The effects of childhood adversity on treatment delays and its components in first-episode psychosis

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Highlights

1. *Treatment delays may be a means by which childhood trauma worsens psychosis outcomes.*
2. *Childhood trauma was associated with delays in help-seeking and system's response.*
3. *Each unit increase in childhood trauma increased treatment delay in psychosis by 25%.*

ABSTRACT

Apart from increasing risk for psychotic disorders, childhood adversity has been associated with worse outcomes. One way in which childhood adversity may worsen outcomes is by lengthening treatment delays, which are associated with negative impacts. We tested the influence of childhood trauma on treatment delays, measured as the duration of untreated psychosis (DUP), and its help-seeking and referral components, in a first-episode psychosis cohort (N= 203). We accounted for pertinent social (e.g., migrant status) and other determinants (i.e., age at onset, diagnosis, symptoms) of treatment delays. Multiple linear regression analyses revealed that for a one-unit increase in Childhood Trauma Questionnaire (CTQ) scores, average overall DUP increased by 25%. Higher CTQ scores also significantly predicted help-seeking and referral DUPs. Patients with schizophrenia-spectrum psychosis had longer help-seeking and total DUPs than those with affective psychosis. More severe positive symptoms predicted longer help-seeking DUPs, while more severe negative symptoms predicted longer referral DUPs. Indicators of social disadvantage did not affect DUP. Our results show that childhood trauma increases DUP by prolonging the help-seeking process *and* delaying access to mental healthcare even after help is sought. Early identification of psychosis among populations with trauma histories seems warranted and can likely positively impact outcomes.

Keywords : childhood adversity, first-episode psychosis, DUP, help-seeking, treatment delays

INTRODUCTION

Childhood adversities represent a range of detrimental experiences known to negatively affect life course and clinical outcomes (Kessler, Davis et al. 1997). These adverse events include

abuse or neglect (emotional, psychological, physical, and sexual); parental loss (death or divorce); mental illness or substance use in the household; and the incarceration of a family member (Anda, Felitti et al. 2006) Adverse experiences and trauma in childhood have been associated with a greater risk of psychopathology in adulthood (Kessler, Davis et al. 1997), including psychotic disorders(Varese, Smeets et al. 2012, Fusar-Poli, Tantardini et al. 2017). Moreover, within first-episode psychosis populations, childhood adversities have been shown to play a role in both the emergence of the disorder (Read, van Os et al. 2005, Fisher, Jones et al. 2010) and various unfavorable clinical outcomes, including the persistence of psychotic psychopathology, inadequate medication adherence, longer and more frequent hospital admissions, and an increased risk of relapse (Lecomte, Spidel et al. 2008, Alvarez, Roura et al. 2011, Trotta, Murray et al. 2015, Pruessner, King et al. 2019, Pruessner, King et al. 2020 (submitted)). Still, key gaps remain in our understanding of the mechanisms by which adversities impact on the development and course of psychosis.

Delays prior to the commencement of treatment have been associated with worse clinical (Penttilä, Jääskeläinen et al. 2014) and functional outcomes (Hill, Crumlish et al. 2012, Iyer, Mustafa et al. 2018) in multiple systematic reviews and meta-analyses. (Marshall, Lewis et al. 2005, Farooq, Large et al. 2009). Such delays have been measured in terms of the duration of untreated psychosis (DUP), which is defined as the duration of time between the onset of frank psychotic symptoms and the commencement of treatment. The consistent association between longer DUP and negative outcomes has led to increased interest in the predictors and determinants of these delays and has provided some of the impetus for early intervention services for psychosis (Norman, Lewis et al. 2005, Malla and McGorry 2019). Such services consider reduc-

ing DUPs an important target given its potential to improve outcomes, and alleviate unnecessary suffering and social loss (Johannessen, McGlashan et al. 2001, Birchwood, Connor et al. 2013). Known predictors of longer DUP include clinical, sociodemographic, and healthcare-related factors such as a pernicious mode and/or younger age of onset, migrant status, social deprivation, being single, increased negative symptoms, social functioning, and referral source among others (Compton, Gordon et al. 2011, Nerhus, Berg et al. 2015, O'Donoghue, Lyne et al. 2016, Stentebjerg-Olesen, Pagsberg et al. 2016, Hastrup, Haahr et al. 2018).

