N = 399$. OR, Odds ratio; CI, Confidence interval. The missing values were imputed with multiple imputations by chain equations. Results without data imputation are shown in Table S2, Supplementary Material.
***$p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

could be potentially explained by specific types of ACEs, controlling for several observable confounders (Table 4). We found that complex ACEs were associated with higher risk of presenting PE (OR 1.73, 95% CI 1.07–1.79, *p*-value <0.05) during the lifetime, controlling for other dimensions of ACEs. After adjusting for observable characteristics, we found a statistically significant association between PE and lifetime complex ACEs (OR 1.78, 95% CI: 1.11–2.85), and suggestive evidence for childhood harmful ACEs (OR 1.49, 95% CI: 0.94–2.36) and adolescence privative ACEs (OR 1.52, 95% CI: 0.93–2.49).

Last, we examined specific ACEs nested in the three main dimensions to examine their association with PE at different developmental periods. The results in Table 5 need to be interpreted with caution, because multiple comparisons in the same data increase the risk of false positives (type I errors), as discussed later in more detail. Several lifetime ACEs were significantly associated with an increased risk of PE. Adjusting for age, gender, educational level, lifetime substance use, psychiatric

Table 4
Bivariate and multivariate associations between the three main types of childhood adversities(ACE) and psychotic experiences.

	Lifetime (0–17 years)		Childhood (0–12)		Adolescence (13–17)	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Woman		1.09		1.01		1.15
		(0.69–1.74)		(0.64–1.59)		(0.72–1.83)
Age		1.00		1.00		1.00
		(0.98–1.02)		(0.98–1.02)		(0.98–1.03)
Complete high school		0.98		0.88		1.05
		(0.59–1.64)		(0.54–1.43)		(0.63–1.75)
Higher education		0.91		0.81		0.97
		(0.54–1.52)		(0.49–1.35)		(0.57–1.64)
Lifetime substance use		1.11*		1.14**		1.12**
		(0.99–1.25)		(1.02–1.27)		(1.00–1.26)
Psychiatric comorbidity		2.11***		2.01***		2.14***
		(1.26–3.54)		(1.20–3.38)		(1.28–3.59)
Social network quality index		0.98		0.97		0.98
		(0.93–1.04)		(0.92–1.02)		(0.93–1.04)
Privative ACE	1.12	1.22	0.80	0.79	1.47*	1.52*
	(0.60–2.07)	(0.63–2.35)	(0.50–1.28)	(0.48–1.29)	(0.93–2.33)	(0.93–2.49)
Harmful ACE	1.18	1.02	1.63**	1.49*	1.03	0.96
	(0.75–1.86)	(0.63–1.65)	(1.05–2.53)	(0.94–2.36)	(0.67–1.57)	(0.62–1.50)
Complex ACE	2.07***	1.73**	1.66	1.39	1.87***	1.60*
	(1.34–3.21)	(1.07–2.79)	(0.65–4.21)	(0.52–3.69)	(1.20–2.93)	(0.98–2.61)
Constant	0.78	0.35	0.98	0.59	0.76	0.29
	(0.45–1.37)	(0.07–1.79)	(0.72–1.34)	(0.14–2.56)	(0.52–1.13)	(0.06–1.42)
Observations	399	399	399	399	399	399

Note: $N = 399$. OR, Odds ratio; CI, Confidence interval.
The missing values were imputed with multiple imputations by chain equations. Results without data imputation are shown in Table S3, Supplementary Material.
$^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.1$.

comorbidity, and social network quality, the highest OR were arrests (OR 1.88, 95% CI: 1.13–3.15), sexual abuse (OR 1.81, 95% CI: 1.07–3.2), alcohol abuse by parents (OR 1.48, 95% CI: 0.97–2.26), school exclusion (OR 1.39, 95% CI: 0.83–2.33), foster or residential care (OR 1.83, 95% CI: 0.83–4.05), and being raised by people that were not their parents (OR 1.37, 95% CI: 0.90–2.10). When analyzing the association between ACES and PE by critical developmental periods, we found a statistically significant association between sexual abuse during childhood (OR 1.81, 95% CI: 1.00–3.29) and arrests during adolescence (OR 1.92, 95% CI: 1.15–3.22), adjusted by the same covariates.

As a robustness test, we examined whether the results held when using data with no imputation for missing values. We found no significant differences between the imputed and non-imputed models, as shown in Supplementary Material (Tables S2, S3, and S4, Supplementary Material). Finally, to understand heterogeneities in the data, we ran the main analysis in Table 3 with perceptual abnormalities PE (hallucinations) and unusual thought content PE (delusions) separately (Table S5, Supplementary Material). Adjusting for confounders, we found suggestive evidence that the number of ACEs during the lifetime (0–17 years of age) were associated with a higher risk of presenting perceptual abnormalities (hallucinations) (OR 1.08, 95% CI: 0.99–1.18).

4. Discussion

This article examined the association between ACEs and PE among patients with substance use disorder attending treatment programs in Chile. We found evidence that ACEs are associated with an increased risk of presenting later PE, with a cumulative risk effect of ACEs on PE. Among the three groups of ACEs examined (i.e. privative, harmful, complex), complex ACEs were associated with a higher risk of presenting PE. Lastly, we found that sexual abuse during childhood and deprivation and complex experiences during adolescence significantly increased the probability of presenting later PE in this population.

Our findings support the idea of a cumulative risk effect of ACEs on PE, with an increase of 10% in the odds of presenting PE for each lifetime ACE exposure, which is consistent with previous research (Evans et al., 2013; McGrath et al., 2017; Morgan et al., 2014, 2020). For instance, Morgan et al. (2020) found that the odds of having a psychotic disorder increased by 50% on average for every additional adversity.

