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Childhood trauma as a risk factor for suicidality in first episode of psychosis: A longitudinal 5-year follow-up study

END OF TERM PROJECT

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1. ABSTRACT

BACKGROUND: Childhood trauma (ChT) is really common, and represents a potential risk factor for future psychotic disorders (PsD), for many other psychiatric disorders, and for suicidality. In addition, suicide is the main cause of premature death in patients with PsD, particularly in the early phases. Therefore, strong evidence connects ChT, PsD, and suicididality. Conversely, there is less evidence supporting the impact of ChT on suicidality in first episode of psychosis (FEP). Only one study reported that a history of ChT in patients with FEP further increased the risk of suicidality, but only two types of ChT were considered, and the follow-up duration was relatively short.

AIMS: To determine the effect of past ChT in patients diagnosed with FEP concerning suicidal ideations (SI) and suicidal behaviours (SB), and identify the types of ChT that further increase the risk for SI and SB in these patients.

METHODS: A cohort study will be performed including 249 patients with FEP between 16 and 40 years, 166 exposed to ChT and 83 non-exposed subjects. Candidate patients will be selected as they are admitted to the "Unitat d'Hospitalització d'Aguts" (UHA) in the Hospital Santa Caterina (HSC) in Girona. Participants will be evaluated during admission and once a year for a five-year follow-up period in order to compare suicidality between the exposed and non-exposed group. Suididality encompasses SI (thoughts and plans) and SB (suicide attempts and complete suicide).

KEYWORDS: Childhood trauma; First episode of psychosis; Suicidality

2. ABBREVIATIONS

ADHD	Attention Deficit – Hyperactivity Disorder
BDNF	Brain-Derived Neurotrophic Factor
CAS	Centre d'Atenció a les Drogodependències
ChT	Childhood Trauma
CS	Complete Suicide
CSM	Centre de Salut Mental
CTQ-SF	Childhood Trauma Questionnaire – Short Form
DUP	Duration of Untreated Psychosis
FEP	First Episode of Psychosis
HDRS	Hamilton Depression Rating Scale
HPA	Hypothalamic-Pituitary-Adrenal
HSC	Hospital Santa Caterina
IQ	Intelligence Quotient
MINI	Mini International Neuropsychiatric Interview
PANSS	Positive and Negative Syndrome Scale
PAS	Premorbid Adjustment Scale
PFC	Prefrontal Cortex
PsD	Psychotic Disorders
PTSD	Post-Traumatic Stress Disorder
SA	Suicidal Attempts
SALT-TMS	Centre de Serveis Assistencials de Llarg Tractament- Trastorns Mentals Severs
SB	Suicidal Behaviours
SI	Suicidal Ideations
UHA	Unitat d'Hospitalització d'Aguts

3. INTRODUCTION

3.1. BACKGROUND

3.1.1. CHILDHOOD TRAUMA

3.1.1.1. Definitions

Childhood trauma (ChT), generally referred to as child abuse and neglect, can be defined as all king of adversities experienced as a child (under 18 years of age) that result in actual or potential harm to the child's health, survival, development or dignity.[1]

Child abuse and neglect, also named child maltreatment, includes all forms of physical and emotional ill-treatment, sexual abuse, neglect, and exploitation. In general terms, five subtypes can be distinguished:[1–3]

- **Emotional or psychological abuse**: verbal assaults on a child's sense of worth or well-being, or any humiliating, degrading, or threatening behavior directed toward a child by an adult or an older person.
- **Physical abuse**: bodily assaults on a child by an adult or an older person that pose a risk of, or result in, injury.
- **Sexual abuse**: sexual contact or conduct between a child and an adult or an older person, including explicit coercion.
- **Emotional neglect**: failure of caretakers to provide basic psychological and emotional needs to children, including love, encouragement, belonging, and support.
- **Physical neglect**: failure to provide basic physical needs to children, such as food, shelter, clothing, safety, and health care.

Nevertheless, childhood adversities are heterogeneous, and many more types of traumatic exposures may be considered: medical illness, exposure to war, life-threatening accidents/conditions, natural disasters, family violence, death of a parent, divorce, and bullying, among others.[4–6]

3.1.1.2. Epidemiology

Adverse childhood experiences are common worldwide. Statistics suggest that about a third of the general population may be affected.[4]

International studies reveal that 25% of adults report having been physically abused as children, and approximately 20% of women and 5–10% of men report having been sexually abused as a child. Moreover, many children are subject to emotional or psychological abuse and to neglect.[7] According to a ChT study, the most common adversities were the death of a parent, physical abuse, and family violence.[6]

Every year 41,000 homicide deaths in children less than 15 years of age are estimated. Since a significant proportion of deaths due to child maltreatment are incorrectly attributed to falls, burns, drowning and other causes, this number underestimates the true scope of the problem. In addition, the broad variety of consequences of child maltreatment, including the social and occupational outcomes, can finally slow a country's economic and social development.[7]

3.1.1.3. Evaluation methods

There is a great variety of questionnaires to explore ChT: 1) questionnaires exploring for both a history of trauma and for symptoms of traumatic experiences, 2) those detecting a history of traumatic exposure alone, 3) others designed to evaluate the impact of trauma.[8]

Regarding the detection of a history of ChT, several questionnaires can be used, such as the Traumatic Life Events Questionnaire (TLEQ), the Adverse Childhood Experience (ACE) Scale, and the Childhood Trauma Questionnaire (CTQ). However, the CTQ is the most widely used and reliable screening tool to detect child abuse and neglect in adults and adolescents.[3]

Originally developed as a 70-item questionnaire, the length of the CTQ was reduced to a 28-item (25 clinical items and 3 validity items) short form (CTQ-SF) revealing very good criterion-related validity.[2] The CTQ-SF is a retrospective self-report measure of

ChT based on a 5-factor structure: emotional abuse, emotional neglect, sexual abuse, physical abuse, and physical neglect.[2,3]

According to its psychometric properties, the internal consistency of the five CTQ factors is extremely high, with the total scale achieving a Cronbach's alpha of 0.95, the construct validity is robust, and the convergent and discriminant validity is also supported. Furthermore, the CTQ exhibit good sensitivity and specificity for all forms of maltreatment. Thus, the CTQ is a sensitive and valid screening questionnaire for ChT.[8,9]

3.1.1.4. Neurobiological alterations

Child abuse and neglect causes stress. As a consequence, trauma experienced by the developing brain leads to several neurobiological alterations, and also alters the immune system.[7,10]

ChT may cause deregulation of the neuroendocrine system, with increased catecholamine and cortisol activity. As levels of cortisol rise, memory and learning are impaired, because of the action of glucocorticoids over the hippocampus and amygdala that leads to decreased hippocampal volumes.[5,10] Furthermore, ChT may result in an accelerated loss of neurons, delay or slowing of myelin formation, inhibition of neurogenesis, and inhibition of brain growth factors. There is also a relationship between traumatic experiences in childhood and a cascade of inflammatory changes in the central nervous system that persists throughout adulthood, with increased levels of interleukin-2 (IL-2), interleukin-6 (IL-6), C-reactive protein (CRP), and tumour necrosis factor (TNF). All these alterations may explain the consequences that childhood trauma can result in.[5]

3.1.1.5. Consequences

Child abuse and neglect is a global problem with serious life-long consequences affecting physical and mental health, and with negative social outcomes.[7,11]

ChT leads to different major medical disorders, including diabetes, asthma,[5] cardiovascular disease, obesity,[5,7] and cancer.[7]

After controlling for other psychosocial risk factors, traumatic experiences during childhood also increase the risk for suicidal behaviours,[5–7,11] as well as for non-suicidal self-injury, and for major psychiatric disorders[5,7,10,11] later in life: post-traumatic stress disorder (PTSD), attention deficit-hyperactivity disorder (ADHD), psychotic disorders, major depressive disorder, bipolar disorder, generalized anxiety disorder, panic disorder, borderline personality disorder, dissociative disorders, eating disorders, and substance abuse, including smoking and alcoholism. It is important to highlight PTSD since this is one of the most prevalent consequences of childhood trauma.[11]

Trauma exposure, besides being a risk factor for all of these disorders, makes depression and anxiety less likely to remit from symptoms, and causes more depressive episodes in bipolar patients, with earlier onset of the disorder.[5]

Other consequences of ChT include psychological difficulties, and alterations in emotional, behavioural, and cognitive arenas. Repeated stress exposure, as a result of trauma, leads to behavioural and emotional deregulation when facing with non-traumatic stressors later in life, with exaggerated stressful responses to later life events.[5] A range of negative occupational and social outcomes may also appear in adulthood as a result of ChT, such as higher criminality and lower educational level.[4]

As the number of child traumas increases over the individual's life, the likelihood of suicidal behaviour and psychiatric disorders becomes higher.[4–6,11]

In summary, childhood trauma is a strong risk factor for suicidal behaviour and psychiatric disorders, emphasizing psychotic disorders, later in life.

3.1.2. FIRST EPISODE OF PSYCHOSIS

3.1.2.1. Definition and diagnosis of psychotic disorders

According to the DSM-V, schizophrenia spectrum and other psychotic disorders (PsD) are defined by abnormalities in one or more of the following five areas:[12]

- **Delusions**: fixed beliefs that are not willing to change despite clear or reasonable conflicting evidence regarding its veracity. Their content includes a

variety of topics: persecutory (defined as a belief that one is going to be harmed, are the most common); referential; somatic; religious; grandiose.

- **Hallucinations**: vivid and clear perception-like experiences that occur without an external stimulus, being not under voluntary control. Auditory hallucinations, experienced as voices that are perceived as distinct from the individual's own thoughts, are the most common.
- **Disorganized thinking (speech):** formal thought disorder, typically deduced from the individual's speech. Disorganized speech may present in form of derailment (individual switching from one topic to another), tangentiality (answers to questions being obliquely or completely unrelated), or incoherence (speech being nearly incomprehensible), and must be severe enough to impair effective communication.
- **Grossly disorganized or abnormal motor behaviour (including catatonia):** manifested in a variety of ways, such as unpredictable agitation, leading to problems in performing daily-living activities. Catatonic behaviour is a pronounced decrease in reactivity to the environment.
- **Negative symptoms**: such as diminished emotional expression, avolition (decrease in motivated self-initiated purposeful activities), alogia (diminished speech output), anhedonia (decreased ability to experience pleasure from positive stimuli), and asociality (lack of interest in social interactions).

Another typical manifestation of psychosis is the lack of insight concerning the nature of these symptoms, with impaired ability to perform critical judgements of reality.[13]

PsD are heterogeneous. Thus, the term "schizophrenia spectrum and other psychotic disorders" includes a wide range of psychiatric disorders: Schizophrenia; Schizotypal (personality) disorder; Delusional disorder; Brief psychotic disorder; Schizophreniform disorder; Schizoaffective disorder; Substance/Medication-induced psychotic disorder; Psychotic disorder due to another medical condition (such as neurological disorders); Other specified schizophrenia spectrum and other psychotic disorder; and Unspecified schizophrenia spectrum and other psychotic disorder. Each PsD is diagnosed by meeting its specific DSM-V criteria.[12]

3.1.2.2. Definition and diagnosis of first episode of psychosis

The definition of first episode of psychosis (FEP) is controversial, since patients with FEP are not homogeneous in regards to psychosis inception and clinical presentation. The psychosis onset can be acute or insidious, and symptoms are heterogeneous, so patients display several combinations of delusions, hallucinations, behavioural alterations, and disorganized thinking. Nevertheless, FEP can be defined as a first lifetime episode of any psychotic illness characterized by the presence of positive psychotic symptoms, such as delusions or hallucinations.[14,15] There may be a prodromal phase characterized by alterations in mental state or behaviour, including changes in mood, thought, behaviour, perception, and global functioning, that appear before the onset of the full-blown psychotic symptoms.[13] The literature is also controversial in regard to the limits of the duration of symptomatology,[13] that may last from just a few days to several weeks or months.[16] In fact, the duration of untreated psychosis (DUP, i.e., period lasting from psychosis onset until start of adequate treatment) can be extremely long, even being between 1-2 years.[15]

The Positive and Negative Syndrome Scale (PANSS) is the most widely used measure for the assessment of symptoms in schizophrenic patients. However, some FEP studies[14,15] based on other PsD in addition to schizophrenia have used the PANSS in order to assess psychotic symptoms. According to these studies, psychosis can be defined as a score of ≥4 (moderate) on PANSS items P1, P3, P5, P6, or G9, for a variable period of time ranging between more than one week and less than 6 months.