Prior research has resolved DUP into two components. *Help-seeking* delays are defined as the duration of time between the onset of symptoms and a first contact with services and represent the process of recognizing a need for help (by the individual or their carers), and the steps taken to obtain it. Although not investigated extensively, longer help-seeking delays have been associated with younger age at onset and poor premorbid adjustment (Bechard-Evans, Schmitz et al. 2007, O'Callaghan, Turner et al. 2010); a schizophrenia-spectrum diagnosis (Bechard-Evans, Schmitz et al., 2007); and lack of family involvement, being male and more negative symptoms (O'Callaghan, Turner et al. 2010). Outside of psychosis, individuals with adverse childhood experiences have been shown to delay help-seeking and have difficulties in maintaining relationships with health professionals (Pearlman and Courtois 2005, Lecomte, Spidel et al. 2008). Following a first contact with healthcare services, *referral* or *systemic* delays represent the length of time between a first healthcare contact and successful engagement with appropriate services or the commencement of treatment. These delays are thought to reflect the functioning of the healthcare system and referral pathways. While limited, prior work has shown associations between lengthier referral delays and a younger age of onset, a non-medical first healthcare contact,

and a schizophrenia-spectrum diagnosis (Bechard-Evans, Schmitz et al. 2007, O'Callaghan, Turner et al. 2010).

Given the influence of sociodemographic factors on treatment delays and the high prevalence of childhood adversity among persons with first-episode psychosis (Reeder, Husain et al. 2017), we hypothesized that childhood adversity would have a significant influence on treatment delays. Indeed, an earlier study reported an association between childhood trauma and lengthier DUPs (Broussard, Kelley et al. 2013). However, it is still unknown if childhood adversity delays the initiation of treatment by delaying help-seeking or referral or both. The present study aims to extend this line of research by determining the effects of childhood trauma not only on overall treatment delays in first-episode psychosis but also on its specific components, i.e., help-seeking DUP and referral DUP.

To determine the independent influence of childhood adversity on DUP and its components, we accounted for other factors known to influence DUP and outcomes in first-episode psychosis samples, such as age at onset, gender, socioeconomic deprivation, minority status, migrant background, positive and negative symptoms and diagnoses ((Bechard-Evans, Schmitz et al. 2007, Birnbaum, Wan et al. 2017, Hastrup, Haahr et al. 2018, Martin, Moro et al. 2019, Ku, Pauselli et al. 2020)). Given the limited research on the predictors of the help-seeking and referral components of DUP, we extended our paper to not only analyze and comment on the contributions of adversity measures to these and but also those of other putative socio-demographic and clinical predictors. Determining who is at risk of having a deferred initiation of treatment (i.e., longer DUPs) is important for developing interventions to reduce treatment delay and thereby, potentially improve the course and prognosis of psychotic disorders.

METHODS

Setting and sample

The present study was conducted at the Prevention and Early Intervention Program for Psychosis, (PEPP-Montreal). All individuals identified as potentially having a first episode of psychosis from a defined epidemiological catchment area (Southwest Montreal, Canada, population of about 350 000) are referred to PEPP-Montreal. PEPP-Montreal's healthcare model combines psychiatric follow-up with assertive case-management, low-dose antipsychotic medications, and psychological and psychosocial interventions for a period of two years (Iyer-JNMD-2015). Patients aged 14 to 35 years with a DSM-IV diagnosis of non-affective or affective psychotic disorder are accepted for treatment. PEPP's referral process includes an open intake system, accepting requests from all sources (including patients themselves, or their families) without requiring any referral forms. All referrals are responded to within 72 hours. Patients are referred elsewhere if they are ultimately determined to have organic causes (e.g., epilepsy), an IQ of less than 70, or previous exposure to antipsychotics of greater than one-month duration. All patients in this study accepted to participate in the research protocol and granted written informed consent. This is part of a larger study approved by the Research Ethics Board at the Douglas Mental Health University Institute.

Delay Measures

Treatment delays were assessed using the Circumstances of Onset and Relapse Schedule (CORS)(Norman, Malla et al. 2004), a semi-structured interview conducted by trained research assistants with the patient and, if needed, a close family member, supplemented by chart reviews

of available health and educational/social records. The interview explores the lifetime history of illness and psycho-developmental history. This chronological account provides a timeline depicting the history of the events that led to the current psychotic episode that prompted the referral. From this information, estimates of important dates can be made, including date of first identifiable psychiatric change (non-psychotic), date of prodrome onset (non-interrupted psychiatric change contiguous with the first psychotic episode), date of first psychotic episode, and date of commencement of first adequate treatment (defined as taking antipsychotic medication for 1 month or start of care at PEPP). Date estimates from the CORS are resolved through consensus between interviewers and the whole research team, including one psychiatrist. The total duration of untreated psychosis (DUP) is defined as the period, in weeks, between the first episode of psychosis and the commencement of adequate treatment (defined as taking antipsychotic medication for 1 month or start of care at PEPP). DUP can be further subdivided into *help seeking* delay (from onset of first psychotic episode to first healthcare contact), and *referral* or *systemic* delay (from first healthcare contact to entry to PEPP). These subdivisions indicate the delays of time to treatment that can be attributed to the patient/family (help-seeking), or to the healthcare system (referral), respectively.