4.1. Harmful or threatening experiences

We found sexual abuse before the age of twelve was associated with an increased risk of later PE (OR 1.81, 95% CI: 1.00–3.29). Similarly, McGrath et al. (2017) found a large effect of sexual abuse on later PE when it occurred during childhood (four to twelve years old, OR 8.5, 95% CI: 3.6–20.2) as compared to adolescence (thirteen to nineteen years old, OR 1.8, 95% CI: 1.0–3.1). Nonetheless, sexual abuse has also been associated with the later onset of psychotic disorders during adolescence (Morgan et al., 2020).

4.2. Deprivation or privative experiences

We found an association between parental alcohol abuse and PE (OR 1.48, 95% CI: 0.97–2.26). Parental alcohol abuse can be considered a deprivation experience as it typically results in less available psychological resources and a poorer and more dysfunctional environment (McLaughlin et al., 2019; Keller et al., 2008). The association between parental substance abuse lost significance when controlled by other variables (OR 0.9, 95% CI: 0.7–1.2). Parental alcohol abuse can lead to other mental and behavioral disorders among their offspring (Keller et al., 2008; Raitasalo et al., 2019).

Dropping out of school was associated with PE (OR 1.39, 95% CI: 0.83–2.33). School exclusion is not consistently included as an adversity measure, even though schools are a primary socialization institution. Patients with mental illness may account for a significant proportion of school dropouts (Hjorth et al., 2016; Porche et al., 2011; Stoep et al., 2003). Most severe mental health problems start during adolescence or early adulthood (Baldessarini et al., 2012; Solmi et al., 2021). Our results suggest that dropping out of school should be included an ACE, especially in the global south, where few children graduate from secondary school (UNESCO, 2019).

Not being raised by parents was also associated with an increased risk of PE (OR 1.48, 95% CI: 0.97–2.26). This is consistent with previous reports describing loss or separation of parents associated with PE and severe mental disorders (Álvarez et al., 2011; McGrath et al., 2017;

Table 5
Bivariate and multivariate associations between specific childhood adversities and psychotic experiences.

Type of ACE [a]	Lifetime (0–17)		Childhood (0–12)		Adolescence (13–17)	
	Unadjusted OR (95% CI)	Adjusted [b] OR (95% CI)	Unadjusted OR (95% CI)	Adjusted [b] OR (95% CI)	Unadjusted OR (95% CI)	Adjusted [b] OR (95% CI)
Privative ACE	1.38 (0.78–2.46)	1.36 (0.73–2.52)	1.00 (0.65–1.55)	0.94 (0.60–1.48)	1.63 (1.05–2.52)	1.59 (0.99–2.55)
Any parent with alcohol problem	1.47 (0.98–2.21)	1.48 (0.97–2.26)	1.24 (0.83–1.86)	1.23 (0.81–1.87)	1.28 (0.85–1.93)	1.31 (0.85–2.01)
Any parent with drug use problem	1.29 (0.76–2.17)	1.18 (0.68–2.06)	1.13 (0.64–2.00)	0.98 (0.53–1.81)	1.25 (0.68–2.31)	1.10 (0.57–2.10)
Any parent left home	1.10 (0.74–1.65)	1.04 (0.68–1.59)	0.91 (0.59–1.38)	0.84 (0.53–1.31)	1.33 (0.77–2.31)	1.40 (0.78–2.50)
Raised by people that weren't their parents	1.55 (1.03–2.34)	1.37 (0.90–2.10)	1.58 (1.02–2.45)	1.39 (0.89–2.19)	1.35 (0.83–2.18)	1.20 (0.72–1.99)
Any parent incarceration	1.17 (0.60–2.30)	0.98 (0.48–1.99)	0.89 (0.41–1.95)	0.70 (0.31–1.60)	1.67 (0.41–6.75)	1.53 (0.35–6.67)
School exclusion	1.48 (0.99–2.20)	1.39 (0.83–2.33)	1.28 (0.59–2.82)	1.10 (0.48–2.50)	1.39 (0.93–2.09)	1.28 (0.79–2.08)
Harmful ACE	**1.36** (0.89–2.07)	**1.17** (0.75–1.83)	**1.55** (1.04–2.31)	**1.39** (0.91–2.12)	**1.15** (0.77–1.71)	**1.10** (0.72–1.69)
Physical maltreatment	1.21 (0.81–1.80)	1.08 (0.71–1.64)	1.33 (0.88–2.00)	1.25 (0.81–1.91)	1.26 (0.80–1.99)	1.20 (0.74–1.94)
Sexual abuse	1.77 (1.10–2.86)	1.81 (1.07–3.06)	2.00 (1.14–3.50)	1.81 (1.00–3.29)	0.98 (0.44–2.16)	0.92 (0.39–2.16)
Intrafamilial violence	1.12 (0.76–1.68)	1.03 (0.68–1.57)	1.29 (0.86–1.93)	1.21 (0.79–1.84)	1.24 (0.80–1.93)	1.22 (0.77–1.93)
Complex ACE	2.14 (1.39–3.30)	1.78 (1.12–2.85)	1.80 (0.72–4.51)	1.43 (0.54–3.77)	1.98 (1.27–3.07)	1.69 (1.04–2.74)
Homelessness	1.58 (0.80–3.12)	1.07 (0.51–2.23)	3.30 (0.37–29.76)	2.40 (0.26–22.47)	1.53 (0.75–3.11)	1.01 (0.47–2.19)
Foster or Residential Care	2.30 (1.08–4.91)	1.83 (0.83–4.05)	1.68 (0.62–4.56)	1.47 (0.52–4.18)	1.67 (0.66–4.23)	1.24 (0.47–3.29)
Arrested	2.17 (1.37–3.45)	1.88 (1.13–3.15)	1.63 (0.15–18.16)	0.89 (0.07–11.02)	2.19 (1.37–3.49)	1.92 (1.15–3.22)
Number of ACEs	1.14 (1.05–1.25)	1.10 (1.00–1.21)	1.10 (0.99–1.21)	1.06 (0.95–1.18)	1.17 (1.04–1.30)	1.12 (0.99–1.26)