Concerning psychometric properties, the reliability and validity of the PANSS has been proved. Firstly, the positive and negative scales show a good interrater reliability, but the reliability of the general psychopathology scale is lower. The internal consistency is relatively high, achieving a Cronbach's alpha of 0.62, 0.92, and 0.55 for the positive, negative and general psychopathology scales, respectively. Moreover, the construct validity is appropriate, and the positive and negative scales held a high criterion-related validity.[17,18]

3.1.2.3. Diagnostic outcomes and stability

Around the period of FEP, symbolising the early phases of PsD, it is often held that there is diagnostic uncertainty making difficult to establish a definitive diagnosis.[14,19] Thus, a follow-up of patients with FEP is required in order to diagnose the different illness outcomes.[14]

Regarding the different outcomes, all PsD mentioned above, as well as bipolar disorder and major depressive disorder (mood disorders with psychotic symptoms), may be all them illness outcomes.[13–15]

Concerning stability, up to 88% of first diagnoses can be sustained after a 6-month follow-up period, while the remainder initial diagnoses may change over time.[19] Thus, the majority of initial diagnoses are stable over time, with first-episode schizophrenia, schizoaffective disorder, bipolar disorder, and major depressive disorder being the most stable and having adequate positive predictive values. Conversely, other psychoses, emphasizing first-episode schizophreniform disorder and brief psychotic disorder, may be considered provisional diagnoses since some of the initial diagnoses will be exchanged for other ones after a follow-up period.[13,19]

3.1.2.4. Epidemiology

According to a FEP epidemiological study, the annual incidence of FEP (considering all psychoses with the exception of psychoses in the context of neurodegenerative diseases) is about 31.6/100,000 across the population aged ≥ 15 years. Over all psychoses, the incidence is higher in males (37.2/100,000) than in females (25.7/100,000), and the mean age at first presentation (35.9 years) is lower in males (32.0 years) than in females (41.8 years).[19]

Schizophrenia spectrum psychoses (i.e., schizophrenia, schizoaffective disorder, or schizophreniform disorder) and affective psychoses (i.e., bipolar disorder, or major depressive disorder with psychotic features) are the most commonly observed, being schizophrenia (7.0/100,000) and major depressive disorder (6.4/100,000) the two most frequent diagnostic outcomes, followed by bipolar disorder (5.2/100,000).[19] However,

it has been also reported that schizophrenia and bipolar disorder are the "core" diagnoses.[14] Regarding gender, schizophrenia spectrum psychoses show higher incidence in males, while in affective psychoses the incidence is indistinguishable between males and females.[19]

Other psychoses are less frequent, but the substance-induced psychotic disorder (in particular by cannabis) is one of the most often found within this group and is not infrequently observed.[13,19] In addition, other diagnoses (especially schizophrenia spectrum psychosis and bipolar disorder) with comorbid substance abuse (mostly cannabis and alcohol) are really usual. In fact, up to 25% (37% of males, 6% of females) of psychotic patients report prior and/or current substance abuse.[19]

3.1.2.5. Neurobiological alterations

In PsD several neurobiological alterations have been observed. The key alteration is the often found increased stress sensitivity, associated with HPA (hypothalamic-pituitary-adrenal) axis dysfunction and consequent elevated glucocorticoid (cortisol) levels.[10,11] Dopamine and cortisol levels are positively associated. Heightened cortisol activity may increase dopamine secretion in the prefrontal cortex (PFC), contributing to the positive symptomatology observed in psychotic disorders. Moreover, the increased dopaminergic activity can further elevate HPA activity and cortisol release. Elevated cortisol levels also cause neurotoxicity in some cerebral structures including hippocampal neurotoxicity, leading to bilateral hippocampal atrophy and resulting in cognitive impairments (memory and learning impairments) and negative symptoms. Furthermore, decreased GR receptors (glucocorticoid receptors) observed in the hippocampus diminish the negative feedback from the hippocampus to the HPA axis, impeding the drop of cortisol levels.

Not only dopamine activity is altered, but also other neurotransmitter systems are aberrant, including reduced functioning of glutamate and GABA neurotransmission in the PFC. In addition, increased serotoninergic activity may play a role in the development of negative symptoms and cognitive impairments. Brain-derived neurotrophic factor (BDNF) may be reduced in the dorsolateral PFC and hippocampus. Since BDNF is a protein necessary for hippocampal neurogenesis, promotes the

survival and growth of GABA and glutamate neurons, and plays an important role in dopaminergic function in the midbrain, reductions in BDNF may explain many of the neurotransmitter abnormalities found in psychotic disorders.

Finally, one possible epigenetic mechanism involved is DNA methylation, with a significant reduction in global DNA methylation observed.[10]

3.1.3. RELATIONSHIP BETWEEN CHILDHOOD TRAUMA AND PSYCHOSIS

3.1.3.1. Epidemiology

High rates of ChT are found in psychotic patients.[10] According to a recent meta-analysis, ChT has an estimated population attributable-risk for psychosis of 33%.[4] Furthermore, an epidemiological cohort of FEP patients reported that 83% of patients had been exposed to at least one stressful exposure and 34% to sexual and/or physical abuse, during their lifetime.[20] Thus, childhood traumatic experiences represent a prominent risk factor for the development of PsD, and also determine the severity of psychotic symptoms.[4,5,10,11,16]

All types of ChT may be considered to increase psychosis risk.[4] It seems probable that individuals exposed to intentional physical harm (maltreatment) as children are more likely to report psychotic symptoms than those exposed to unintentional physical harm (accidents),[11] but currently there is no evidence suggesting that any specific type of traumatic event is a stronger predictor of psychosis than any other.[4]

As the number of traumatic exposures increases over the individual's life the risk of psychosis will be higher, indicating a cumulative effect of trauma on psychosis outcomes.[4,5,11] Other variables, such as age of trauma exposure or gender, may be related to psychosis risk, but further investigation in these areas is required.[4,11] However, it has been suggested that the earlier the age of trauma exposure as children the sooner the onset of psychotic symptoms.[16]

3.1.3.2. Neurobiological pathways

Traumatic experiences during critical developmental periods, like childhood and adolescence, may lead to pathogenic stress reactions.[10,11] In addition, individuals with a genetic predisposition to psychosis show increased stress sensitivity, and exhibit much greater distress reactions in response to traumatic events in childhood. These facts suggest that such traumatic events may precipitate the onset of psychotic disorders by exacerbating already elevated stress levels.[10] Therefore, probably both genetic and environmental mechanisms play a role, in which trauma may alter gene expression through epigenetic pathways modifying stress sensitivity and thus precipitating the onset of psychosis.[10,11] However, the relationship between trauma and psychosis remains significant even when controlling for potentially confounding variables, such as genetic liability for psychosis (family history of psychosis or other psychiatric disorders) and drugs and cannabis use.[4,10]

The final result of trauma is a full stress sensitization syndrome, a "stress cascade" that leads to the neurobiological alterations commented above for PsD. In response to stress or early trauma, increased HPA axis activity and consequent elevated glucocorticoid release may occur, causing hippocampal neurotoxicity and also altering dopamine secretion. Furthermore, BDNF levels are diminished by stress, and stress may impact glutamate, GABA, and serotonin transmission, being plausible that early trauma could lead to some of the neurotransmitter system abnormalities associated with PsD.[10]

ChT is associated with the differential methylation of various promoters, being such changes in DNA methylation a possible epigenetic mechanism by which traumatic experiences can lead to the neurobiological abnormalities observed in psychotic disorders.[10] Moreover, a BDNF-Val66Met polymorphism may moderate the relationship between trauma and psychosis.[11]

Regarding psychotic symptomatology, although there is some evidence for a connection between ChT and negative and cognitive symptoms, positive symptomatology seems to be the most associated with early trauma. A positive feedback loop may be an important mechanism in the development of positive

symptoms: as glucocorticoid levels increase in response to trauma, dopaminergic activity raises, and the increased dopamine can further elevate HPA activity and cortisol release.[10]

3.1.3.3. Influence of childhood trauma over psychotic patients

Psychotic patients with a history of childhood traumatic events have a more severe clinical profile compared with those individuals without a history of trauma.[11]

Firstly, there is a significant association between elevated levels of childhood stress and greater symptom severity in psychotic patients.[10] Victims of ChT exhibit high rates of positive symptoms, particularly hallucinations, whose content may be related to patients' traumatic experiences.[10,11]

In addition, these psychotic patients are more prone to present with additional problems, similar to that of non-psychotic individuals with ChT. Thus, they exhibit higher rates of substance abuse, depression, anxiety, and more dissociative symptoms. They also experience negative perceptions of the self and low self-esteem. The prevalence of PTSD in psychotic patients is much greater than in the general population. Other additional problems found in psychotic samples with ChT are emotional instability, worse social functioning, poorer compliance with treatment, and lower remission rates.[11] Moreover, victims of sexual and physical abuse report higher levels of suicidal ideation and behaviour.[20]

3.1.4. SUICIDALITY

3.1.4.1. Definitions

Self-directed violence encompasses a variety of violent behaviours, including acts of fatal and nonfatal suicidal behaviour, and also non-suicidal intentional self-harm, such as self-mutilation, where the intention is not to kill oneself.

Suicide is the fatal event of self-directed violence, but there are many other definitions surrounding suicide. Regarding the spectrum of "suicidality", several terms must be distinguished: suicidal behaviour, suicidal ideations, and death wish.

Suicidal behaviour (SB) encompasses fatal and nonfatal components, through three important definitions:

- **Complete suicide (CS)** is defined as all those self-injurious acts that result in loss of life and are associated with at least some intent to die as a result of the behaviour.
- **Suicide attempts (SA)** are defined as potentially self-directed harmful actions that are associated with at least some intent to die as a result of the behaviour. It is worth mentioning that suicide attempts may or may not result in actual injury.
- **Preparatory actions** toward imminent suicidal behaviour are those acts that are taken in order to injure one-self, but are stopped by self or others from starting the self-injurious behaviour before the potential for harm has begun.

SB does not include the term "**death wish**", which is often defined as an affirmative response to a question similar to "do you ever wish to go to sleep and not wake up?" or "have you ever felt like life is not worth living?". Although "death wish" is present, it is probably necessary but not sufficient for SI and SB.

Suicidal ideations (SI) are thoughts (passive ideations) about the desire to die or active thoughts (planning) about killing one-self, not accompanied by preparatory actions. A passive ideation may be a thought like "The world would be better if I weren't here" or "I wish that I was dead". An active thought may be for instance "I'm thinking about ways to end my life".[(5)]

3.1.4.2. Epidemiology

Suicide is a global health problem. An estimated 804,000 suicide deaths happened worldwide in 2012, representing an annual global age-standardized incidence rate of 11.4 per 100,000 population, in accordance with the most recent information available from the 2014 WHO report "Preventing Suicide: A Global Imperative".[(21)] In addition, suicide accounts for approximately 1% of all deaths.[(22)] When interpreting this data, it is important to keep in mind that any suicide rate can be underestimated. For instance,

since intentional self-harm is typically not attributed to young children, suicide rates generally exclude individuals aged <10-15 years.[5]

Concerning suicide rates, these are subject to an important variation by age, gender, race/ethnicity, and geographic region.[5,21] Suicide rates increase with age.[22] In fact, the highest suicide rates throughout European nations are reported among people aged >65 years, and also between 45–59 years.[5] Moreover, suicide represents 17.6% of all deaths among young adults aged 15-29 in high-income countries. Following road traffic accidents, suicide is ranked the second leading cause of death globally and in Europe among this age group.[21] Globally, suicide rates are disproportionately higher in high-income countries than in low- and middle-income countries, with the highest suicide rates reported in European nations.[5] For all age groups and across almost all nations, suicide is much more common in males, considering that 3.5-4 males commit suicide for every female.[5,15,21,22] Considering ethnicity, suicide rates are two times higher among whites than non-whites.[5] It has been also reported that Protestants commit more suicides than Catholics or Jews, and higher suicide rates are found among unemployed, single, divorced, or widowed people.[22]

Regarding the prevalence of SI and nonfatal SB, there is also a marked variation by age, ethnicity, gender, and other demographic and social characteristics across and within nations. According to the World Mental Health Surveys, the general lifetime prevalence of suicidal ideation, plans, and attempts is 9.2%, 3.1%, and 2.7%, respectively,[5] being higher in young population.[5,22] As opposed to CS (which is more frequent among men), women attempt suicide more often than men.[15,22] Finally, 60% of transitions from ideation to plan and attempt are expected to occur within the first year after ideation onset in both adults and children.[5]

3.1.4.3. Risk factors

Suicide is the final consequence of a combination and interaction of a variety of genetic, psychological, biological, societal, cultural and environmental factors.[5,23] Generally, the most common risk factors for CS identified in the literature are:[5]

- History of or current mental disorders, particularly clinical depression, schizophrenia, and bipolar disorder
- History of or current alcohol and substance abuse
- Economic adversities/downturns and unemployment
- Easy access to lethal methods (e.g., access to firearms)
- Family history of suicide or violence, including physical or sexual abuse
- Marital difficulties (divorce) or Major loss (relational, social, work, or financial)
- Previous SA(s)
- Feelings of hopelessness, and fearlessness about death
- Impulsive or aggressive tendencies
- Cultural and religious beliefs (e.g., suicide is resolution of a personal dilemma)
- Exposure to SB of other people, including from media
- Lack of social support and isolation, a feeling of being cut off from others
- Barriers to access mental health care
- Deteriorating physical health and chronic medical conditions (e.g., chronic pain)
- Unwillingness to search for help owing to the stigma attached to mental health and substance abuse disorders or to suicidal thoughts
- Bullying (more recently identified)

90% of suicides can be due to mental illness in high-income countries, being depression the most frequently identified risk factor, and 22% of all suicides are attributed to alcohol use.[5,21] According to a recent review, the strongest predictors for CS may be older age and prior SA or SI.[22]

The most common risk factors for SI and nonfatal SB cited in the literature are: (many of them are also associated with CS)[5]

- Major depressive disorder
- Schizophrenia
- PTSD
- Disruptive behaviour disorders
- Some forms of dementia
- Benzodiazepine and/or antidepressant use

Depression (particularly severe depression), the same as in CS, is the strongest risk factor for SI and SB. In other psychiatric disorders, such as schizophrenia, the risk is further increased if comorbidities such as depression are present. Furthermore, there is evidence supporting that a previous SA is the strongest predictor for repeating this action later in life.[5,22]

3.1.4.4. Protective factors

Protective factors are associated with lower risk of suicidal behaviours. The most important are:[5]

- Effective clinical care for mental, physical, and substance abuse disorders
- Easy access to clinical interventions
- Family and community support for help seeking and continuing medical and mental health care relationships
- Skills in problem solving, and nonviolent ways of dealing with arguments
- Cultural/religious beliefs discouraging suicide and supporting survival instincts

3.1.4.5. Evaluation methods

Several methods can be applied in order to evaluate suicidality, such as the Brief Psychiatric Rating Scale (BPRS), the Clinical Global Impression for Severity of Suicidality (CGI-SS), the Suicide Intent Scale (SIS), and the Scale for Suicide Ideation (SSI). Another useful instrument is the M.I.N.I. International Neuropsychiatric Interview (M.I.N.I. 6.0), which is the most widely employed psychiatric structured diagnostic interview instrument worldwide. The M.I.N.I. is a short diagnostic structured interview for DSM-IV and ICD-10 psychiatric disorders, containing sixteen different sections, and being one of these specifically to evaluate suicidal risk (section C). Kappa coefficient, sensitivity and specificity are substantial for most diagnoses, and inter-rater and test-retest reliability are also good.[24,25]

3.1.4.6. Neurobiological alterations

The complete neurobiological bases of suicide are not well understood yet, although some cerebral alterations have been identified so far.