Predictor measures

Childhood trauma was assessed with the Childhood Trauma Questionnaire (CTQ), a validated and widely used 25-item inventory that explores five different domains of trauma exposure. Individual items are rated on a five-point Likert scale, and scores of each item are summed to constitute five subdomains (physical neglect, emotional neglect, physical abuse, emotional abuse, and sexual abuse). Total CTQ scores were calculated by adding up scores in the respective subscales. Given the lack of basis for any hypotheses about specific components of CTQ being more or less associated with DUP or its components, we focused on total CTQ score.

Data was also collected by trained research assistants at baseline (upon entry into treatment) on other known influences of treatment delays including age at onset, gender, socioeconomic deprivation, minority status, migrant background, positive and negative symptoms and diagnoses. Additional socio-demographic variables included age, gender, living situation (dichotomized as living with others or living alone), education (dichotomized as completed high school or not), visible minority status (dichotomized as non-white or white), and migrant background (non-migrant, first-generation, and second-generation). Social and material deprivation were determined by linking the participants' postal codes with the deprivation database provided by the *Institut National de Sante Publique de Quebec* (INSPQ). The INSPQ utilizes data from the Canadian census on six different social determinants of health to create composite indices for both social and material deprivation(Pampalon, Hamel et al. 2009). These indices reflect social disadvantage at the neighborhood level, a method that has proven to predict health outcomes in different metropolitan areas (Su, Gong et al. 2017). A variable reflecting a composite score of deprivation was created as follows: low deprivation (both social and material scores in the 2 lowest quintiles), high deprivation (both social and material scores in the 2 highest quintiles), and intermediate (rest of the possible quintile combinations). Participants were defined as having a migrant background if they had been born outside of Canada ('first-generation'), or if at least one of their parents was ('second-generation') (Statistics Canada 2020). This variable was dichotomized between having a migrant (first or second generation), or a non-migrant background. Finally, the Statistics Canada definition was adopted to assign the status of visible ethnic minority: "persons, other than Aboriginal peoples, who are non-Caucasian in race or non-white" (Statistics Canada 2020). Again, this variable was dichotomized between being part of a visible minority group or not.

Primary diagnosis (schizophrenia-spectrum or affective) and secondary diagnosis (presence or absence of substance abuse) were determined by SCID-IV. SCID-IV diagnoses were recorded based on consensus between the interviewer and the research team, including one experienced psychiatrist.

Clinical symptoms were measured using the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen 1984), global score out of 30) and the Scale for the Assessment of Negative Symptoms (SANS)(Andreasen 1984) , global score out of 30). Symptom assessments were done by trained staff who had achieved high inter-rater reliability rates (intra-class correlation range = 0.82-0.98). The Global Assessment of Function scale (GAF) (Hall 1995), global score out of 100) and the Social and Occupational Functioning Assessment Scale (SOFAS; (Goldman, Skodol et al. 1992), global score out of 100) were also used to characterize the sample at base-line.

Data Analysis

Descriptive statistics regarding the demographic and clinical characteristics of the sample are provided first. Continuous variables were explored for normality; logarithmic transformations were implemented for those variables with considerable skewness (i.e., the delay variables). Predictor testing began with univariate explorations to determine the individual and unadjusted influence of total CTQ score and each of the other demograpic and clinical predictor variables on treatment delays — categorical variables were analyzed with student's t-tests or ANOVA, and continuous variables with Pearson correlations. As exploratory analyses, we also examined the relationship between the five specific CTQ domains (emotional neglect, emotional abuse, physical neglect, physical abuse, and sexual abuse) and DUP, help-seeking and referral delays.

Finally, we examined the influence of all predictors in a multiple regression model, which allowed us to determine the independent effect of each predictor (including total childhood trauma) on total, help-seeking, and referral treatment delays. Analyses were conducted using the R statistical software core packages (3.2.3) (Venables and Smith 2015).

RESULTS

Sample characteristics

Our sample included 203 participants. Demographic and clinical characteristics of participants are illustrated in Table 1. The majority of participants were male (69.3%), of non-visible minority status (62.8%), and had a schizophrenia-spectrum diagnosis (68.6%). The near totality of participants came from deprived neighborhoods (97% lived in medium or high deprivation). The majority had finished high school (70.1%) and were living with others (friends or family, 88.2%) upon entry into PEPP.

Prevalence of Childhood Adversity

Total CTQ scores ranged from 25-100 (mean = 43.46, SD = 14.8). Overall, 54.5% of our sample met criteria for at least one experience of childhood adversity. The most common adversities to which individuals in our sample had been exposed were emotional neglect (25.7% of the sample) and emotional abuse (25.3% of the sample). See Ancillary Table 1 for distribution of CTQ subscale scores.