Note. $N = 399$.OR: Odds ratio; CI: Confidence interval. The missing values were imputed with multiple imputations by chain equations. Results without data imputation are shown in Table S4, Supplementary Material.

[a] Each model included one childhood adversity at a time as predictor of psychotic experiences.

[b] Adjusted for gender, age, educational (abandoned education, completed high school and higher education), lifetime drug use, lifetime psychopathology and social network quality index.

Varese et al., 2012). For example, Álvarez et al. (2011) found that the loss of one or both parents increased four times the risk of having more than one psychotic episode (OR 5.25, 95% CI: 1.03–26.68), while Varese et al. (2012) found in their metanalysis a significant association between parental death and later psychosis onset (OR 2.3, 95% CI: 1.63–3.24).

4.3. Complex experiences

Foster or residential care was also associated with later PE, even though this was not statistically significant after controlling for other variables (OR 1.83, 95% CI: 0.83–4.05). Institutional care is not a commonly measured ACE in psychosis or PE studies. Bentall et al. (2012) found that patients that had been in institutional care had greater odds of presenting paranoid ideation (OR 12.68, 95% CI: 3.56–45.11). Being arrested during adolescence was associated with PE after controlling for other factors (OR 1.92, 95% CI: 1.15–3.22). Rates of arrest or incarceration in persons with PE are higher than those found in the general population (Ford, 2015; James and Glaze, 2006). However, the association might be bidirectional (Kelleher et al., 2013), as psychotic-like symptoms are a risk factor of violent recidivism among juvenile offenders (Colins et al., 2013), but also PE might appear after having contact with the criminal justice system (Ford, 2015).

4.4. Critical period

Our findings also suggest that the time when ACEs occurred may be important. Considering the existence of critical periods in which individuals may be more susceptible to adverse environmental stimuli is essential to understanding the consequences of adversity. It is also essential when designing clinical or public health interventions (McLaughlin et al., 2019; Morgan et al., 2020; Varese et al., 2012). Early detection of social adversity and appropriate intervention may reduce its effect on mental health.

4.5. Strenghts and limitations

Our study has some limitations. First, retrospective reports of adverse childhood experiences may be inaccurate due to limitations in individuals' perception and forgetfulness (Reuben et al., 2016). Memory in these stages of development may be biased due to the judgment and interpretation of situations and context. Nonetheless, previous literature has consistently shown that childhood adversity increases the risk for poor physical and cognitive health later in life (Reuben et al., 2016), and repeated measurements over time have shown more reliability (Dube et al., 2004). We measured early adversities using a broad range from zero to twelve years old to limit the risk of recall bias (Halfon and Forrest, 2017). Second, we did not use a random sample of participants, which may affect the generalization of results to a broader population with substance use disorder. Nevertheless, the relatively large sample and comprehensive evaluation of patients are among this study's main strengths. Substance use disorder individuals represent a hard-to-reach population due to stigma and marginality from support networks, including access to mental health services. As a result, they are typically

underrepresented in clinical studies and household surveys (Tourangeau, 2014), which are the most common source of information about adversity and its association with PE or psychosis (McGrath et al., 2017, 2015; Morgan et al., 2020; Tourangeau, 2014; Varese et al., 2012). Third, as mentioned before, Table 5 shows multiple comparisons using the same data, which increases the risk of false-positive results (type-1 errors), and therefore some statistically significant results might be spurious. The main model in Table 3, shows that ACEs rises the risk of presenting PE, consistent with previous studies. Our sample allows further exploring whether this association holds in different developmental stages and to examine this association for more specific ACEs related to harm, deprivation, and complex experiences. While the results in Table 5 need to be interpreted with caution, these exploratory findings are not incidental to the main focus of our article; on the contrary, they are expected results derived from a large body of research. Our results have relevant implications for research and practice focused on specific periods and mental health prevention strategies; although they need to be assessed critically. Fourth, our analysis did not integrate mediators between adversity and PE, such as substance abuse. We decided not to interact substance abuse and ACEs due to the lack of variability of substance use within our sample. Houston et al. (2008) found both additive and multiplicative interaction between cannabis and sexual abuse in the general population, but these results have not been consistently replicated in other studies (Sideli et al., 2020).

Lastly, our study was conducted in the global south, and thus it contributes to deepening our understanding of how social determinants shape mental health in this underrepresented context (Crossley et al., 2019). This is particularly important due to unique socioeconomic characteristics in this area, such as inequality, violence, and poverty, which may affect normal development.