Firstly, alterations in the serotonin (5-HT) neurotransmitter system in the brainstem or serotoninergic targets in the forebrain are present in suicidal individuals, being suicide linked to serotonin deficits.[5,26,27] 5-HT is synthetized by neurons set inside the midline raphe nuclei in the brain stem with widespread targets topographically organized.[27] Reduced serotoninergic input represents a crucial element in the vulnerability to SB. Findings of reduced 5-hydroxyindoleacetic acid (5-HIAA), the major serotonin metabolite, in cerebral spinal fluid (CSF) in suicide attempters, independently of other previous psychiatric diagnosis, supports evidence for the involvement of serotonin in suicide.[5,26,27] Polymorphisms of tryptophan hydroxylase (enzyme that modifies the biosynthesis of serotonin) gene contribute to the decrease of serotonergic activity.[26,27] Furthermore, post–mortem studies of suicide victims suggest a role of the two serotoninergic receptor subtypes located in the ventromedial PFC in suicide, revealing decreased density of the 5–HT_{1A} presynaptic receptor, and a compensatory up-regulation of the 5–HT_{2A} postsynaptic receptor in this cortical area.[26,27]

SB is also linked to the response to stress. Chronic stress leads to HPA axis hyperactivity, elevated cortisol release, and increased CSF content of corticotrophin–releasing hormone.[5,26] Moreover, chronic stress may be associated with reduced neurotrophin expression, leading to structural abnormalities in PFC and hippocampus and reduced hippocampal plasticity. The reduction of both neurotrophins and BDNF trkB–receptor (tyrosine kinase receptor B) mRNA in these areas may play a role in SB. In addition, decreased PFC activity, observed in positron emission tomographic studies, and impaired serotoninergic response are associated with high impulsivity and higher preparation and lethality of SA.[5,26]

Other structural abnormalities involve amygdala, whose function is critical regarding some behavioural patterns related to suicidality, including fear, anxiety, aggression and the recognition and response to danger. Therefore, amygdaline alterations may also increase the risk of SB.[26]

Lastly, the lateral septal nucleus activity is involved in the hedonic process, being this structure associated with anhedonia and hopelessness if altered. Anhedonia, hopelessness and other depressive symptoms are strongly related to SI.[26]

All these cerebral structures, involved in the integration of hedonic processes, emotional memory, impulsivity and decision–taking, may precipitate in suicide when abnormally working. In summary, the vulnerability to SB is associated with the specific PFC serotoninergic abnormalities and the consequent alteration of all the PFC-dependent cognitive tasks. Thus, the result may be a reduced ability to make decisions when facing stressful events and negative emotional contexts, leading to the selection of a wrong decision and lastly ending in SB.

3.1.5. SUICIDALITY IN CHILDHOOD TRAUMA

There is consistent evidence showing a significant association between childhood adversities and elevated risk of suicidality in adulthood. ChT is an independent risk factor for SI and SB later in life.[5,6]

Neurobiological alterations commented above for ChT, including stress-related responses (involving HPA axis and neurotrophins), elevated levels of inflammation in the central nervous system, and increased levels of IL-6, may be associated with SB.[5,10]

According to studies based on suicidality in ChT, lifetime prevalence of SA and SI in affected children is 2.7% and 9.4%, respectively. Among those individuals that have been attempters, 29.3% report physical abuse, 24.8% report family violence, and 14.5% report sexual abuse as children. All adversities are significantly associated with suicidality, although physical and sexual abuse may be the strongest risk factors for both onset and persistence of suicidality. Concerning the onset of SB across the lifespan, adversities are more predictive of SB in adolescence and early adulthood.[6] Another important aspect is the strong dose-response relationship reported between the number of traumas and suicidal outcomes, meaning that the greater the number of adversities as children the higher the suicidal risk.[5,6]

In addition, it is worth mentioning that not only ChT is a risk contributor for SB, but also most of the psychiatric disorders that trauma exposure can lead to. Therefore, depression, bipolar disorder, PsD including schizophrenia, PTSD, anxiety, substance

abuse, and ADHD, are further independent risk factors associated with SB in this population.[5]

ADHD is associated with impulsive decision making and this way increases suicidal risk.[28] In fact, impulsivity is robustly associated with early trauma exposure and suicides characterized by impulsivity are more likely in patients with ChT.[5]

3.1.6. SUICIDALITY IN FIRST EPISODE OF PSYCHOSIS

There is strong evidence connecting PsD with high suicide rates.[14,15,23,28] Neurobiological alterations explained above for both psychosis and suicide support the connection between them, emphasizing elevated levels of stress and the consequent alteration in neurotrophins expression and structural abnormalities in PFC.[5,10,26]

Suicide represents 2-5% of deaths in FEP patients,[23] being the main cause of premature death among psychotic samples and an important health concern.[14,23] Furthermore, between 20% and 40% of patients with PsD will attempt suicide during their lifetime.[14]

Although the risk of suicidality is high during all of lifetime, rates of SB decrease throughout psychotic patients' lifetime. The risk is particularly elevated during the early phases of PsD, with the highest rates of suicidality reported before or shortly after first admission to treatment (especially during the period of untreated psychosis).[14,15,23] Therefore, the risk is especially elevated during the first year of follow-up, decreases dramatically after 1 year, and then seems to increase again after 2 years. Moreover, suicidal risk may remain for at least 7 years or longer following psychosis onset. According to prospective FEP studies based on adult samples, SA rates range between 10% and 28% prior to first treatment for psychosis, up to 11.3% during the first 2 years following the establishment of treatment, and up to 18%-20% when considering longer follow-up periods of 4, 5 or even 7 years.[14] Of those individuals who attempt suicide, more than half are reported to make the attempts during the period of untreated psychosis.[15]

It has been suggested that the younger the age of psychosis onset the higher the rates of lifetime suicidality. Thus, in early-onset FEP up to 12.4% of patients attempt suicide during the first 2-year period, showing greater rates of suicidality than in adult-onset psychoses.[14,15,23,28]

Concerning gender, women are more likely to repeat SA and to use less harmful methods. Conversely, men are more likely to successfully complete a suicide since they use more lethal methods. In addition, males of higher socioeconomic levels are more prone to commit self-harmful behaviours during FEP.[28]

Suicidal risk is considered not to vary according to whether the diagnostic outcome is schizophrenia or affective spectrum psychosis.[14]

The most robust risk factors for SA are history of previous SI or SB and severity of depressive symptoms, as well as being the strongest predictors at presentation for future SA both in early- and adult-onset psychosis.[14] In fact, depressive symptoms are one of the most common comorbidities in suicidal psychotic patients.[28]

Other important risk factors are alcohol and drug abuse, greater insight, positive psychotic symptoms, a greater number of admissions, family history of suicide, and longer DUP, highlighting this last factor as one of the most mentioned by the literature[14,15,23] and associated with more violent SA.[28]

Finally, we emphasize child's sexual and physical abuse as an important risk factor for attempting suicide in FEP patients.[20]

3.1.7. IMPACT OF CHILDHOOD TRAUMA ON SUICIDALITY IN FIRST EPISODE OF PSYCHOSIS

ChT has several negative outcomes later in life, emphasizing PsD and suicidality. Despite the important connection between these 3 variables, currently there is a shortage of studies focused on the impact of ChT on suicidality in FEP patients. Therefore, more research is required in this area.

Only a 18-month follow-up study in FEP [(20)] found that first-episode patients with past sexual and/or physical abuse were more likely to make SA during treatment, and also more prone to have experienced past SA and other psychiatric disorders (particularly PTSD and substance use disorder) before psychosis onset. Other findings in this population were poorer functional levels before the onset of psychosis and less compliance to treatment. Moreover, elevated prevalence of ChT was reported among psychotic patients, with 34% exposed to sexual and/or physical abuse and 83% to any stressful event.

3.2. STUDY JUSTIFICATION

Currently exists a highly demonstrated association between ChT and psychosis,[4,10,11] between ChT and suicidality,[5,6] and also between FEP and suicidality.[14,15,23,28] Conversely, there is less evidence supporting the impact of ChT on suicidality in FEP. Since both ChT and FEP are strongly associated with suicidality, the interaction of trauma and psychosis can further increase the risk for SB, as reported in the already commented 18-month follow-up study in FEP (Relative risk (RR) = 2.4).[20] This study focused on outcomes of just 2 types of ChT (i.e., sexual and physical abuse) in FEP, while impact of other child adversities (such as neglect) was not analysed. In addition, the duration of the follow-up in this study was relatively short, and it is likely that the impact of ChT on suicidality may manifest later in time. In fact, evidence suggests that in psychoses the suicidal risk may remain elevated at least for 7 years following psychosis onset.[14] Thus, longer follow-up periods in FEP are required in order to better analyse the impact of ChT concerning suicidality. Furthermore, FEP-based studies often include neither all the spectrum of psychoses nor the early-onset psychoses.

Our longitudinal 5-year follow-up study will include all first-admission psychotic episodes (with the exception of psychoses in the context of neurodegenerative diseases, severe head injury or brain damage, and mental retardation) in patients aged 16-40 years in Girona, so both early- and adult-onset psychoses will be considered having in mind that psychotic symptoms can appear at earlier age if past ChT. Several types of trauma exposure, including all forms of both child abuse and neglect, will be considered. Moreover, all the spectrum of suicidality will be evaluated, from SI to nonfatal and fatal SB.

Therefore, our study will provide new evidence in this area, as current studies concerning this matter didn't consider many types of ChT and their follow-up period was shorter, and will contribute to increase the insight into this issue. The study also will have a great clinical impact, paving the way for the implementation of future strategies into the daily clinical practice concerning both the detection and treatment of traumatic events among psychotic patients, and consequently decreasing suicidality, which is so frequently observed in these patients.

4. HYPOTHESIS

4.1. PRIMARY HYPOTHESIS

A history of ChT in patients diagnosed with FEP will increase by two times the risk for SI and SB (RR=2), comparing with those psychotic patients with no exposure to trauma as children.

4.2. SECONDARY HYPOTHESIS

Not all of child adversities will increase the risk for SI and SB in the same proportion. Depending on the type of ChT, the obtained RR will be different.

5. OBJECTIVES

5.1. PRIMARY OBJECTIVE

The main aim of the study is to determine the effect of past ChT in patients diagnosed with FEP concerning SI and SB.

5.2. SECONDARY OBJECTIVE

To identify which traumas are the most strongly associated with increased suicidal risk, i.e., the types of ChT that further increase the risk for SI and SB in patients diagnosed with FEP.

6. METHODOLOGY

6.1. STUDY DESIGN

This study will be a prospective cohort, a 5-year follow-up study.

6.2. STUDY POPULATION

The target population of the study will be patients diagnosed with FEP.

6.2.1. Inclusion criteria

- **FEP**: first lifetime episode of any PsD (also including affective psychoses) defined as the presence of psychotic symptoms (i.e., delusions, hallucinations, disorganized thinking, disorganised or abnormal motor behaviour, or negative symptoms), mainly delusions or hallucinations, according to the DSM-V criteria for PsD.[(12)]
- Patients aged **16-40 years**

6.2.2. Exclusion criteria

- Psychosis in the context of a previous diagnosis of neurodegenerative disease
- History of severe head injury or brain damage
- Low intelligence quotient (IQ): mental retardation

6.3. SAMPLING

6.3.1. Sample selection

The sampling method used will be conveniently consecutive non-probabilistic. This sampling consists on selecting patients diagnosed with FEP, who meet the inclusion and exclusion criteria, as they are admitted to the "Unitat d'hospitalització d'Aguts" (UHA) in the Hospital Santa Caterina (HSC) in Girona.