Initial Univariate Analyses

The initial analyses of the variables known to influence treatment delays was conducted with univariate regression analyses for the continuous variables (Ancillary Table 1,2) and t-tests/ANOVAs for nominal variables (Ancillary Tables 3,4). Higher scores of childhood trauma were associated with longer total, help-seeking and referral treatment delays. Higher scores on each of the five domains of trauma (emotional neglect, emotional abuse, physical neglect, physical abuse, and sexual abuse) were associated with longer total delays. In addition, higher scores of emotional neglect and emotional abuse were associated with longer help-seeking and referral delays, and higher scores of sexual abuse were associated with longer referral delays.

Those who were younger upon onset of the first episode of psychosis and males had significantly longer total and help-seeking delays. Belonging to a visible minority group or having a migrant background did not significantly impact on treatment delays.

Higher levels of negative symptoms at baseline were significantly correlated with longer total and referral delays. In contrast, positive symptom scores were not significantly associated with delays. Having a diagnosis of schizophrenia-spectrum disorder was associated with longer total and help-seeking delays when compared with affective psychoses, but not longer referral delays.

Main Analyses

The final multivariate regression models included age at onset, gender, socioeconomic deprivation, minority status, migrant background, total childhood trauma scores, baseline scores of positive and negative symptoms, substance abuse diagnosis and main diagnosis (Table 2). With all other variables controlled for, longer total treatment delays remained significantly associated with CTQ score and with having a schizophrenia-spectrum disorder diagnosis. This model explained 19% of the variance in total DUP. For every 1-unit increase in the total CTQ score, rep-

resenting the endorsement of at least one additional experience related to a childhood adversity sub-domain , the average DUP of participants increased by 25%**.**

A similar picture emerged for help-seeking delays, although the effect of childhood trauma just approached statistical significance ($p = 0.05$). In addition, higher positive symptom scores significantly predicted longer help-seeking delays. This model explained 11% of the total variance.

Regarding referral delays, childhood trauma was still significantly associated, but in contrast to results for help-seeking delays, increased negative, but not positive, symptoms predicted longer referral delays. Unlike for total and help-seeking delays, the type of diagnosis had no influence on this measure. Longer referral delays were also associated with a younger age at onset of first psychotic episode. The final model explained 12% of the variance in referral DUP. For every 1-unit increase in the total CTQ score, the average referral delay increased by 21%.

DISCUSSION

The present study aimed to examine the influence of childhood adversity on treatment delays in first-episode psychosis. Notably, childhood trauma was associated with length of total delay prior to treatment initiation, as well as with lengthier systemic referral delay and a tendency for longer help-seeking treatment delay. In contrast, belonging to a visible minority, having a migrant background, or living with socioeconomic deprivation did not have a significant influence on treatment delays. In addition, patients with SSD diagnoses had longer delays in help-seeking that were in turn associated with increased levels of positive symptoms. Additionally, negative symptoms were associated with lengthier delays during the referral process. These findings add

to the extensive literature on the impact of childhood adversities on health and social outcomes in psychosis.

a) Childhood trauma [i]

Multiple lines of evidence have documented a strong association between childhood trauma and psychotic disorders. Individuals who develop psychosis are almost three times more likely to have a history of childhood trauma compared to the general population (Varese, Smeets et al. 2012). Furthermore, experiences of childhood trauma have been linked to worse clinical outcomes in psychosis (Pruessner, King et al. 2019), including severity of hallucinations and delusions (Bailey, Alvarez-Jimenez et al. 2018), persistence of symptoms (Trotta, Murray et al. 2015, Pruessner, King et al. 2019) , and impaired cognitive performance (Schalinski, Teicher et al. 2018). Similarly, longer delays in receiving treatment have been linked with the severity of hallucinations and delusions (Birnbaum, Wan et al. 2017), persistence of symptoms (Dama, Shah et al. 2019), and lower remission rates (Penttilä, Jääskeläinen et al. 2014). Our findings add to this literature by suggesting that one possible mechanism through which childhood trauma may worsen outcomes in psychotic disorders is by lengthening treatment delays. After accounting for other known predictors, the influence of childhood trauma on DUP was noteworthy, with every unit increase in CTQ lengthening DUP by 25% and CTQ scores being relatively wide-spread in our sample (range = 25-100; mean = 43.46, SD = 14.8) .