4.6. Implications for mental health research

PE render the behavioral expression of distributed risk for psychotic disorders (Kaymaz and van Os, 2010) and represent transdiagnostic clinical markers of psychopathology severity (Kelleher and Cannon, 2016). Psychotic disorders, on the other hand, have a considerable economic and social cost, as their early appearance underpins the quality of life, social support, productivity, and educational achievement (Dominguez et al., 2011; Kelleher and Cannon, 2016). Therefore, early detection of symptoms and associated risk factors is essential in health and educational contexts (Thompson and Broome, 2020). Early detection of adversity provides a window of opportunity to prevent the development of psychiatric disorders resulting from latent and cumulative risk within the life course (Muenzenmaier et al., 2015; Vásquez Núñez, 2020). This implies formalizing services and instruments that acknowledge adversity within the life trajectories of patients and especially children. Reducing the risk of exposure to ACEs is imperative, especially in highly vulnerable populations (Calkins et al., 2017; Thompson and Broome, 2020). Lastly, limited assessment of ACEs may imply erroneously attributing effects to highly correlated unobserved experiences (for instance, household poverty). Thus, future research should include more extensive and comprehensive social adversity measures.

5. Conclusion

In conclusion, we examined the association between ACEs and PE among patients SUD in Chile. Our results suggest that early exposure to ACEs is a risk factor for later PE in this population. Also, the type of ACE and the period when they occurred is important, suggesting the existence of critical periods where the individual is more susceptible to adverse environmental stimuli. Specifically, sexual abuse during childhood and deprivation and complex experiences during adolescence significantly increased the probability of presenting later PE in individuals with substance use disorder.

Authorship statement

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All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in Psychiatry Research.

Declaration of Competing Interest

Nicolas Crossley has received personal fees from Janssen, outside the submitted work. Juan Undurraga has served as a consultant for Johnson & Johnson. None of the other authors have conflicts of interest to declare.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2022.114733.

References

Álvarez, M.J., Roura, P., Osés, A., Foguet, Q., Solà, J., Arrufat, F.X., 2011. Prevalence and clinical impact of childhood trauma in patients with severe mental disorders. J. Nervous Mental Dis. 199 (3), 156–161. https://doi.org/10.1097/NMD.0b013e31820c751c.

Arendt, M., Rosenberg, R., Foldager, L., Perto, G., Munk-Jorgensen, P., 2005. Cannabis-induced psychosis and subsequent schizophrenia-spectrum disorders: follow-up schizophrenia-spectrum disorders: follow-up study of 535 incident cases study of 535 incident cases. Br. J. Psychiatry 187, 510–515. https://doi.org/10.1192/bjp.187.6.510.

Baldessarini, R.J., Tondo, L., Vázquez, G.H., Undurraga, J., Bolzani, L., Yildiz, A., Khalsa, H.-M.K., Lai, M., Lepri, B., Lolich, M., Maffei, P.M., Salvatore, P., Faedda, G. L., Vieta, E., Tohen, M., 2012. Age at onset versus family history and clinical outcomes in 1,665 international bipolar-I disorder patients. World Psychiatry 11 (1), 40–46. https://doi.org/10.1016/j.wpsyc.2012.01.006.

Bellis, M.A., Lowey, H., Leckenby, N., Hughes, K., Harrison, D., 2014. Adverse childhood experiences: retrospective study to determine their impact on adult health behaviours and health outcomes in a UK population. J. Public Health (Bangkok) 36 (1), 81–91. https://doi.org/10.1093/pubmed/fdt038.

Bentall, R.P., Wickham, S., Shevlin, M., Varese, F., 2012. Do specific early-life adversities lead to specific symptoms of psychosis? A study from the 2007 the Adult Psychiatric Morbidity Survey. Schizophr Bull 38, 734–740. https://doi.org/10.1093/schbul/sbs049.

Bernardi, L., Huinink, J., Settersten, R., 2018. The life course cube: a tool for studying lives. Adv. Life Course Res. 41, 100258 https://doi.org/10.1016/j.alcr.2018.11.004.

Bielas, H., Barra, S., Skrivanek, C., Aebi, M., Steinhausen, H.-.C., Bessler, C., Plattner, B., 2016. The associations of cumulative adverse childhood experiences and irritability with mental disorders in detained male adolescent offenders. Child Adolesc. Psychiatry Ment. Health 10 (1), 34. https://doi.org/10.1186/s13034-016-0122-7.

Blanchard, M.M., Jacobson, S., Clarke, M.C., Connor, D., Kelleher, I., Garavan, H., Harley, M., Cannon, M., 2010. Language, motor and speed of processing deficits in adolescents with subclinical psychotic symptoms. Schizophr. Res. 123 (1), 71–76. https://doi.org/10.1016/j.schres.2010.05.028.

Bobes, J., 1998. A Spanish validation study of the mini international neuropsychiatric interview. Eur. Psychiatry 13 (S4), 198S–199S. https://doi.org/10.1016/S0924-9338(99)80240-5.

Calkins, M.E., Moore, T.M., Satterthwaite, T.D., Wolf, D.H., Turetsky, B.I., Roalf, D.R., Merikangas, K.R., Ruparel, K., Kohler, C.G., Gur, R.C., Gur, R.E., 2017. Persistence of psychosis spectrum symptoms in the Philadelphia Neurodevelopmental Cohort: a