The candidate psychotic patients, once stabilized, will be informed about the study and invited to participate voluntarily by the signature of the informed consent (**Annex 1**). In the case of subjects aged 16 and 17 years, the consent will have to be given by their parents or legal tutor, also once patients are stabilized, since their opinion must be considered anyway.

6.3.2. Sample size

GRANMO application will be used to calculate the sample size of the study. We assume that the event rate in exposed is 0.2, since up to 20% of psychotic patients attempt suicide during the first 4-7 years following psychosis onset. According to dropout rates reported in some FEP-follow-up studies, we consider an anticipated dropout rate in this study of 20%. The minimum expected relative risk is 2, and the non-exposed/exposed ratio is 0.5.

Accepting an alpha risk of 0.05 and a beta risk of 0.20 in a two-sided test, 166 exposed to ChT and 83 non-exposed subjects are necessary to recognize as statistically significant a RR greater than or equal to 2 for SI or SB in FEP patients with past ChT comparing with non-exposed psychotic patients.

6.4. VARIABLES

6.4.1. Independent variable

The independent variable is the history of ChT (particularly physical neglect, emotional neglect, physical abuse, emotional abuse, and sexual abuse), that will be measured with the CTQ – SF.

6.4.2. Dependent variables

Dependent variables include all the spectrum of suicidality: SI (passive thoughts or plans), nonfatal SB (SA), and fatal SB (CS). CS will be identified by the death certificate. SI and SB will be evaluated by the section C of the MINI, as well as by the item 3 of the Hamilton Depression Rating Scale (HDRS).

6.4.3. Covariates

- *Age at psychosis onset*: measured in years
- *Gender*: male/female
- *Education/schooling*: measured with the PAS (Premorbid Adjustment Scale).
- *Labour situation*: student; unemployed; employed; pensioner; work absence for illness.

- *Family history (first/second degree) of psychoses, bipolar disorder, depression, or CS*: evaluated by interviewing patient or relatives.
- *Premorbid functioning* (up to 1 year before FEP onset): measured with the PAS.
- *DUP* (i.e., period lasting from psychosis onset until start of adequate treatment): measured in days.
- *Compliance to treatment:* yes/no
- *SB prior to FEP onset*: evaluated by the MINI (section C).
- *History of/current substance and/or alcohol misuse (abuse and dependence):* evaluated by the MINI (sections J and K).
- *History of/current depression, bipolar disorder, PTSD, ADHD, anxiety:* diagnosed by meeting the DSM-V criteria (bipolar disorder and ADHD), applying the section I of the MINI (PTSD), or using the HDRS (depression and anxiety).

6.5. MEASURE INSTRUMENTS

1) ***ChT***: the history of ChT will be assessed using the 28-item CTQ-SF (**Annex 2**), a retrospective self-report measure suitable for individuals ≥ 12 years validated in Spanish language. The Spanish CTQ-SF shows adequate psychometric properties and a favourable fit of the 5-factor structure, providing support for the reliability and validity of the Spanish version.[29] This questionnaire contains 25 clinical items, distributed in five clinical subscales about: physical neglect, emotional neglect, physical abuse, emotional abuse, and sexual abuse. Thus, five items are included in each subscale. The CTQ-SF also contains a three-item Minimization/Denial validity subscale, developed specifically to detect socially desirable responses and underreporting of maltreatment (attempts by individuals to minimize their childhood abuse experiences). In each item, a 5-point frequency of occurrence is used: 1-never true, 2-rarely true, 3-sometimes true, 4-often true, and 5-very often true. Therefore, each clinical subscale score ranges from 5 (no history of abuse or neglect) to 25 (very extreme history of

abuse and neglect).[2,3] According to CTQ manual's cut-off scores for the severity of child abuse and neglect, the total scores are classified in: "none to minimal", "low to moderate", "moderate to severe", and "severe to extreme".[3]

2) ***FEP***: the diagnosis of FEP will be made according to the DSM-V criteria (presence of psychotic symptoms). The PANSS (**Annex 3**) will be applied by a clinician (when the psychotic patient is more stable) in order to assess the severity of psychotic symptoms. The PANSS evaluates 30 different symptoms distributed among three scales: a positive scale (7 items); a negative scale (7 items); and a general psychopathology scale (16 items). In each of the thirty items a 7-point score is used, ranging from 1 (absence of the symptom) to 7 (symptom is extremely severe). Thus, the minimum total score is 30 (meaning that none of the items is present) and the maximum is 210 (all of items in extreme presentation), although scores are often given separately for each scale.[18] In FEP, the most noteworthy items are P1 (delusions), P3 (hallucinations), P5 (grandiosity), P6 (suspiciousness), G9 (unusual thought content), and G12 (lack of insight), with a score of ≥4 (moderate) in any of them.[14,15]

3) ***Suicidality***: will be evaluated by several ways. The cases of CS will be identified by the death certificate. In this document, all the deaths given an underlying cause of intentional self-harm or an injury/poisoning of undetermined intent will be considered a suicide.[5] SI and SB will be evaluated by both the section C of the MINI (**Annex 4**) and the item 3 of the HDRS (**Annex 5**).

   The MINI has been validated in Spanish, and reliability and validity of this instrument for children and adolescents (MINI-KID) have been proved.[24,25] In the MINI section C, suicidal ideation, plans, and attempts are investigated through 6 different questions, whose answer is yes/no. Each affirmative response to a question is given a different score. By summing each positive-response score a low, moderate, or high suicidal risk is obtained.[25]

   The item 3 (suicide) of the HDRS is scored as follows: 0- absent; 1- feels life is not worth living; 2- whishes about being death; 3- suicidal ideations; 4- suicidal attempts.

4) ***Depression and anxiety***: both will be measured with the HDRS (**Annex 5**), a 17-item scale developed to assess the severity of depression, validated in Spanish language, with well-reported validity and reliability. Each item includes 3 or 5 responses, whose score ranges from 0 to 2 or from 0 to 4, respectively. Thus, the total score ranges between 0 and 52 points: 0-6 (no depression); 7-17 (mild depression); 18-24 (moderate depression); 25-52 (severe depression).[30] In addition, two of the HDRS items evaluate anxiety: psychic anxiety (item 10) and somatic anxiety (item 11). As explained above, one item contemplates suicide as well.

5) ***Bipolar disorder, PTSD, and ADHD***: diagnoses of bipolar disorder and ADHD will be made by meeting the DSM-V criteria for bipolar disorder and ADHD, respectively.[12] PTSD will be diagnosed by using the MINI section I (**Annex 4**). In this section, several questions (distributed in 5 subsections: I1, I2, I3, I4, I5) must be answered (yes/no). Not all of questions must be responded initially, but a specific number of positive responses in each subsection are required in order to be able to answer the following subsection questions. If in the final I5 question a "yes" response is obtained, the diagnosis of current PTSD is made.

6) ***Alcohol and substance misuse (abuse and dependence)***: will be detected as well by the MINI (sections J and K). The section J assesses alcohol dependence and abuse, and the section K substance dependence and abuse (**Annex 4**). To respond the several questions include in each section the same method explained above for the section I is applied. This means that, if a diagnosis of alcohol of substance dependence is made, the following questions to evaluate abuse are not required.

7) ***Premorbid functioning***: will be measured with the PAS (**Annex 6**), a scale indicated to evaluate the lifetime functioning up to one year before FEP onset. In the PAS, four lifetime periods are distinguished: Childhood (up through age 11); Early adolescence (ages 12-15); Late adolescence (ages 16-18); and Adulthood (Age 19 and above). Thus, for instance, if FEP onset is when the patient is 16 years, all lifetime periods until 15 years (one year before) must be evaluated, childhood and early adolescence in this case. The PAS evaluates five

areas (five scales) concerning functioning: sociability and withdrawal, peer relationships, scholastic performance, adaptation to school, and social-sexual aspects of life, this last one from early adolescence on. Moreover, includes a section with general questions regarding quality of life (for all age groups): Education; Employment for pay or functioning in school during a period of 3 years up to 6 months before first hospitalization or onset of first episode; Change in work or school performance within a period of a year up to 6 months before first hospitalization or first episode; Frequency of job change, if working, or interruption of school attendance during a period of 3 years up to 6 months before first hospitalization or first episode; Establishment of Independence; Global assessment of highest level of functioning achieved in patient's life; Social-personal adjustment; Degree of interest in life; Energy level. The PAS measures the maximum functioning or adjustment in each of the five areas. Each area score ranges from 0 (maximum level of functioning) to 6 (worst level) points. An overall score for the whole scale is obtained by averaging the five scales scores. The lower the global score the better the patient's premorbid functioning. The scale is also available in Spanish language.[31,32]

6.6. DATA COLLECTION AND VISITS CHRONOGRAM

Visits that will be performed and data that will be collected at each time during the study are specified in the following Visits Chronogram, which will be applied to each participant:

DATA COLLECTION AND VISITS CHRONOGRAM						
Data collection	**Baseline**	**First year**	**Second year**	**Third year**	**Fourth year**	**Fifth year**
• Informed consent	X					
• Demographic features: Age, gender	X					
• Education level	X					
• Labour situation	X					
• Complete patient's clinical history	X					
• IQ	X					
• Diagnosis of FEP	X					
• Diagnostic outcome	X[1]	X[2]				
• DUP	X					
• **History of ChT**	X	X	X	X	X	X
• Family history (first/second degree) of psychoses, bipolar disorder, depression, or completed suicide	X					
• Premorbid functioning	X					
• Suicidal behaviour prior to FEP onset	X					
• History of substance and/or alcohol misuse	X					
• Current substance and/or alcohol misuse	X	X	X	X	X	X
• History of depression	X					
• Current depression	X	X	X	X	X	X
• Bipolar disorder	X	X				
• History of PTSD	X					
• Current PTSD	X	X	X	X	X	X
• History of anxiety	X					
• Current anxiety	X	X	X	X	X	X
• History of ADHD	X					
• Current ADHD	X	X	X	X	X	X
• Compliance to treatment		X	X	X	X	X
• **Suicidality: SI, SA, CS**	X	X	X	X	X	X
Number of visits	indeterminate	1	1	1	1	1
Centre where the visits will be performed	UHA Hospital Sta. Caterina	*	*	*	*	*

[1] *Provisional diagnosis (because of the difficulty of establishing a definitive diagnosis in the early phases)*

[2] *Definitive diagnosis*

**Depending on the patient: Centre de Salut Mental (CSM), Centre d'Atenció a les Drogodependències (CAS), Centre de Serveis Assistencials de Llarg Tractament- Trastorns Mentals Severs (SALT-TMS).*

Data obtained from participants at baseline and during the following visits will be registered in the Case Report Form (**Annex 7**), and according to this form data will be reported in the study database.

The first evaluation of participants will be while they are admitted to the UHA in the HSC. In this first exhaustive evaluation, demographic and clinical data will be obtained, with a complete patient's clinical history including the investigation of neurodegenerative diseases and brain damage, and measure of the IQ in order to ensure appropriately inclusion and exclusion criteria. Collected data at baseline is specified in the Visits Chronogram. The number of visits required at baseline is indeterminate, as it will depend on the psychotic patient. Information will be obtained by asking both the patient and relatives, in order to increase the reliability of collected data.

Later on, one visit per year will be performed, using as much as possible one of the visits that patients will have scheduled in their respective centres. The centre will be different depending on the patient. For instance, if the diagnostic outcome is a substance-induced psychotic disorder the following visits may be in the CAS, and if the patient suffers from a severe mental disorder probably visits will be in the TMS. The Visits Chronogram specifies which data will be collected during the follow-up period. As opposed to the history of psychiatric disorders that will be assessed only at baseline, the history of ChT will be evaluated during the whole study duration, because of the secrecy that often surrounds this issue and the difficulty to talk about that. Thus, as the familiarity between patient and interviewer increases throughout the follow-up, detecting ChT will be easier.

7. STATISTICAL ANALYSIS

Statistical analysis will be performed using Statistical Package for Social Sciences (SPSS) for *Windows®*.

7.1. DESCRIPTIVE - UNIVARIATE

ChT will be statistically considered a categorical variable (history/no history of ChT, and types of ChT experienced: physical abuse or neglect, emotional abuse or neglect, or sexual abuse). SI (including plans), SA, and CS will be treated as binary categorical variables (yes/no). In the same way, most covariates will be considered as categorical, with the exception of age, DUP, and all questionnaires/scales scores, which are quantitative variables. Categorical variables will be expressed as relative frequencies and percentages. Quantitative variables will be described by mean ± standard deviation (when normal distribution) or median and interquartile range (if variables without normal distribution).

7.2. BIVARIATE

Comparisons of variables between exposed and non-exposed group will be carried out using Student-t test or Mann-Whitney test (for quantitative variables) and Chi-square test or Fisher exact test (for categorical variables). Both comparisons of suicidality between exposed and non-exposed to ChT (primary objective) and comparisons of suicidality concerning exposure to the different types of ChT (secondary objective) will be performed using Chi-square test.