Perhaps more importantly, the present findings demonstrate that the influence of childhood trauma on treatment delays exists at both help-seeking (individual) and referral (systemic) levels. Regarding help-seeking, childhood trauma has been shown to impact psychological processes

later in life, including response to environmental cues and self-regulation (Pollak 2008), which may contribute to delayed decision-making. Further, individuals with experiences of childhood trauma have been known to avoid healthcare for a variety of mental and physical health issues (Anda, Felitti et al. 2006, Dube, Fairweather et al. 2009, Strine, Dube et al. 2012, Alcalá 2016). It has been suggested that poor attachment, i.e., a maladaptive pattern of emotional closeness and dependency towards others, which is often present in individuals with a history of childhood trauma, may be a factor leading to symptom dismissal or denial of a need for help. Indeed, qualitative work with adults with experiences of childhood trauma has suggested that some of these individuals prefer to self-manage their health issues and are reluctant to admit a need for help (Stige, Traeen et al. 2013). Additionally, individuals with experiences of childhood trauma may have difficulties with trusting authority figures such as healthcare professionals, thus delaying formal treatment seeking when in need. Finally, given the importance of parents and families in help-seeking for psychosis (Connor, Greenfield et al. 2016), a lack of or poor social support in young adulthood, which is common among those with childhood trauma (Pepin and Banyard 2006, Sperry and Widom 2013), may contribute to delays in help-seeking during a first episode of psychosis.

Our results also indicated that the process of reaching and engaging with appropriate services for psychosis is delayed in individuals with a history of childhood abuse, even once an initial contact with healthcare services is made. The same reasons individuals may delay help-seeking may also impact the referral process to specialized care, which represents both the response from providers and services, but also the individuals' ongoing engagement with care and the help-seeking process. There was no significant association of trauma with positive symptoms in our sample, sug-

gesting that referral delays do not seem attributable to lower psychosis symptom burden in these individuals exposed to childhood trauma. Nonetheless, individuals with trauma histories are more likely to have additional symptoms and problems such as anxiety, depression, maladaptive risk-taking and emotional dysregulation that may impede the timely identification of their psychosis symptoms. Our post-hoc tests revealed small but significant correlations between trauma and depression scores on the Calgary Depression Scale (r =0.16) but not with anxiety (assessed using the anxiety item on the Brief Psychiatric Rating Scale).

The higher presence of traits such as hostility, uncooperativeness, or impulse control (Ajnakina, Trotta et al. 2016) in individuals with trauma histories may also complicate both the identification of psychosis in help-seeking individuals and the referral process. Attachment may also play a role, as individuals with psychotic disorders with an insecure attachment style are less likely to keep in contact with services (McGonagle, Bucci et al. 2019). Young individuals with trauma histories are also likely to be in contact with numerous systems of care (e.g., justice, youth protection services, social services) and may inadvertently fall through cracks between these various systems.

Replicating an earlier study (Broussard, Kelley et al. 2013), we found that each of the five domains of the CTQ was associated with overall DUP. Our findings that emotional neglect and abuse were specifically associated with help-seeking and referral delays, and sexual abuse with referral delays extend and nuance what we know about this association.

b) Other sociodemographic factors

Our results are in line with four previous studies reporting no differences in treatment delays in psychosis depending on ethnicity (McGovern and Cope 1991, Cole, Leavey et al. 1995, Archie,

Akhtar-Danesh et al. 2010, Singh, Brown et al. 2015). In one study, however, one minority group but not others had longer DUPs (Basu, Subramaniam et al. 2015). We only analyzed ethnicity as a binary variable which may have masked the influence of different specific ethnicities on DUP, an investigation of which was precluded by our sample only including 77 visible minority individuals.

With respect to socioeconomic deprivation, our sample was rather homogeneous, and thus this might have hampered our ability to detect differences in DUP based on deprivation indices.

In addition, younger age and male sex are known negative predictors of help-seeking for mental health problems (Bechard-Evans, Schmitz et al. 2007)). The restricted range of age of onset of our cohort might have limited the ability of our model to identify differences based on age, but there was a non-significant trend towards shorter help-seeking delays with increasing age. Similarly, the distribution of gender observed in our sample, typical of a first-episode cohort, where roughly 70% of it is composed of male patients, might have hampered our ability to find significant differences.

c) Diagnosis and symptoms

Patients with schizophrenia-spectrum disorders had significantly longer total DUPs than their affective psychosis counterparts. However, this effect appears to be specific to help-seeking delays, since there was no difference in referral times. This pattern had been previously documented in this same setting (Bechard-Evans, Schmitz et al. 2007). It is well-known that patients with SSD have a heavier psychopathological burden(Torrent, Reinares et al. 2018), poorer long-term functional outcomes (Jarbin, Ott et al. 2003), and lower rates of educational achievement and

employment (Perala, Suvisaari et al. 2007). Individuals who later develop schizophrenia-spectrum disorders have higher rates of premorbid cognitive deficits when compared to those who develop affective psychotic disorders (Seidman, Giuliano et al. 2006, Agnew-Blais, Buka et al. 2015). How cognition might affect help seeking is still not clear, and the challenge of assessing cognition and help-seeking in individuals who will later develop psychosis is reflected in the paucity of studies on this issue.