prospective two-year follow-up. World Psychiatry 16 (1), 62–76. https://doi.org/10.1002/wps.20386.
Cociña, M., Frei, R., & Larragaña, O. (2017). Desiguales. Orígenes, cambios y desafíos de la brecha social en Chile | Programa De Las Naciones Unidas Para El Desarrollo. UNDP. https://www.undp.org/es/chile/publications/desiguales-or%C3%ADgenes-cambios-y-desaf%C3%ADos-de-la-brecha-social-en-chile (accessed 11 November 2022).
Colins, O.F., Vermeiren, R.R., Noom, M., Broekaert, E., 2013. Psychotic-like symptoms as a risk factor of violent recidivism in detained male adolescents. J. Nerv. Mental Dis. 201 (6), 478–483. https://doi.org/10.1097/NMD.0b013e3182948068.
Crossley, N.A., Alliende, L.M., Ossandon, T., Castañeda, C.P., González-Valderrama, A., Undurraga, J., Castro, M., Guinjoan, S., Díaz-Zuluaga, A.M., Pineda-Zapata, J.A., López-Jaramillo, C., Reyes-Madrigal, F., León-Ortíz, P., de la Fuente-Sandoval, C., Czepielewski, L.S., Gama, C.S., Zugman, A., Gadelha, A., Jackowski, A., Bressan, R., 2019. Imaging social and environmental factors as modulators of brain dysfunction: time to focus on developing Non-Western societies. Biol. Psychiatry Cogn. Neurosci. Neuroimaging 4 (1), 8–15. https://doi.org/10.1016/j.bpsc.2018.09.005.
Degenhardt, L., Saha, S., Lim, C.C.W., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonso, J., Andrade, L.H., Bromet, E.J., Bruffaerts, R., Caldas-de-Almeida, J.M., de Girolamo, G., Florescu, S., Gureje, O., Haro, J.M., Karam, E.G., Karam, G., Kovess-Masfety, V., Lee, S., Lepine, J.P., on behalf of the WHO World Mental Health Survey Collaborators, 2018. The associations between psychotic experiences and substance use and substance use disorders: findings from the World Health Organization World Mental Health surveys: psychotic experiences and substance use. Addiction, 113 (5), 924–934. https://doi.org/10.1111/add.14145.
DeVylder, J.E., Oh, H.Y., Kelleher, I., 2018. Commentary on Degenhardt et al. (2018): cause or consequence? Disentangling the relationship between psychosis and substance use. Addiction, 113 (5), 935–936. https://doi.org/10.1111/add.14186.
Valenzuela, E., Bórquez, I., Dupré, S., López, A., Maldonado, L., Fernández, G., Mateo, M., Cooper, R., Díaz, R., Chamorro, C., 2020. Evaluación De Resultados De Los Programas De Tratamiento y Rehabilitación Del Servicio nacional Para La Prevención y Rehabilitación Del Consumo De Drogas y Alcohol. SENDA. Centro de Estudios Justicia y Sociedad, Pontificia Universidad Católica de Chile. http://www.dipres.gob.cl/597/articles-214466_r_ejecutivo_institucional.pdf. accessed 11 July 2022.
Dominguez, M.D.G., Wichers, M., Lieb, R., Wittchen, H.-U., van Os, J., 2011. Evidence that onset of clinical psychosis is an outcome of progressively more persistent subclinical psychotic experiences: an 8-year Cohort study. Schizophr. Bull. 37 (1), 84–93. https://doi.org/10.1093/schbul/sbp022.
Dube, S.R., Williamson, D.F., Thompson, T., Felitti, V.J., Anda, R.F., 2004. Assessing the reliability of retrospective reports of adverse childhood experiences among adult HMO members attending a primary care clinic. Child Abuse Negl. 28 (7), 729–737. https://doi.org/10.1016/j.chiabu.2003.08.009.
Elder, G.H., 1998. The Life Course as Developmental Theory. Child Dev. 69 (1), 1. https://doi.org/10.2307/1132065.
Evans, G.W., Li, D., Whipple, S.S., 2013. Cumulative risk and child development. Psychol. Bull. 139 (6), 1342–1396. https://doi.org/10.1037/a0031808.
Evans, G.W., Li, D., Whipple, S.S., 2013. Cumulative risk and child development. Psychol. Bull. 139, 1342–1396. https://doi.org/10.1037/a0031808.
Ford, E., 2015. First-episode psychosis in the criminal justice system: identifying a critical intercept for early intervention. Harv. Rev. Psychiatry 23 (3), 167–175, 10.1097/HRP.0000000000000066.
Fox, S.E., Levitt, P., Nelson III, C.A., 2010. How the timing and quality of early experiences influence the development of brain architecture. Child Dev. 81 (1), 28–40. https://doi.org/10.1111/j.1467-8624.2009.01380.x.
George, L., 2013. Life-Course Perspectives on Mental Health. Handbook of the Sociology of Mental Health, 2nd Edition. Springer, pp. 585–602.
Ghose, S., 2018. Substance-induced psychosis: an indicator of development of primary psychosis? Am. J. Psychiatry 175 (4), 303–304. https://doi.org/10.1176/appi.ajp.2018.17121395.
Halfon, N., Forrest, C.B., 2017. The emerging theo- retical framework of life course health development. In: Halfon, N., Forrest, C.B., Lerner, R.M., Faustman, E. (Eds.), Handbook of Life Course Health-Development Science. Springer, Cham.
Harris, Kathleen Mullan, Schorpp, Kristen M, 2018. Integrating biomarkers in social stratification and health research. Annu. Rev. Sociol. 44 (1) https://doi.org/10.1146/annurev-soc-060116-053339, 11.1-11.25.
Henrich, J., Heine, S.J., Norenzayan, A., 2010. The weirdest people in the world? Behav. Brain Sci. 33 (2–3), 61–83. https://doi.org/10.1017/S0140525X0999152X.
Hjorth, C.F., Bilgrav, L., Frandsen, L.S., Overgaard, C., Torp-Pedersen, C., Nielsen, B., Bøggild, H., 2016. Mental health and school dropout across educational levels and genders: a 4.8-year follow-up study. BMC Public Health 16 (1), 976. https://doi.org/10.1186/s12889-016-3622-8.
Hjorthøj, C., Starzer, M.S.K., Benros, M.E., Nordentoft, M., 2020. Infections as a risk factor for and prognostic factor after substance-induced psychoses. Am. J. Psychiatry 177 (4), 335–341. https://doi.org/10.1176/appi.ajp.2019.19101047.
Hughes, K., Bellis, M.A., Hardcastle, K.A., Sethi, D., Butchart, A., Mikton, C., Jones, L., & Dunne, M.P. (2017). The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. Lancet Public Health, 2(8), e356–e366. doi:10.1016/S2468-2667(17)30118-4.
James, D.J., & Glaze, E. (2006). Mental Health Problems of Prison and Jail Inmates [WWW Document], n.d. . Bureau of Justice Statistics. URL https://bjs.ojp.gov/library/publications/mental-health-problems-prison-and-jail-inmates (accessed 7 December 2022).
Houston, J.E., Murphy, J., Adamson, G., Stringer, M., Shevlin, M., 2008. Childhood sexual abuse, early cannabis use, and psychosis: testing an interaction model based on the national comorbidity survey. Schizophr. Bull. 34, 580–585. https://doi.org/10.1093/schbul/sbm127.