7.3. MULTIVARIATE

Three Cox proportional hazards regression models at the subject level will be fitted to quantify the multivariate-adjusted risk of CS risk, the SI risk, and the SA risk between the exposed and non-exposed group. The models will include the variables of age, gender, education, labour situation, family history of suicide or psychiatric disorders, personal history of/current psychiatric disorders (depression, anxiety, bipolar disorder, PTSD, ADHD) and alcohol and substance misuse, SB prior to FEP onset, DUP,

compliance to treatment, and premorbid functioning as independent variables. The validity of the proportionality assumption for each predictor variable will be graphically verified. Results will be expressed as absolute numbers and percentages, means, standard deviations, hazard ratios, and 95% confidence intervals (95% CI). Statistical tests will be considered to be significant for a two-tailed p-value <0.05.

8. ETHICAL CONSIDERATIONS

This project will be evaluated and approved by the CEIC (Comitè d'Ètica d'Investigació Clínica) Institut d'Assistència Sanitària de Girona.

This study will be conducted in accordance to the human rights and to the ethical tenets defined on the World Medical Association Declaration of Helsinki of "Ethical Principles for Medical Research Involving Human Subjects" of 2013.

Before being included, all participants will be informed appropriately about the study and given the information sheet. Subjects will be invited to participate voluntarily by the signature of the informed consent. In the case of subjects aged 16 and 17 years, the informed consent will be given to their parents or legal tutor, but patient's opinion will be considered anyway.

The access to all the obtained information will be warranted and confidentiality regulation will be respected. Confidentiality of participants' personal data will be in accordance to "Ley Orgánica 15/1999, de 13 de diciembre, de Protección de Datos de Carácter Personal". Personal data will be able to be object of automatic treatment. Participants of the study have the right to access, modify, oppose or remove their personal data contained in the file at any time.

9. STUDY LIMITATIONS

The first limitations that may be considered are the typical of a cohort study, including the long duration of the study (a five-year follow-up period) and the possible loss of participants during the follow-up. Although the duration of the study is relatively long, this is necessary in order to evaluate suicidality in a more reliable way, since suicidality rates may remain high for several years following psychosis onset. In addition, the prospective assessment concerning suicidality is more reliable than if data were obtained retrospectively.

Another limitation of the study may be the lack of reliability concerning psychotic patients, with some uncertainty as to whether what patients report about ChT can be trusted. However, the reliability of psychotic patients' maltreatment reports has repeatedly been recognised.

A third limitation can be the secrecy that often surrounds childhood traumatic experiences, which may lead to reject ChT in our psychotic-patient sample when actually present. In spite of that, the repetitive assessment of trauma over the entire duration of our study allows to forge a trusting relationship between the patient and the interviewer, providing a bigger chance for patients to talk about this difficult issue than during a single interview. In the same way, the retrospective assessment of ChT also may lead to reject childhood adversities when present, so data could be affected by memory bias if patients don't remember their traumatic events as children.

Finally, it is likely that our FEP sample is not representative enough, since it is an inpatient-based sample, without including outpatients. Focusing on inpatients may lead to the potential bias of selecting individuals suffering from more severe forms of FEP. In favour of this study, and as opposed to most of the FEP studies which are usually restricted to a few diagnostic categories (usually schizophrenia), we include almost all diagnostic categories associated with psychosis, increasing the representativeness of our sample.

10. CLINICAL AND HEALTHCARE IMPACT

This study will provide new evidence and a better insight into the impact of ChT on suicidality in FEP patients and which types of ChT further increase the risk of suicidality among this population. Since such traumatic events are quite common in patients with psychosis, clinicians should be aware of their importance and explore their presence in FEP patients.

Therefore, from results obtained in this study, new strategies in order to detect ChT among FEP patients can be implemented into the daily clinical practice. Only in that way, psychotic patients suffering from the consequences of ChT may be benefited from appropriate treatments, such as psychoeducation, stabilization, and the development of safe coping and social skills. If successful treatments are implemented in this population, rates of SI and fatal/nonfatal SB will decrease.

In summary, this study will have a great clinical impact, paving the way for future new strategies into the daily clinical practice concerning both the detection and treatment of such traumatic events among psychotic patients, and consequently decreasing suicidality, which is so frequently observed in these patients.

11. WORK PLAN AND CHRONOGRAM SCHEME

This study will be performed in 7 years and 2 months, and organized in the following phases:

1. <u>COORDINATION PHASE</u> (**6 months**) [*Principal investigator and all investigators*]:

1.1. Study setting-up: during this first period the initial idea and protocol will be designed. The principal investigator will have the functions of initiating, managing and ensuring the funding and resources for the study, and also will have to select the investigators.

1.2. Follow-up meetings: the first in person meeting will take place with all investigators in the HSC, where the principal investigator will present them the project design and execution plan, and will provide them the appropriate information to ensure that the study will be adequately conducted.

1.3. Framework establishment: the principal investigator will ensure the participation of the different centres of the province, where the follow-up period will be performed.

1.4. Final project design

1.5. Project evaluation and approval: the principal investigator will ensure the obtainment of the approval from the CEIC (Comitè d'Ètica d'Investigació Clínica) Institut d'Assistència Sanitària de Girona.

2. <u>PARTICIPANTS' INCLUSION, EVALUATION AND DATA COLLECTION PHASE</u> (**6 years**) [*Principal investigator, all investigators and collaborators*]:

2.1. Participants recruitment period: from April of 2015 to April of 2016 it will take place the inclusion of patients from the UHA, until the sample size is achieved. The principal investigator will ensure the obtainment of all participants' informed consent.

2.2. Participants evaluation period: this period will start simultaneously with participants' recruitment, but will end five years after the last participant is included in the study. Thus, the evaluation period lasts 6 years. In order to evaluate participants once a year (after the first evaluation during hospitalization), the principal investigator will have to schedule the annual visits for all patients in their respective centres, that

will coincide as much as possible with one of the visits that patients will have already programmed. Subjects' evaluation will be performed by the several investigators and collaborators, applying the same visits chronogram to all them.

2.3. Data collection and processing: data will be registered in the study database according to the Case Report Form for each participant. Data from subjects who die of suicide will be facilitated by the Department of Legal and Forensic Medicine in the "Jutjats de Girona", via the death certificate. Data collection will finish one month after ending evaluation period. All data collection procedures will be made by the psychiatrists of the UHA. The principal investigator will ensure the obtainment of death certificates of CS.

2.4. In person meetings: seven meetings in the hospital will take place, where the principal investigator will ensure the quality and homogeneity of recruiting and data collection. Moreover, the progress of the study will be discussed, and motivation and internal collaboration of all participating staff will be ensured.

3. <u>DATA STATISTICAL ANALYSIS PHASE</u> (**3 months**) [*Statistical consultant*]:

3.1. Monitoring analysis: four statistical analysis will be performed throughout the study in order to control its progress.

3.2. Final analysis: at the end of the study, when all data have been collected.

4. <u>FINAL REPORT PHASE</u> (**4 months**) [*Principal investigator and all investigators*]:

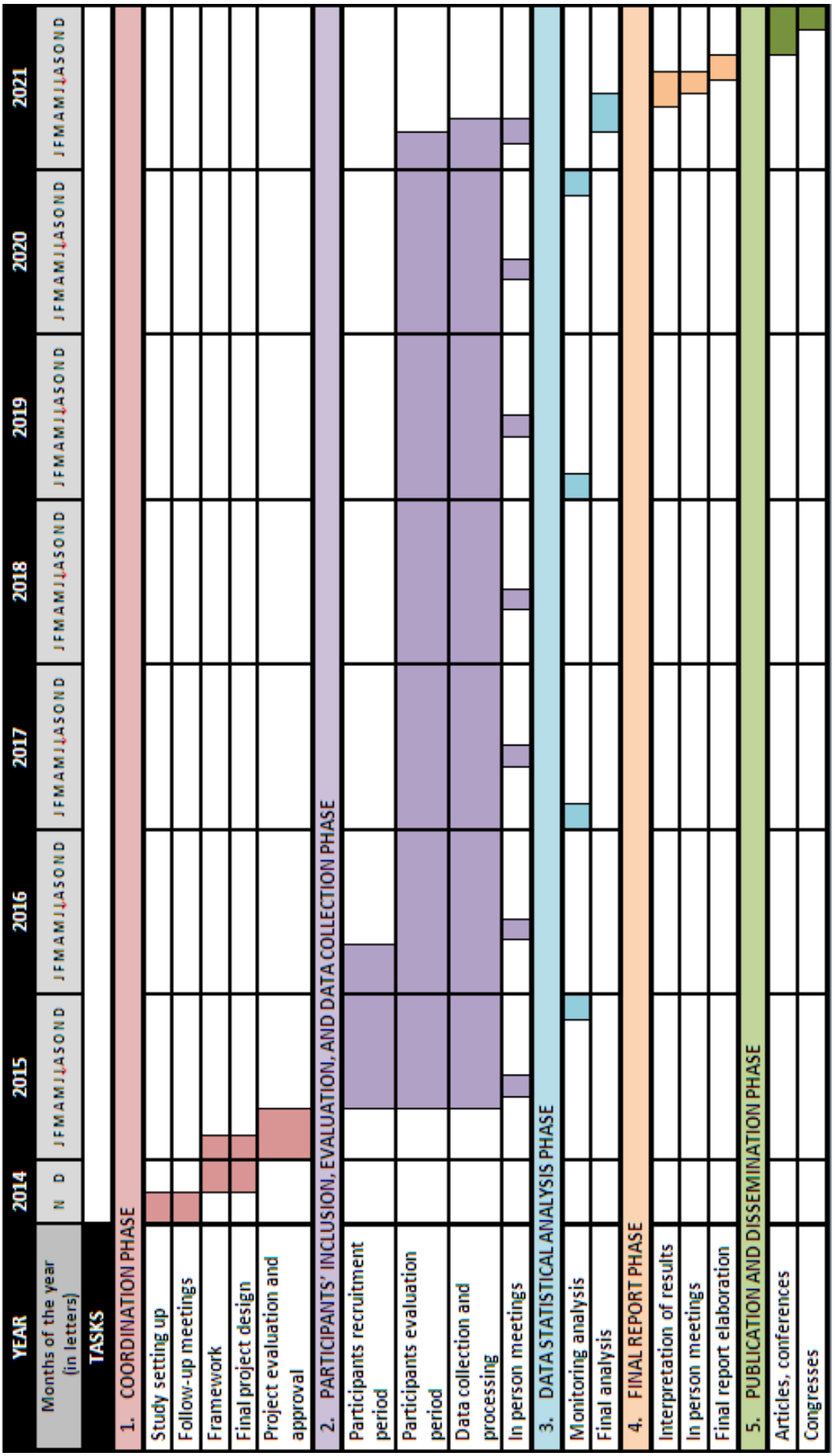
4.1. Interpretation of results: all the results will be analysed and interpreted and investigators will perform the final discussion and conclusions of the study.

4.2. In person meetings: there will be a last meeting in July of 2021 to discuss all the findings, performed as well in the HSC.

4.3. Final report elaboration

5. <u>PUBLICATION AND DISSEMINATION PHASE</u> (**4 months**) [*Principal investigator*]:

The final results of this study will be published and disseminated in journal articles, reports, or conference presentations.


YEAR
2014
2015
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2021
Months of the year (in letters)
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TASKS
1. COORDINATION PHASE
Study setting up
Follow-up meetings
Framework
Final project design
Project evaluation and approval
2. PARTICIPANTS' INCLUSION, EVALUATION, AND DATA COLLECTION PHASE
Participants recruitment period
Participants evaluation period
Data collection and processing
In person meetings
3. DATA STATISTICAL ANALYSIS PHASE
Monitoring analysis
Final analysis
4. FINAL REPORT PHASE
Interpretation of results
In person meetings
Final report elaboration
5. PUBLICATION AND DISSEMINATION PHASE
Articles, conferences
Congresses

12. FEASIBILITY

The IAS (*Institut d'Assistència Sanitària*) provides assistance for mental health and addictions to 840,000 inhabitants along the Sanitary Region of Girona. To do so, the IAS has a decentralized framework including 24 centres along the whole sanitary region. Taking into account the annual incidence of FEP across the population aged ≥ 15 years (31.6/100,000) and the estimated population in Girona province, 265 FEP patients may be available every year to participate in our study. Since our sample size is 249 patients, it means that in a 1-year period we can accomplish the whole sample.

Moreover, there is a good continuity and coordination between the different centres and levels of assistance. In this study, different centres along the province will be involved during the follow-up period (depending on the patient), so it is necessary to count on an appropriately coordinated mental health network.

On the other hand, healthcare professionals of the IAS are available to carry out this study.

Thus, our study is feasible regarding availability of the sample, of the professionals, and of a well communicated mental health network.

13. BUDGET

ITEM	COST PER UNIT	NUMBER OF UNITS	TOTAL COST
PERSONNEL COSTS			
Statistical consultant	35 €/hour	120 hours	
			x 1 person
			4,200 €
		Subtotal:	**4,200 €**
MATERIAL COSTS			
Questionnaires, scales, and informed consent printing	0,30 €/unit	21 units/participant	
		x 249 participants	**1,568 €**
		Subtotal:	**1,568 €**
PUBLICATION COSTS			
Article publication charges	1,200 €	4 publications	**4,800 €**
		Subtotal:	**4,800€**
		TOTAL COST	**10,568 €**

All of psychiatrists, psychologists, and nurses that will visit and attend study participants in the HSC and in other centres (CSM, CAS) in Girona will be part of the study staff, so they are not considered in this estimated budget. In the same way, the principal investigator is neither considered, since will be a psychiatrist of the UHA in the HSC.