Results from previous studies have provided contradicting results with respect to the association between symptoms and treatment delays. In one study, positive, but not negative, symptom scores were associated with longer DUPs (Drake, Haley et al. 2000). In contrast, a different study only found an association between negative symptoms and DUP (Drake, Haley et al. 2000, Clarke, Browne et al. 2007). Our ability to separate both components of treatment delay might provide a clue to clarify these discrepancies: in the present report, help-seeking delays were significantly increased by the degree of positive symptom severity at admission, while scores of negative symptoms were associated with delayed referrals. It is plausible that individuals with more severe psychopathology are less likely to seek help and that individuals with less severe psychotic symptoms are faster to identify a need for help. Our findings are in line with earlier reports that patients with negative symptoms had longer pathways to care than patients with predominant positive symptomatology (Platz, Umbricht et al. 2006), in part due to the under-identification of insidious features of psychosis by community healthcare workers such as general practitioners (Simon, Lauber et al. 2005).

Strengths and Limitations

Strengths of the present study include the use of the CORS, a follow-back method (van Os, Schaub et al. 2021) that allows for a systematic and rigorous estimation of treatment delays, and the differentiation of its help-seeking and referral components. Moreover, our sample was well-characterized due to our research protocol and trained staff with high levels of reliability.

Our findings should be considered in light of certain limitations. First, our study relied on participants' recollection of exposure to trauma in childhood, which can be limited by retrospective recall bias. Nevertheless, the measure we used has been reliably used in psychosis and shown to have adequate sensitivity (Lardinois, Lataster et al. 2011, Stowkowy, Liu et al. 2016) Second, our variable measuring material deprivation is an area-based measure calculated from census data, and it thus does not gauge socioeconomic deprivation at the individual level. This might explain why we did not observe any differences depending on this determinant. However, area-based methods have proven to reliably and accurately predict health outcomes (Ross and Mirowsky 2001) and are robust indicators of the socioeconomic environment in which individuals live. Further, our sample of first-episode psychosis service users was limited to those aged 14-35, were relatively homogenous in terms of social and material deprivation, and came from one clinical setting. As such, generalizability of our findings to other groups experiencing psychosis, in different contexts, is limited.

Finally, our relatively small sample size precluded testing how trauma and other predictors interact to contribute to overall treatment delays. For instance, gender differences have been noted in childhood trauma experiences, with more pronounced impact on the course of psychosis among males (Pruessner, King et al. 2019). While gender did not independently influence DUP in our study, research with larger sample sizes is needed to test if gender moderates the influence of childhood trauma on DUP. Future research with larger sample sizes should also use sophisticated path analyses to examine the mediating role of treatment delays in the relationship between childhood trauma and treatment outcomes in psychosis.

Implications

Our results add to the literature documenting the effects of childhood trauma on mental health, and point towards potential mechanisms through which such effects might be channelled, in addition to known neurobiological mechanisms (Van Winkel, Van Nierop et al. 2013, Faravelli, Mansueto et al. 2017). If proven, this will highlight the importance of screening for childhood trauma in clinical populations accessing mental health services. Similarly, these findings underscore the importance of comprehensive youth mental health services, where a history of childhood trauma could signal the need for a more intensive and coordinated follow-up, and focused interventions. By the same token, targeted outreach/early detection may be necessary for youth at high risk of trauma, for example, in criminal justice or foster care systems. Finally, childhood trauma should keep gaining recognition as a public health problem that needs to be treated as a priority and for which decisive policies need to be delineated.

Conclusion

Overall, treatment delay is a complex phenomenon influenced by diverse factors at the individual-, societal-, service-, and health-system levels. This study contributes to our understanding of treatment delays in first-episode psychosis through new evidence suggesting that childhood adversity plays a role in overall, help-seeking and systemic delays experienced by this population.