Kalmakis, K.A., Chandler, G.E., 2014. Adverse childhood experiences: towards a clear conceptual meaning. J. Adv. Nurs. 70, 1489–1501. https://doi.org/10.1111/jan.12329.
Kaymaz, N., van Os, J., 2010. Extended psychosis phenotype – yes: single continuum – unlikely: a commentary on 'Why we need more debate on whether psychotic symptoms lie on a continuum with normality' by David (2010). Psychol. Med. 40 (12), 1963–1966. https://doi.org/10.1017/S0033291710000358.
Kelleher, I., Cannon, M., 2016. Putting psychosis in its place. Am. J. Psychiatry 173 (10), 951–952. https://doi.org/10.1176/appi.ajp.2016.16070810.
Kelleher, I., Keeley, H., Corcoran, P., Ramsay, H., Wasserman, C., Carli, V., Sarchiapone, M., Hoven, C., Wasserman, D., Cannon, M., 2013. Childhood trauma and psychosis in a prospective cohort study: cause, effect, and directionality. Am. J. Psychiatry 170 (7), 734–741. https://doi.org/10.1176/appi.ajp.2012.12091169.
Keller, P.S., Cummings, E.M., Davies, P.T., Mitchell, P.M., 2008. Longitudinal relations between parental drinking problems, family functioning, and child adjustment. Dev. Psychopathol. 20 (1), 195–212. https://doi.org/10.1017/S0954579408000096.
Kessler, R.C., McLaughlin, K.A., Green, J.G., Gruber, M.J., Sampson, N.A., Zaslavsky, A. M., Aguilar-Gaxiola, S., Alhamzawi, A.O., Alonso, J., Angermeyer, M., Benjet, C., Bromet, E., Chatterji, S., de Girolamo, G., Demyttenaere, K., Fayyad, J., Florescu, S., Gal, G., Gureje, O., Williams, D.R., 2010. Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. Br. J. Psychiatry 197 (5), 378–385. https://doi.org/10.1192/bjp.bp.110.080499.
Kessler, R.C., Üstün, T.B., 2004. The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). Int. J. Methods Psychiatr. Res. 13 (2), 93–121. https://doi.org/10.1002/mpr.168.
Lien, Y.J., Kao, Y.C., Liu, Y.P., Chang, H.A., Tzeng, N.S., Lu, C.W., Lin, S.J., Loh, C.H., 2015. Relationships of perceived public stigma of mental illness and psychosis-like experiences in a non-clinical population sample. Soc. Psychiatry Psychiatr. Epidemiol. 50 (2), 289–298. https://doi.org/10.1007/s00127-014-0929-6.
Luby, J., Belden, A., Botteron, K., Marrus, N., Harms, M.P., Babb, C., Nishino, T., Barch, D., 2013. The effects of poverty on childhood brain development: the mediating effect of caregiving and stressful life events. JAMA Pediatr. 167 (12), 1135. https://doi.org/10.1001/jamapediatrics.2013.3139.
Mackie, C.J., Castellanos-Ryan, N., Conrod, P.J., 2011. Developmental trajectories of psychotic-like experiences across adolescence: impact of victimization and substance use. Psychol. Med. 41 (1), 47–58. https://doi.org/10.1017/S0033291710000449.
McGrath, J.J., McLaughlin, K.A., Saha, S., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonso, J., Bruffaerts, R., de Girolamo, G., de Jonge, P., Esan, O., Florescu, S., Gureje, O., Haro, J.M., Hu, C., Karam, E.G., Kovess-Masfety, V., Lee, S., Lepine, J.P., Lim, C.C.W., Kessler, R.C., 2017. The association between childhood adversities and subsequent first onset of psychotic experiences: a cross-national analysis of 23 998 respondents from 17 countries. Psychol. Med. 47 (7), 1230–1245. https://doi.org/10.1017/S0033291716003263.
McGrath, J.J., Saha, S., Al-Hamzawi, A., Alonso, J., Bromet, E.J., Bruffaerts, R., Caldas-de-Almeida, J.M., Chiu, W.T., de Jonge, P., Fayyad, J., Florescu, S., Gureje, O., Haro, J.M., Hu, C., Kovess-Masfety, V., Lepine, J.P., Lim, C.C.W., Mora, M.E.M., Navarro-Mateu, F., Kessler, R.C., 2015. Psychotic experiences in the general population: a cross-national analysis based on 31 261 respondents from 18 countries. JAMA Psychiatry 72 (7), 697. https://doi.org/10.1001/jamapsychiatry.2015.0575.
McGrath, J.J., Saha, S., Al-Hamzawi, A., Andrade, L., Benjet, C., Bromet, E.J., Browne, M. O., Caldas de Almeida, J.M., Chiu, W.T., Demyttenaere, K., Fayyad, J., Florescu, S., de Girolamo, G., Gureje, O., Haro, J.M., ten Have, M., Hu, C., Kovess-Masfety, V., Lim, C.C.W., Kessler, R.C., 2016. The bidirectional associations between psychotic experiences and DSM-IV mental disorders. Am. J. Psychiatry 173 (10), 997–1006. https://doi.org/10.1176/appi.ajp.2016.15101293.
McLaughlin, K.A., Sheridan, M.A., 2016. Beyond cumulative risk: a dimensional approach to childhood adversity. Curr. Dir. Psychol. Sci. 25 (4), 239–245. https://doi.org/10.1177/0963721416655883.
McLaughlin, K.A., Sheridan, M.A., Lambert, H.K., 2014. Childhood adversity and neural development: deprivation and threat as distinct dimensions of early experience. Neurosci. Biobehav. Rev. 47, 578–591. https://doi.org/10.1016/j.neubiorev.2014.10.012.
McLaughlin, K., Weissman, D., Bitrán, D., 2019. Childhood adversity and neural development: a systematic review. Annu. Rev. Dev. Psychol. 15 (1) https://doi.org/10.1146/annurev-devpsych-121318- 084950, 11.1-11.36.
Miguel, P.M., Pereira, L.O., Silveira, P.P., Meaney, M.J., 2019. Early environmental influences on the development of children's brain structure and function. Dev. Med. Child Neurol. 61 (10), 1127–1133. https://doi.org/10.1111/dmcn.14182.
Montoya Gonzalez, L.E., Restrepo Bernal, D.P., Mejía-Montoya, R., Bareño-Silva, J., Sierra-Hincapié, G., Torres de Galvis, Y., Marulanda-Restrepo, D., Gómez-Sierra, N., Gaviria-Arbeláez, S, 2016. Sensibilidad y especificidad entre la Entrevista Diagnóstica Internacional Compuesta versión 3.0 (World Mental Health, CIDI) con la Evaluación Clínica Estandarizada versión I (SCID-I) en la Encuesta de Salud Mental de la ciudad de Medellín, 2012. Rev. Colomb. Psiquiatr. 45 (1), 22–27. https://doi.org/10.1016/j.rcp.2015.07.001.
Moreno, C., Nuevo, R., Chatterji, S., Verdes, E., Arango, C., Ayuso-Mateos, J.L., 2013. Psychotic symptoms are associated with physical health problems independently of a mental disorder diagnosis: results from the WHO World Health Survey. World Psychiatry 12 (3), 251–257. https://doi.org/10.1002/wps.20070.
Morgan, C., Gayer-Anderson, C., 2016. Childhood adversities and psychosis: evidence, challenges, implications. World Psychiatry 15 (2), 93–102. https://doi.org/10.1002/wps.20330.