On the other hand, all of validated questionnaires and scales that will be applied to patients are available in all centres, meaning that their cost is mainly associated with printing expenses.

All in person meetings performed during the whole duration of the study neither suppose additional expenses, because these will be performed in the same HSC.

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15. ANNEXES

ANNEX 1: INFORMATION SHEET AND INFORMED CONSENT

FULL D'INFORMACIÓ AL PACIENT

Títol de l'estudi:

Els traumes infantils com a factors de risc de ideació i conducta suïcida en pacients amb un primer episodi psicòtic: Estudi longitudinal de seguiment a 5 anys

Benvolgut/da,

Agraïm la seva participació en aquest estudi que estem realitzant des de la Xarxa de Salut Mental a la província de Girona. El suïcidi és una causa molt important de mort a nivell mundial, i encara és més important en persones que tenen alguna malaltia mental. Amb la seva participació estarà contribuint a millorar els coneixements que tenim actualment sobre quines són les causes que porten als pacients psicòtics a voler suïcidar-se, i d'aquesta manera poder prevenir d'una manera més eficaç que es produeixin aquests fatals esdeveniments.

Per tant, estem molt interessats en fer un seguiment dels nostres participants durant 5 anys per tal de conèixer qualsevol desig de morir o intent de suïcidi que puguin presentar durant aquest temps, i alhora investigar els antecedents que aquests puguin tenir en relació a esdeveniments traumàtics a la infància (abusos, maltractaments físics o psicològics...).

A continuació li expliquem amb detall quins són els motius pels que demanem la seva participació en aquest estudi, per tal que pugui decidir amb més criteri si està interessat/da o no a col·laborar en l'estudi. Llegeixi detingudament la següent informació i prengui's el temps que cregui convenient per fer-ho. Li recordem que la seva participació és totalment voluntària, i que si decideix no participar, això no afectarà de cap manera al tracte del professionals sanitaris cap a vostè.

1. Per a què necessiten fer-me un seguiment durant 5 anys?

Els estudis de seguiment aporten molta evidència científica quan el que es busca és conèixer les conseqüències d'algun esdeveniment, en aquest cas dels traumes infantils en pacients psicòtics. El que necessitem per dur a terme el nostre estudi és recollir totes les dades dels participants, referents a salut física i mental, en el moment en què entren a l'estudi i durant els següents 5 anys, ressaltant sobretot els antecedents traumàtics viscuts a la infància. Durant el seguiment, investigarem sobretot els pensaments de suïcidi o temptatives que puguin presentar els participants durant aquest temps. És molt important pel nostre estudi saber d'una manera fiable si els nostres participants es volen suïcidar durant el seguiment que farem.

2. Quina és la finalitat de l'estudi?

La finalitat d'aquest estudi és conèixer si els pacients amb un primer episodi psicòtic que a més hagin patit algun esdeveniment traumàtic durant la seva infància són més propensos a tenir

pensaments o conductes suïcides. El que esperem amb aquest estudi és avançar una mica més en el coneixement del suïcidi i les seves causes en pacients amb psicosi. Totes les dades que obtinguem dels participants seran utilitzades exclusivament amb finalitat de recerca.

3. En què consistirà la meva participació?

Els participants seran entrevistats en el moment en què entrin a l'estudi, per elaborar una història clínica (antecedents personals i familiars) i fer una avaluació psiquiàtrica completa. Per fer aquesta avaluació, cada participant haurà de respondre una sèrie de breus qüestionaris que seran proporcionats i avaluats per l'equip mèdic. Aquesta primera fase serà realitzada a l'hospital Santa Caterina, mentre els participants estan ingressats a la Unitat d'Hospitalització d'Aguts.

En els següents 5 anys, els participants tindran simplement una visita anual amb el seu psiquiatra. Per tant, només hi haurà 5 visites en tot el seguiment. Aquestes visites coincidiran amb alguna de les visites habituals que cada pacient ja tingui concertada amb el seu psiquiatra, independentment de si hagués entrat o no a l'estudi. Per tant, els participants no hauran d'anar a visitar-se més vegades de les que ho haurien fet si no haguessin entrat a formar part del nostre estudi. Aquestes visites es faran doncs al mateix centre on els participants siguin visitats pel seu psiquiatra, ja sigui al Centre de Salut Mental o al Centre d'Atenció a les drogodependències, en funció de cada participant. Durant aquesta visita anual, els pacients hauran de respondre també algun breu qüestionari com van fer a l'inici de l'estudi.

4. La meva participació serà confidencial?

Les dades personals dels nostres participants són totalment confidencials. Només hi tindran accés els membres de l'equip investigador i personal autoritzat, tal i com obliga la Llei Orgànica 15/1999 de 13 de desembre, de Protecció de Dades de Caràcter Personal. Per tant, totes les dades dels participants que siguin enregistrades a la base de dades del nostre estudi es mantindran estrictament confidencials.

5. El fet de participar en l'estudi em pot perjudicar d'alguna manera?

No, cap participant es pot veure perjudicat pel fet de formar part d'aquest estudi. Només hauran de respondre les preguntes que el seu psiquiatra els faci a cada visita i omplir algun qüestionari, com s'ha comentat.

6. És possible canviar la meva decisió un cop he acceptat participar en l'estudi?

Si, en qualsevol moment els participants poden canviar d'opinió i decidir abandonar l'estudi, i sense haver de donar cap explicació. Recordem que la participació és totalment voluntària.

7. A qui em puc dirigir per a demanar més informació?

En cas que tingui qualsevol dubte o vulgui més informació, pregunti al seu entrevistador o contacti amb l' adreça de correu electrònic que ell li proporcionarà.

FULL DE CONSENTIMENT INFORMAT

Títol de l'estudi:

Els traumes infantils com a factors de risc de ideació i conducta suïcida en pacients amb un primer episodi psicòtic: Estudi longitudinal de seguiment a 5 anys

Jo (Nom i cognoms): _____

- He llegit detingudament i he entès tot el full d'informació que m'han entregat
- He rebut suficient informació sobre l'estudi
- L'entrevistador m'ha explicat de manera entenedora tot el procediment
- Tots els meus dubtes han estat resolts de manera satisfactòria
- Entenc que totes les meves dades seran tractades de manera estrictament confidencial
- Entenc quin serà el meu paper com a participant de l'estudi
- Entenc que la meva participació és voluntària, i que en qualsevol moment de l'estudi puc decidir deixar de participar i, a més, sense haver de donar cap explicació

Per tant, accepto participar en l'estudi "Els traumes infantils com a factors de risc de ideació i conducta suïcida en pacients amb un primer episodi psicòtic: Estudi longitudinal de seguiment a 5 anys".

Signatura del participant o tutor/s legal/s

_____

Signatura de l'entrevistador

_____

Girona, _____ de _____ de 201_____

HOJA DE INFORMACIÓN AL PACIENTE

Título del estudio:

Los traumas infantiles como factores de riesgo de ideación y conducta suicida en pacientes con un primer episodio psicótico: Estudio longitudinal de seguimiento a 5 años

Estimado/a:

Agradecemos su participación en este estudio que estamos realizando desde la Red de Salud Mental en la provincia de Girona. El suicidio es una causa muy importante de muerte a nivel mundial, y es aún más importante en personas que tienen alguna enfermedad mental. Con su participación estará contribuyendo a mejorar los conocimientos que tenemos actualmente sobre cuáles son las causas que llevan a los pacientes psicóticos a querer suicidarse, y de esta manera poder prevenir de una manera más eficaz que se produzcan estos fatales eventos.

Por lo tanto, estamos muy interesados en hacer un seguimiento de nuestros participantes durante 5 años para conocer cualquier deseo de morir o intento de suicidio que puedan presentarse durante este tiempo, y al mismo tiempo investigar los antecedentes que éstos puedan tener en relación a eventos traumáticos en la infancia (abusos, maltratos físicos o psicológicos...).

A continuación le explicamos con detalle cuáles son los motivos por los que pedimos su participación en este estudio, para que pueda decidir con más criterio si está interesado / a o no a colaborar en el estudio. Lea detenidamente la siguiente información y tómese el tiempo que crea conveniente para hacerlo. Le recordamos que su participación es totalmente voluntaria, y que si decide no participar, esto no afectará de ninguna manera al trato de los profesionales sanitarios hacia usted.

1. ¿Para qué necesitan hacerme un seguimiento durante 5 años?

Los estudios de seguimiento aportan mucha evidencia científica cuando lo que se busca es conocer las consecuencias de algún evento, en este caso de los traumas infantiles en pacientes psicóticos. Lo que necesitamos para llevar a cabo nuestro estudio es recoger todos los datos de los participantes, referentes a salud física y mental, en el momento en que entran en el estudio y durante los siguientes 5 años, resaltando sobre todo los antecedentes traumáticos vividos en la infancia. Durante el seguimiento, investigaremos todo los pensamientos de suicidio o tentativas que puedan presentar los participantes durante este tiempo. Es muy importante para nuestro estudio saber de una manera fiable si nuestros participantes se quieren suicidar durante el seguimiento que haremos.

2. ¿Cuál es la finalidad del estudio?

La finalidad de este estudio es conocer si los pacientes con un primer episodio psicótico que además hayan sufrido algún evento traumático en su infancia son más propensos a tener pensamientos o conductas suicidas. Lo que esperamos con este estudio es avanzar un poco más en el conocimiento del suicidio y sus causas en pacientes con psicosis. Todos los datos que obtengamos de los participantes serán utilizados exclusivamente con fines de investigación.

3. ¿En qué consistirá mi participación?

Los participantes serán entrevistados en el momento en que entren en el estudio, para elaborar una historia clínica (antecedentes personales y familiares) y hacer una evaluación psiquiátrica completa. Para hacer esta evaluación, cada participante deberá responder una serie de breves cuestionarios que serán proporcionados y evaluados por el equipo médico. Esta primera fase será realizada en el hospital Santa Caterina, mientras los participantes están ingresados en la Unidad de Hospitalización de Agudos.

En los siguientes 5 años, los participantes tendrán simplemente una visita anual con su psiquiatra. Por tanto, sólo habrá 5 visitas en todo el seguimiento. Estas visitas coincidirán con alguna de las visitas habituales que cada paciente ya tenga concertada con su psiquiatra, independientemente de si hubiera entrado o no en el estudio. Por tanto, los participantes no tendrán que ir a visitar más veces de las que lo habrían hecho si no hubieran entrado a formar parte de nuestro estudio. Estas visitas se harán pues en el mismo centro donde los participantes sean visitados por su psiquiatra, ya sea en el Centro de Salud Mental o al Centro de Atención a las drogodependencias, en función de cada participante. Durante esta visita anual, los pacientes deberán responder también algún breve cuestionario como hicieron al inicio del estudio.

4. ¿Mi participación será confidencial?

Los datos personales de nuestros participantes son totalmente confidenciales. Sólo tendrán acceso a ellos los miembros del equipo investigador y personal autorizado, tal y como obliga la Ley Orgánica 15/1999 de 13 de diciembre, de Protección de Datos de Carácter Personal. Por lo tanto, todos los datos de los participantes que sean registrados en la base de datos de nuestro estudio se mantendrán estrictamente confidenciales.

5. ¿El hecho de participar en el estudio me puede perjudicar de alguna manera?

No, ningún participante puede verse perjudicado por el hecho de formar parte de este estudio. Sólo deberán responder las preguntas que su psiquiatra les haga en cada visita y llenar algún cuestionario, como se ha comentado.

6. ¿Es posible cambiar mi decisión una vez he aceptado participar en el estudio?

Si, en cualquier momento los participantes pueden cambiar de opinión y decidir abandonar el estudio, y sin tener que dar ninguna explicación. Recordemos que la participación es totalmente voluntaria.

7. ¿A quién me puedo dirigir para pedir más información?

En caso de que tenga cualquier duda o quiera más información, pregunte a su entrevistador o contacte con la dirección de correo electrónico que él le proporcionará.

HOJA DE CONSENTIMIENTO INFORMADO

Título del estudio:

Los traumas infantiles como factores de riesgo de ideación y conducta suicida en pacientes con un primer episodio psicótico: Estudio longitudinal de seguimiento a 5 años

Yo (Nombre y apellidos): _____

- ■ He leído detenidamente y he entendido toda la hoja de información que me han entregado
- ■ He recibido suficiente información sobre el estudio
- ■ El entrevistador me ha explicado de manera clara todo el procedimiento
- ■ Todas mis dudas han sido resueltas de manera satisfactoria
- ■ Entiendo que todos mis datos serán tratados de forma estrictamente confidencial
- ■ Entiendo cuál será mi papel como participante del estudio
- ■ Entiendo que mi participación es voluntaria, y que en cualquier momento del estudio puedo decidir dejar de participar y, además, sin tener que dar ninguna explicación

Por lo tanto, acepto participar en el estudio "Los traumas infantiles como factores de riesgo de ideación y conducta suicida en pacientes con un primer episodio psicótico: Estudio longitudinal de seguimiento a 5 años".