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Table 1. Demographic characteristics of participants

	N	(%)		N	(%)
Gender			**Minority**		
Male	144	69.6%	Yes	77	37.20%
Female	63	30.40%	No	130	62.80%
Diagnosis			**Substance Use Diagnosis**		
SSD	142	68.60%	No	95	46.30%
AP	65	31.40%	Yes	110	53.70%
Highschool			**Living Alone**		
No	61	29.90%	Yes	24	11.80%
Yes	143	70.10%	No	180	88.20%
Deprivation			**CTQ**	**N**	**mean (SD)**
High	100	48.30%		203	43.5 (14.8)
Medium	101	48.80%			
Low	6	2.90%			
	N	**mean (SD)**		**N**	**mean (SD)**
SAPS	206	11.58(3.4)	**SANS**	207	11.3(4.25)
GAF	206	30.58(9.58)	**SOFAS**	184	43.0 (13.05)

Age at episode onset	207	22.78(4.66)			

SSD – schizophrenia spectrum diagnosis, AP-affective psychosis diagnosis, CTQ –Childhood Trauma Questionnaire, SAPS – Scale for the Assessment of Positive Symptoms, SANS - Scale for the Assessment of Negative Symptoms, GAF –The Global Assessment of Function scale , SOFAS-Social and Occupational Functioning Assessment Scale

Table 2. Multiple regression models for total DUP and components

	Total DUP (N=203)					Help-seeking DUP (N=204)				Referral DUP (N=203)		
COEFF	**Std.β**	**OR (95% CI)**	**t**	***p***	**Std.β**	**OR 95%CI**	**t**	***p***	**Std.β**	**OR 95%CI**	**t**	***p***
Age (onset)	-0.11	0.89 (-0.13 – 0.01)	-1.62	0.11	-0.12	0.89 (-0.18 – 0.02)	-1.68	0.09	-0.21	0.81 (-0.16 - 0.023)	-3.05	<0.01
Gender (male)	-0.08	0.92 (-0.1 – 0.41)	-1.22	0.22	-0.08	0.92 (-0.15-0.56)	-1.09	0.28	-0.03	0.97 (-0.3 – 0.45)	-0.42	0.68
Deprivation (low)	-0.05	0.95 (-1.2 – 0.63)	-0.82	0.41	-0.06	0.94(-0.88 – 1.6)	-0.92	0.36	-0.01	0.99 (-1.5 – 1.0)	-0.16	0.87
Migrant Status (non-migrant)	0.03	1.03 (-0.3 – 0.49)	0.39	0.70	0.01	1.01 (-0.5 – 0.61)	0.05	0.96	<0.01	1.01 (-0.6 – 0.5)	0.06	0.95
Visible minority (yes)	-0.08	0.92 (-0.1 – 0.49)	-1.08	0.28	-0.09	0.91 (-0.2 – 0.61)	-1.16	0.25	-0.01	0.99 (-0.35 – 0.47)	-0.11	0.91
CTQ (total)	0.03	1.03 (0.01 – 0.04)	3.28	<0.01	0.14	1.15 (-0.001 – 0.24)	1.96	0.05	0.19	1.21 (0.006 – 0. 25)	2.73	0.01
SAPS (global)	0.08	1.08 (-0.03 – 0.11)	1.19	0.23	0.15	1.16 (-.0.01 – 0.2)	2.02	0.04	-0.05	0.95 (-0.13 – 0.06)	-0.62	0.53
SANS (global)	0.07	1.07 (-0.03 – 0.09)	1.01	0.31	-0.08	0.92 (-0.11 – 0.04)	-1.11	0.27	0.17	1.18 (0.02 – 0.18)	2.30	0.02
Substance Dx	0.02	1.02 (-0.3 – 0.2)	0.25	0.80	-0.01	0.99 (-0.32 –	-0.07	0.94	-0.06	0.94 (-0.2 – 0.47)	-	0.45

(Yes)						0.37)					0.75	
Diagnosis (SSD)	0.49	1.63 (0.23 – 0.76)	-3.56	<0.01	0.59	1.8 (0.23-0.95)	-3.34	<0.01	0.05	1.05 (-0.5 – 0.23)	0.71	0.48
MODEL	**R^2**		**F**	***p***	**R^2**		**F**	***p***	**R^2**		**F**	***p***
	0.19		4.64	<0.01	0.13		2.87	<0.01	0.12		2.55	0.01

DUP – Duration of Untreated Psychosis, CTQ –Childhood Trauma Questionnaire, SAPS – Scale for the Assessment of Positive Symptoms, SANS - Scale for the Assessment of Negative Symptoms , SSD – schizophrenia spectrum diagnos

Ancillary Tables

Ancillary table 1	Correlations between childhood trauma domains and treatment delay variables
Ancillary table 2	Bivariate Correlations between continuous predictors and treatment delay
Ancillary table 3	t-tests/ANOVA total DUP (log) by nominal variables
Ancillary table 4	t-tests/ANOVA help-seeking DUP (log) by nominal variables
Ancillary table 5	t-tests/ANOVA referral DUP (log) by nominal variables

Ancillary Table 1. Correlations between childhood trauma domains and treatment delay variables