Morgan, C., Gayer-Anderson, C., Beards, S., Hubbard, K., Mondelli, V., Di Forti, M., Murray, R.M., Pariante, C., Dazzan, P., Craig, T.J., Reininghaus, U., Fisher, H.L., 2020. Threat, hostility and violence in childhood and later psychotic disorder: population-based case–control study. Br. J. Psychiatry 217 (4), 575–582. https://doi.org/10.1192/bjp.2020.133.

Morgan, C., Reininghaus, U., Reichenberg, A., Frissa, S., team, SELCoH study, Hotopf, M., Hatch, S.L, 2014. Adversity, cannabis use and psychotic experiences: evidence of cumulative and synergistic effects. Br. J. Psychiatry 204 (5), 346–353. https://doi.org/10.1192/bjp.bp.113.134452.

Muenzenmaier, K.H., Seixas, A.A., Schneeberger, A.R., Castille, D.M., Battaglia, J., Link, B.G., 2015. Cumulative effects of stressful childhood experiences on delusions and hallucinations. J. Trauma Dissociation 16 (4), 442–462. https://doi.org/10.1080/15299732.2015.1018475.

Noble, K.G., Houston, S.M., Brito, N.H., Bartsch, H., Kan, E., Kuperman, J.M., Akshoomoff, N., Amaral, D.G., Bloss, C.S., Libiger, O., Schork, N.J., Murray, S.S., Casey, B.J., Chang, L., Ernst, T.M., Frazier, J.A., Gruen, J.R., Kennedy, D.N., Van Zijl, P., Sowell, E.R., 2015. Family income, parental education and brain structure in children and adolescents. Nat. Neurosci. 18 (5), 773–778. https://doi.org/10.1038/nn.3983.

Porche, M.V., Fortuna, L.R., Lin, J., Alegria, M., 2011. Childhood trauma and psychiatric disorders as correlates of school dropout in a national sample of young adults: childhood trauma and school dropout. Child Dev. 82 (3), 982–998. https://doi.org/10.1111/j.1467-8624.2010.01534.x.

Raitasalo, K., Holmila, M., Jääskeläinen, M., Santalahti, P., 2019. The effect of the severity of parental alcohol abuse on mental and behavioural disorders in children. Eur. Child Adolesc. Psychiatry 28 (7), 913–922. https://doi.org/10.1007/s00787-018-1253-6.