Firma del participante o tutor/es legal/es Firma del entrevistador

_____ _____

Girona, _____ de _____ de 201_____

ANNEX 2: CHILDHOOD TRAUMA QUESTIONNAIRE - SHORT FORM (CTQ-SF)

O	T	R	F
When I was growing up...	Quando eu estava crescendo...	When I was growing...	Enquanto eu crescia...
I didn't have enough to eat.	Eu não tinha o suficiente para comer.	I hadn't enough to eat	Eu não tive o suficiente para comer.
I knew that there was someone to take care of me and protect me.	Eu sabia que havia alguém para me cuidar e me proteger.	I knew that there was somebody to care about me and protect me.	Eu soube que havia alguém para me cuidar e proteger.
People in my family called me things like "stupid", "lazy", or "ugly".	As pessoas da minha família me chamavam de coisas do tipo "estúpido", "preguiçoso" ou "feio de doer".	People in my family called me things like "stupid", "lazy", or "too ugly".	As pessoas da minha família me chamaram de coisas do tipo "estúpido (a)", "preguiçoso (a)" ou "feio (a)".
My parents were too drunk or high to take care of the family.	Meus pais estavam muito bêbados ou drogados para cuidar da família.	My parents were too drunk or drugged to take care of the family.	Meus pais estiveram muito bêbados ou drogados para poder cuidar da família.
There was someone in my family who helped me feel that I was important or special.	Havia alguém em minha família que me ajudava a sentir-se especial ou importante.	There was somebody in my family who helped me to feel that I was special or important.	Houve alguém na minha família que ajudou a me sentir especial ou importante.
I had to wear dirty clothes.	Eu tinha que usar roupas sujas.	I had to wear dirty clothes.	Eu tive que usar roupas sujas.
I felt loved.	Eu me senti amado.	I felt loved.	Eu me senti amado (a).
I thought that my parents wished I had never been born.	Eu achava que meus pais desejavam que eu nunca tivesse nascido.	I thought that my parents wished that I had never been born.	Eu achei que meus pais preferiam que eu nunca tivesse nascido.
I got hit so hard by someone in my family that I had to see a doctor or go to the hospital.	Eu apanhei tanto de alguém da minha família que por isso tive que ir ao hospital ou consultar com um médico.	I got beaten so much by somebody from my family that therefore I had to go to a hospital or to see a doctor.	Eu apanhei tanto de alguém da minha família que tive de ir ao hospital ou consultar um médico.
There was nothing I wanted to change about my family.	Não havia nada que eu quisesse mudar na minha família.	There was nothing I wanted to change in my family.	Nunca quis mudar nada na minha família.
People in my family hit me so hard that it left me with bruises or marks.	Alguém em minha família me bateu tanto que me deixou com marcas ou equimoses.	Somebody in my family hit me so much that it left me with marks or bruises.	Alguém da minha família me bateu tanto que me deixou com machucados roxos.
I was punished with a belt, a board, a cord, or some other hard object.	Eu apanhei com cinto, vara, corda ou outro objeto duro.	I got beaten with a belt, stick, cord or other hard object.	Eu apanhei com cinto, vara, corda ou outras coisas que machucaram.
People in my family looked out for each other.	As pessoas em minha família cuidavam umas das outras.	People in my family took care each other.	As pessoas da minha família cuidavam umas das outras.
People in my family said hurtful or insulting things to me.	As pessoas em minha família diziam coisas que me machucavam ou me ofendiam.	People in my family said things that hurt or offended me.	Pessoas da minha família disseram coisas que me machucaram ou me ofenderam.
I believe that I was physically abused.	Eu acredito que fui abusado fisicamente.	I believe that I was physically abused.	Eu acredito que fui maltratado (a) fisicamente.
I had the perfect childhood.	Eu tive uma infância perfeita.	I had the perfect childhood.	Eu tive uma ótima infância.
I got hit or beaten so badly that it was notice by someone like a teacher, neighbor, or doctor.	Eu apanhei tanto que isso foi notado por um professor, vizinho ou médico.	I got beaten so much that was seen by a teacher, neighbor or doctor.	Eu apanhei tanto que um professor, vizinho ou médico chegou a notar.
I felt that someone in my family hated me.	Eu sentia que alguém na minha família me odiava.	I felt that someone in my family hated me.	Eu senti que alguém da minha família me odiava.
People in my family felt close to each other.	As pessoas da minha família se sentiam próximas umas das outras.	People of my family felt close to each other.	As pessoas da minha família se sentiam unidas.
Someone tried to touch me in a sexual way, or tried to make me touch them.	Alguém tentou me tocar ou me fez tocar-lhe de uma maneira sexual.	Somebody tried to touch me or make me touch them in a sexual way.	Tentaram me tocar ou me fizeram tocar de uma maneira sexual.
Someone threatened to hurt me or tell lies about me unless I did something sexual with them.	Alguém ameaçou me machucar ou contar mentiras sobre mim se eu não lhe fizesse algo sexual.	Somebody threatened to hurt me or tell lies about me if I didn't make sexual things with them.	Ameaçaram me machucar ou contar mentiras sobre mim se eu não fizesse algo sexual.
I had the best family in the world.	Eu tive a melhor família do mundo.	I had the best family in the world.	Eu tive a melhor família do mundo.
Someone tried to make me do sexual things or watch sexual things.	Alguém tentou me forçar a fazer algo sexual ou assistir coisas sobre sexo.	Somebody tried to force me to make something sexual or to watch sexual things.	Tentaram me forçar a fazer algo sexual ou assistir coisas sobre sexo.
Someone molested me.	Alguém me molestou.	Somebody molested me.	Alguém me molestou.
I believe that I was emotionally abused.	Eu acredito que fui abusado emocionalmente.	I believe that I was emotionally abused.	Eu acredito que fui maltratado (a) emocionalmente.
There was someone to take me to the doctor if I needed it.	Havia alguém para me levar ao médico caso precisasse.	There was someone to take me to the doctor if I needed it.	Houve alguém para me levar ao médico quando eu precisei.
I believe that I was sexually abused.	Eu acredito que fui abusado sexualmente.	I believe that I was sexually abused.	Eu acredito que fui abusado (a) sexualmente.
My family was a source of strength and support.	Minha família foi uma fonte de força e apoio.	My family was a source of encouragement and support.	Minha família foi uma fonte de força e apoio.

Taken from: Grassi-Oliveira R, Milnitsky Stein L, Pezzi JC. Translation and content validation of the Childhood Trauma Questionnaire into Portuguese language. Rev Saúde Pública. 2006; 40(2): 249-55.

ANNEX 3: POSITIVE AND NEGATIVE SYNDROME SCALE (PANSS)

Adaptación española de V. Peralta y M. J. Cuesta

Nombre del paciente _____ Número _____
Entrevistador _____ Periodo de observación _____ Fecha _____

	A	D	L	M	MS	S	E
SINDROME POSITIVO (PANSS-P)							
1. Delirios	1	2	3	4	5	6	7
2. Desorganización	1	2	3	4	5	6	7
3. Comportamiento alucinatorio	1	2	3	4	5	6	7
4. Excitación	1	2	3	4	5	6	7
5. Grandiosidad	1	2	3	4	5	6	7
6. Suspicacia/perjuicio	1	2	3	4	5	6	7
7. Hostilidad	1	2	3	4	5	6	7
SINDROME NEGATIVO (PANSS-N)							
1. Embotamiento afectivo	1	2	3	4	5	6	7
2. Retraimiento afectivo	1	2	3	4	5	6	7
3. Contacto pobre	1	2	3	4	5	6	7
4. Retraimiento social	1	2	3	4	5	6	7
5. Dificultad en el pensamiento abstracto	1	2	3	4	5	6	7
6. Ausencia de Espont. y fluidez en la conversación	1	2	3	4	5	6	7
7. Pensamiento estereotipado	1	2	3	4	5	6	7
PSICOPATOLOGÍA GENERAL (PANSS-PG)							
1. Preocupaciones somáticas	1	2	3	4	5	6	7
2. Ansiedad	1	2	3	4	5	6	7
3. Sentimientos de culpa	1	2	3	4	5	6	7
4. Tensión motora	1	2	3	4	5	6	7
5. Manierismos y posturas	1	2	3	4	5	6	7
6. Depresión	1	2	3	4	5	6	7
7. Retardo motor	1	2	3	4	5	6	7
8. Falta de colaboración	1	2	3	4	5	6	7
9. Inusuales contenidos del pensamiento	1	2	3	4	5	6	7
10. Desorientación	1	2	3	4	5	6	7
11. Atención deficiente	1	2	3	4	5	6	7
12. Ausencia de juicio e "introspección"	1	2	3	4	5	6	7
13. Trastornos de la volición	1	2	3	4	5	6	7
14. Control deficiente de impulsos	1	2	3	4	5	6	7
15. Preocupación	1	2	3	4	5	6	7
16. Evitación social activa	1	2	3	4	5	6	7

Taken from: Escala de los síndromes positivo y negativo PANSS. Madrid: Universidad Complutense de Madrid; 1994.

ANNEX 4: M.I.N.I. INTERNATIONAL NEUROPSYCHIATRIC INTERVIEW

C. RIESGO DE SUICIDIO

	Durante este último mes:			
C1	¿Ha pensado que sería mejor morirse o ha deseado estar muerto?	NO	SI	1
C2	¿Ha querido hacerse daño?	NO	SI	2
C3	¿Ha pensado en el suicidio?	NO	SI	3
C4	¿Ha planeado suicidarse?	NO	SI	4
C5	¿Ha intentado suicidarse?	NO	SI	5
	A lo largo de su vida:			
C6	¿Alguna vez ha intentado suicidarse?	NO	SI	6

¿HAY AL MENOS 1 RESPUESTA CODIFICADA **SI**?

NO SI

SI **SI**, ESPECIFICAR EL NIVEL DE RIESGO DE SUICIDIO COMO SIGUE:

C1 o C2 o C6 = SI : LIGERO
C3 o (C2 + C6) = SI : MODERADO
C4 o C5 o (C3 + C6) = SI : ALTO

RIESGO DE SUICIDIO ACTUAL

LIGERO
MODERADO
ALTO

I. TRASTORNO POR ESTRES POST-TRAUMÁTICO (opcional)

I1	¿En alguna ocasión se ha enfrentado o ha experimentado un acontecimiento extremadamente traumático, en el curso del cual otras personas han muerto y/o otras personas o usted mismo han estado amenazadas de muerte o en su integridad física EJ. DE ACONTECIMIENTOS TRAUMÁTICOS: ACCIDENTE GRAVE, ATRACO, VIOLACIÓN, ATENTADO, INCENDIO, DESCUBRIMIENTO DE UN CADÁVER, MUERTE SÚBITA EN EL ENTORNO, GUERRA, CATÁSTROFE NATURAL.	→ NO	SI	1
I2	¿Durante el último mes, ha revivido de manera penosa este acontecimiento (ej: sueños, recuerdos intensos, visiones o reacciones físicas)?	→ NO	SI	2
I3	**Durante el último mes:**			
a	¿Ha evitado pensar en este acontecimiento o en las cosas que se lo pudiesen recordar?	NO	SI	3
b	¿Se siente mal al recordar alguna parte importante de lo que sucedió?	NO	SI	4
c	¿Ha disminuido su interés en cosas que le agradaban o en actividades sociales?	NO	SI	5
d	¿Se siente alejado o extraño con respecto a los demás?	NO	SI	6
e	¿Ha notado que sus sentimientos se han bloqueado?	NO	SI	7
f	¿Ha sentido como si su vida se hubiese empobrecido, debido a este trauma?	NO	SI	8
	¿HAY AL MENOS 3 RESPUESTAS CODIFICADAS SI EN I3 ?	→ NO	SI	
I4	**Durante el último mes:**			
a	¿Ha tenido dificultades para dormir?	NO	SI	9
b	¿Ha estado especialmente irritable o ha tenido crisis de enfado?	NO	SI	10
c	¿Ha tenido dificultades para concentrarse?	NO	SI	11
d	¿Ha estado nervioso o en alerta constante?	NO	SI	12
e	¿Se sobresaltaba por cualquier cosa?	NO	SI	13
	¿HAY AL MENOS 2 RESPUESTAS CODIFICADAS SI EN I4 ?	→ NO	SI	
I5	¿Durante el último mes, estos problemas han interferido en su trabajo o sus actividades sociales o le han causado un profundo malestar?	NO	SI	14

¿I5 HA CODIFICADO SI ?