	Total DUP (log)	**Help-seeking DUP (log)**	**Referral DUP (log)**	**CTQ. EN**	**CTQ.EA**	**CTQ.PN**	**CTQ.PA**	**CTQ. SA**	**CTQ Total**
Total DUP (log)	1	0.57***	0.51***	0.23**	0.22*	0.19*	0.15*	0.17*	0.289***
Help-seeking DUP (log)		1	0.01	0.14*	0.19*	0.14*	0.04	0.11	0.203***
Referral DUP (log)			1	0.16*	0.14*	0.14*	0.05	0.16*	0.161**
CTQ.EN				1	0.57***	0.60***	0.31***	0.25***	0.78***
CTQ.EA					1	0.41***	0.55***	0.48***	0.86***
CTQ.PN						1	0.26***	0.27***	0.66***
CTQ PA							1	0.37***	0.68***
CTQ.SA								1	0.64***
CTQ Total									1

DUP – Duration of Untreated Psychosis, CTQ –Childhood Trauma Questionnaire, EN Emotional neglect, EA – Emotional abuse, PN, physical neglect, PA-physical abuse, SA- sexual abuse
*$*p < .05$, $**$ $p \leq .001$., ***p<0.000*

Ancillary Table 2: Correlations between continuous predictors and treatment delay variables

	Total DUP (log)	Help DUP (log)	Referral DUP (log)	Age (onset)	CTQ (total)
Total DUP (log)	1	0.615**	0.402**	-0.117**	0.289**
Help DUP (log)		1	0.000	-0.119**	0.203**
Referral DUP (log)			1	-0.215**	0.161*
Age (onset)				1	-0.100
CTQ (total)					1
SAPS (global)					
SANS (global)					

DUP – Duration of Untreated Psychosis, CTQ –Childhood Trauma Questionnaire, , SAPS – Scale for the Assessment of Positive Symptoms, SANS - Scale for the Assessment of Negative Symptoms

Ancillary table 2 t-tests/ANOVA <u>total DUP</u> (log) by nominal variables

DUP total	**Gr.**	**N**	**Mean**	**SD**	**Gr.**	**N**	**Mean**	**SD**
Gender	male	141	2.85	1.78	female	62	2.53	1.72
Minority	No	129	2.83	1.83	Yes	74	2.62	1.64
Substance Dx	No	94	2.59	1.77	Yes	109	2.90	1.75
Diagnosis	SSD	138	3.15	1.61	AP	65	1.91	1.77

t-test	**t**	**DF**	**p (2-tailed)**
Gender	1.21	201	0.22
Minority	0.82	166	0.42
Substance Dx	1.24	196	0.21
Diagnosis	4.81	115	<0.01
ANOVA	**N**	**F**	**p**
Deprivation	203	0.56	0.57
Migrant Status	203	0.07	0.92

DUP – Duration of Untreated Psychosis, SSD – schizophrenia spectrum diagnosis, AP-affective psychosis diagnosis

Ancillary table 3 t-tests/ANOVA help-seeking DUP (log) by nominal variables

DUP HS		Gr.	N	Mean	SD	Gr.	N	Mean	SD
	Gender	male	141	1.63	0.19	female	62	1.30	0.29
	Minority	No	129	1.70	0.20	Yes	74	1.24	0.26
Dx	Substance	No	94	1.39	2.47	Yes	109	1.66	2.15
	Diagnosis	SSD	138	1.94	0.19	AP	65	0.67	0.27

t-test		t	DF	p (2-tailed)
	Gender	0.96	201	0.33
	Minority	1.37	201	0.17
Dx	Substance	-0.84	201	0.39
	Diagnosis	3.79	201	<0.01

ANOVA		N	F	p
	Deprivation	203	0.82	0.44
Status	Migrant	203	0.80	0.45

DUP – Duration of Untreated Psychosis, SSD – schizophrenia spectrum diagnosis, AP-affective psychosis diagnosis

Ancillary table 4 t-tests/ANOVA referral DUP (log) by nominal variables

DUP R	Gr.	N	Mean	SD	Gr.	N	Mean	SD
Gender	male	140	0.46	2.34	female	62	0.18	2.25
Minority	No	129	0.34	0.20	Yes	73	0.44	0.27
Substance Dx	No	94	0.44	2.13	Yes	108	0.32	2.47
Diagnosis	SSD	137	0.47	0.20	AP	65	0.18	0.29

t-test	t	DF	p (2-tailed)
Gender	0.81	200	0.43
Minority	0.29	200	0.77
Substance Dx	0.35	200	0.72
Diagnosis	-0.81	200	0.41

ANOVA	N	F	p
Deprivation	202	0.44	0.64
Migrant Status	202	0.16	0.86

DUP – Duration of Untreated Psychosis, SSD – schizophrenia spectrum diagnosis, AP-affective psychosis diagnosis