Reuben, A., Moffitt, T.E., Caspi, A., Belsky, D.W., Harrington, H., Schroeder, F., Hogan, S., Ramrakha, S., Poulton, R., Danese, A., 2016. Lest we forget: comparing retrospective and prospective assessments of adverse childhood experiences in the prediction of adult health. J. Child Psychol. Psychiatry 57 (10), 1103–1112. https://doi.org/10.1111/jcpp.12621.

Roddy, S., Tiedt, L., Kelleher, I., Clarke, M.C., Murphy, J., Rawdon, C., Roche, R.A.P., Calkins, M.E., Richard, J.A., Kohler, C.G., Cannon, M., 2012. Facial emotion recognition in adolescents with psychotic-like experiences: a school-based sample from the general population. Psychol. Med. 42 (10), 2157–2166. https://doi.org/10.1017/S0033291712000311.

Saha, S., Scott, J., Varghese, D., McGrath, J., 2012. Social support and delusional-like experiences: a nationwide population-based study. Epidemiol. Psychiatr Sci. 21 (2), 203–212. https://doi.org/10.1017/S2045796011000862.

Schalinski, I., Teicher, M.H., Nischk, D., Hinderer, E., Müller, O., Rockstroh, B., 2016. Type and timing of adverse childhood experiences differentially affect severity of PTSD, dissociative and depressive symptoms in adult inpatients. BMC Psychiatry 16 (1), 295. https://doi.org/10.1186/s12888-016-1004-5.

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59 (Suppl 20), 22-33;quiz 34-57.

Sheridan, M.A., McLaughlin, K.A., 2014. Dimensions of early experience and neural development: deprivation and threat. Trends Cogn. Sci. (Regul. Ed.) 18 (11), 580–585. https://doi.org/10.1016/j.tics.2014.09.001.

Sideli, L., Murray, R.M., Schimmenti, A., Corso, M., La Barbera, D., Trotta, A., Fisher, H. L., 2020. Childhood adversity and psychosis: a systematic review of bio-psycho-social mediators and moderators. Psychol. Med. 50 (11), 1761–1782. https://doi.org/10.1017/S0033291720002172.

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., Salazar de Pablo, G., Il Shin, J., Kirkbride, J.B., Jones, P., Kim, J.H., Kim, J.Y., Carvalho, A.F., Seeman, M.V., Correll, C.U., Fusar-Poli, P, 2021. Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. Mol. Psychiatry. https://doi.org/10.1038/s41380-021-01161-7.

StataCorp, 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.

Stoep, A.V., Wiess, N., Elena, K., Doug, C., Cohen, P., 2003. What proportion of failure to complete secondary school in the US population is attributable to adolescent psychiatric disorder? J. Behav. Health Serv. Res. 30 (1), 119–124. https://doi.org/10.1097/00075484-200301000-00009.

Thompson, A., Broome, M., 2020. Risk Factors for Psychosis: Paradigms, Mechanisms, and Prevention. Academic Press.

Thompson, A.D., Nelson, B., Yuen, H.P., Lin, A., Amminger, G.P., McGorry, P.D., Wood, S.J., Yung, A.R., 2014. Sexual trauma increases the risk of developing psychosis in an ultra high-risk “Prodromal” population. Schizophr. Bull. 40 (3), 697–706. https://doi.org/10.1093/schbul/sbt032.

Tourangeau, R., 2014. Hard-to-survey Populations. Cambridge University Press.

Trotta, A., Murray, R.M., Fisher, H.L., 2015. The impact of childhood adversity on the persistence of psychotic symptoms: a systematic review and meta-analysis. Psychol. Med. 45 (12), 2481–2498. https://doi.org/10.1017/S0033291715000574.

UNESCO (2019). Combining data on out-of-school children, completion and learning to offer a more comprehensive view on SDG 4 [WWW Document], n.d. . UNICEF Global Development Commons. URL https://gdc.unicef.org/resource/combining-data-out-school-children-completion-and-learning-offer-more-comprehensive-view (accessed 14 October 2021).

van Nierop, M., Bak, M., Graaf, R., Ten Have, M., van Dorsselaer, S., 2016. The functional and clinical relevance of childhood trauma-related admixture of affective, anxious and psychosis symptoms. Acta Psychiatr. Scand. 133, 91–101. https://doi.org/10.1111/acps.12437.

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., Read, J., van Os, J., Bentall, R.P., 2012. Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. Schizophr. Bull. 38 (4), 661–671. https://doi.org/10.1093/schbul/sbs050.

Vásquez Núñez, J., 2020. La influencia de la exposición a experiencias sociales adversas tempranas sobre el padecimiento de trastornos psiquiátricos de adolescentes y jóvenes infractores de ley [WWW Document], n.d.. Pontificia Universidad Católica de Chile. URL https://repositorio.uc.cl/handle/11534/49537 (accessed 11 July 2022).

von Hippel, P., & Lynch, J. (2013). Efficiency gains from using auxiliary variables in imputation. 1–10. 10.48550/arXiv.1311.5249.

White, I.R., Royston, P., Wood, A.M., 2011. Multiple imputation using chained equations: issues and guidance for practice. Stat. Med. 30 (4), 377–399. https://doi.org/10.1002/sim.4067.

Zhao, Y., Long, Q., 2016. Multiple imputation in the presence of high-dimensional data. Stat. Methods Med. Res. 25 (5), 2021–2035. https://doi.org/10.1177/0962280213511027.