NO	SI
TRASTORNO POR ESTRES POST-TRAUMATICO ACTUAL	

J. DEPENDENCIA Y ABUSO DE ALCOHOL

J1	¿Durante los últimos 12 meses ha tomado 3 ó más bebidas alcohólicas en menos de 3 horas en 3 o más ocasiones?	→ NO	SI	1
J2	**Durante los últimos 12 meses:**			
a	¿Ha necesitado beber más cantidad de alcohol para lograr los mismos efectos que cuando comenzó a beber?	NO	SI	2
b	¿Cuando ha reducido la cantidad de alcohol, le temblaban las manos, sudaba o se sentía agitado? ¿Ha bebido para evitar estos síntomas o para evitar la resaca, p. ej. temblores, sudor, agitación?. CODIFICAR **SI**, SI ALGUNA ES AFIRMATIVA	NO	SI	3
c	¿Cuando ha bebido alcohol, ha terminado bebiendo más de lo que en un principio se había planteado?	NO	SI	4
d	¿Ha intentado reducir o dejar de beber alcohol pero ha fracasado?	NO	SI	5
e	¿Los días en los que ha bebido, ha empleado mucho tiempo en obtener alcohol, bebiendo o recuperándose de sus efectos?	NO	SI	6
f	¿Debido a la bebida, ha empleado menos tiempo, trabajando, disfrutando de sus distracciones, en estar con los demás?	NO	SI	7
g	¿Ha seguido bebiendo a pesar de saber que la bebida le causa problemas de salud, físicos o mentales?	NO	SI	8
	¿HAY AL MENOS 3 RESPUESTAS CODIFICADAS **SI** EN **J2** ?	**NO**	**SI** → ***DEPENDENCIA ALCOHOLICA ACTUAL***	
	¿PRESENTA EL PACIENTE DEPENDENCIA ALCOHOLICA?	NO	→ SI	
J3	**Durante los últimos 12 meses:**			
a	¿Ha estado intoxicado, embriagado o con "resaca", en más de una ocasión cuando tenía otras responsabilidades, estudios, trabajo, casa? ¿Esto le ha ocasionado algún problema? CODIFICAR **SI** SOLO SI ESTO LE HA OCASIONADO PROBLEMAS	NO	SI	9
b	¿Ha estado intoxicado en alguna situación en la que tuviese un riesgo físico, ej: conduciendo un coche, navegando, utilizando maquinaria, etc.?	NO	SI	10
c	¿Ha tenido algún problema legal por haber bebido? (ej. arrestos o conductas delictivas)	NO	SI	11
d	¿Ha seguido bebiendo aunque esto le haya ocasionado problemas con la familia o en su entorno?	NO	SI	12
	¿HAY AL MENOS 1 RESPUESTA CODIFICADA **SI** EN J3 ?	**NO**	**SI** → ***ABUSO DE ALCOHOL ACTUAL***	

K. TRASTORNOS LIGADOS AL CONSUMO DE SUSTANCIAS PSICOACTIVAS (NO ALCOHOLICAS)

K1	Ahora voy a enseñarle/ leerle (ENSEÑAR LA LISTA DE SUSTANCIAS/ LEER LA SIGUIENTE LISTA), una lista de drogas y de medicamentos y usted me indicará si en el transcurso de los últimos 12 meses ha tomado en más de una ocasión alguno de estos productos con el propósito de sentirse mejor o cambiar de humor.	→ NO	SI	

ENMARCAR CADA PRODUCTO CONSUMIDO:

Estimulantes : anfetaminas, «speed», Ritalín, píldoras adelgazantes.
Cocaína : cocaína, «coke», crack, «speedball».
Opiáceos : heroína, morfina, opio, metadona, codeína, meperidina, fentanil.
Alucinógenos : L.S.D., «ácido», mescalina, PCP, «polvo de ángel», «hongos», éxtasis.
Inhalantes : «cemento», pegamento, éther.
Cannabinoides : hachis, «hasch», THC, cannabis, «hierba», «shit», mota, grifa, pasto, etc.
Tranquilizantes : Valium, Trankimazín, Halción, Lexatín, Orfidal, barbitúricos, Rohypnol ("reina").
Varios: Anabolizantes, Esteroides. ¿Toma otras substancias?

ESPECIFICAR LA (O LAS) SUBSTANCIA(S) MÁS CONSUMIDA(S): _____

_____

ESPECIFICAR LO QUE SE EXPLORA A CONTINUACIÓN:

- SI CONSUME VARIAS SUBSTANCIAS (AL MISMO TIEMPO O SECUENCIALMENTE): CADA SUBSTANCIA O CLASE DE SUBSTANCIAS POR SEPARADO, UNICAMENTE LA SUBSTANCIA (O CLASE DE SUBSTANCIAS) MÁS CONSUMIDA. _
- SI SOLO CONSUME UNA SUBSTANCIA (O CLASE DE SUBSTANCIAS), UNICAMENTE UNA SUBSTANCIA (O CLASE DE SUBSTANCIAS) _

_

K2	**Considerando su consumo de [NOMBRE DE LA SUBSTANCIA O LA CLASE DE SUBSTANCIAS SELECCIONADAS], en el transcurso de los 12 últimos meses:**			
a	¿Ha constatado que necesitaba tomar más cantidad de (NOMBRE DE LA SUBSTANCIA O LA CLASE DE SUBSTANCIAS SELECCIONADAS) para obtener los mismos efectos que cuando comenzó a tomarla?	NO	SI	1
b	¿Cuando reducía o dejaba de tomar drogas tenía síntomas de abstinencia (dolores, temblores, fiebre, desfallecimiento, diarrea, náuseas, sudoración, palpitaciones, dificultades para dormir, o se sentía agitado, ansioso, irritable o deprimido)? ¿Utilizaba otras cosas para evitar encontrarse mal (SÍNTOMAS DE ABSTINENCIA), o para sentirse mejor? CODIFICAR SI, SI ALGUNA ES AFIRMATIVA	NO	SI	2
c	¿Ha comprobado que cuando consumía, (NOMBRE DE LA SUBSTANCIA O LA CLASE DE SUBSTANCIAS SELECCIONADAS) terminaba tomando más cantidad de lo que era su intención?	NO	SI	3

d	¿Ha tratado de reducir o dejar de consumir (NOMBRE DE LA SUBSTANCIA O LA CLASE DE SUBSTANCIAS SELECCIONADAS) pero no lo ha conseguido?	NO	SI	4
e	¿Los días que ha consumido (NOMBRE DE LA SUBSTANCIA O LA CLASE DE SUBSTANCIAS SELECCIONADAS) ha empleado mucho tiempo (> de 2 horas) en obtener, tomar esta sustancia, recuperarse de sus efectos, o pensando en ella(s)?	NO	SI	5
f	¿Ha tenido menos tiempo para trabajar, disfrutar de sus distracciones, o estar con su familia o amigos por consumir droga?	NO	SI	6
g	¿Ha seguido consumiendo (NOMBRE DE LA SUBSTANCIA O LA CLASE DE SUBSTANCIAS SELECCIONADAS) a pesar de saber que esto le causa problemas de salud o mentales?	NO	SI	7

¿HAY AL MENOS 3 RESPUESTAS CODIFICADAS **SI** EN **K2** ?

NO **SI**

ESPECIFICAR LA (S) SUBSTANCIA(S) :

_____

DEPENDENCIA de SUBSTANCIA(S) ACTUAL

¿PRESENTA EL PACIENTE DEPENDENCIA A SUBSTANCIA(S) ? → NO SI

K3 **En el transcurso de los 12 últimos meses:**

a	¿Ha estado intoxicado, embriagado, con resaca, a causa de (NOMBRE DE LA SUBSTANCIA O LA CLASE DE SUBSTANCIAS SELECCIONADAS) en más de una ocasión, cuando tenía otras responsabilidades académicas, laborales o en su casa? ¿Esto le ocasionó algún problema? CODIFICAR **SI**, SI ALGUNA ES AFIRMATIVA	NO	SI	8
b	¿Ha estado intoxicado por (NOMBRE DE LA SUBSTANCIA O LA CLASE DE SUBSTANCIAS SELECCIONADAS), en alguna situación en la que tuviese un riesgo físico (ej: conduciendo un coche, navegando, utilizando maquinaria, etc.)?	NO	SI	9
c	¿Ha tenido algún problema legal por consumir (NOMBRE DE LA SUBSTANCIA O LA CLASE DE SUBSTANCIAS SELECCIONADAS), ej. arrestos o conductas delictivas?	NO	SI	10
d	¿Ha seguido consumiendo (NOMBRE DE LA SUBSTANCIA O LA CLASE DE SUBSTANCIAS SELECCIONADAS) aunque esto le ocasionara problemas con su familia o con otras personas?	NO	SI	11

¿HAY AL MENOS 1 SI EN K3 ?

NO **SI**

ESPECIFICAR LA (LAS) SUBSTANCIA(S) :

_____

ABUSO DE SUBSTANCIA(S) ACTUAL

Taken from: Sheehan D, Lecrubier Y, Sheehan K, Amorim P, Janavs J, Weiller E, et al. M.I.N.I. Mini International Neuropsychiatric Interview [Internet]. Madrid: Instituto IAP; 1998. p. 1–28. Available from: http://www.iiap.es/files/mini.pdf

ANNEX 5: HAMILTON DEPRESSION RATING SCALE (HDRS)

Institut d'Assistència Sanitària

ESCALA DE HAMILTON PER VALORAR LA DEPRESSIÓ (HRS-D)

Punts	Avaluació dels darrers dies, fins la setmana previa.	Data	Data	Data	Data	Diferència inicial-alta
0-4	**1. Estat d'ànim deprimit** (actitud malencònica, pessimista vers el futur, sentiment de tristesa, tendència al plor) 0. Absent 1. Aquests estats no són assenyalats si no s'interroga el subjecte 2. Són assenyalats verbalment de forma espontània 3. Són comunicats no verbalment (p.e. expressió facial, actitud, veu, tendència a plorar) 4. El subjecte comunica aquests estats afectius mitjançant comunicacions espontànies verbals i no verbals					
0-4	**2. Culpabilitat** 0. Absent 1. Auto-retrets, sensació d'haver causat perjudici o decebut a la gent 2. Idees de culpa o meditació sobre errors i/o males accions del passat 3. La malaltia actual és un càstig. Idees delirants de culpabilitat 4. Escolta veus d'acusació o de denúncia i/o té al.lucinacions visuals amenaçants					
0-4	**3. Suïcidi** 0. Absent 1. Li sembla que la vida no val la pena viure-la 2. Desitja morir-se 3. Té idees suïcides 4. Intents de suïcidi					
0-2	**4. Insomni inicial** 0. Cap dificultat en adormir-se 1. Dificultats eventuals (p.e. més de mitja hora) 2. Té dificultats cada nit per adormir-se					
0-2	**5. Insomni mig** 0. No en té 1. El pacient està inquiet i alterat durant la nit 2. Es desperta durant la nit					
0-2	**6. Insomni tardà** 0. No en té 1. Es desperta de matinada, però es torna a dormir 2. No es pot tornar a dormir.					
0-4	**7. Treball i activitats** 0. Cap dificultat 1. Sentiments d'incapacitat, negligència, indecisió i vacil.lació en les activitats professionals o de diversió 2. Pèrdua d'interès per les activitats professionals i afeccions, descrites directament o indirectament per desatenció, indecisió, titubeig (té la impresió que s'ha d'esforçar en el seu treball o al realitzar una activitat) 3. Disminució de les activitats o de la productivitat 4. Va deixar de treballar a causa de la malaltia actual					
0-4	**8. Inhibició** (alentiment del pensament, de la parla i/o conducta) 0. Normal 1. Lleuger retard durant l'entrevista 2. Evident retard durant l'entrevista 3. Entrevista dificultosa 4. Complet estupor					
0-4	**9. Agitació**					

	0. Cap 1. Enervament 2. Juga amb les mans, els cabells 3. Agitat, no pot estar-se quiet 4. Es cargola les mans, es mossega les ungles, es mossega els llavis					
0-4	**10. Ansietat psíquica** 0. Cap 1. Tensió i irratibilitat 2. Preocupació per assumptes menors 3. Actitud aprensiva 4. Temors					
0-4	**11. Ansietat somàtica** 0. Absent 1. Discreta (molèsties gastrointestinals. Indigestió, meteorisme, boca seca, diarrera, eructosi) 2. Mitjana 3. Greu (trastorns cardiovasculars, palpitacions, cefalees) 4. Trastorns respiratoris, hiperventilació, sospirs, poliúria, transpiració					
0-2	**12. Símptomes somàtics digestius** 0. Cap 1. Pèrdua de la gana, sensació de pesadesa d'abdomen 2. Dificultat per menjar si no se l'obliga. Necessitat de laxants, purgants					
0-2	**13. Símptomes somàtics generals** 0. Cap 1. Pesadesa en els membres inferiors, espatlla o cap, cefalees, dolors musculars, pèrdua d'energia i fatigabilitat. 2. Anoteu 2 si qualsevol d'aquests símptomes són molt presents					
0-2	**14. Símptomes genitals** 0. Pèrdua de la libido, alteracions menstruals 1. Absent 2. Lleugers 3. Incapacitant					
0-4	**15. Hipocondriasi** 0. Absent 1. Atenció concentrada en el propi cos 2. Preocupació per la pròpia salut 3. Queixes freqüents, demandes d'ajuda, etc. 4. Idees delirants hipocondríaques					
0-2	**16. Pèrdua de discerniment** 0. Reconeix que està deprimit i malalt 1. Reconeix que està malalt però ho atribueix al menjar, al clima, al cansament, a un virus, etc. 2. Nega estar malalt					
0-2	**17. Pèrdua de pes** 0. No n'hi ha 1. Lleugera o incerta 2. Certa o important					
0-2	18. Canvis diürns (no suma a la P.Total) 0. No hi ha variació 1. Variació poc important 2. Variació marcada					
0-52	PUNTUACIÓ TOTAL					

Valors orientatius (Vázquez C. 1995):

- **0 – 6 : sense depressió**
- **7 – 17 : depressió lleu**
- **18 – 24 : depressió moderada**
- **25 – 52 : depressió greu**

Taken from: Hospital Santa Caterina de Girona

ANNEX 6: PREMORBID ADJUSTMENT SCALE (PAS)

Appendix: Premorbid Adjustment Scale

Childhood (up through age 11)

1. Sociability and withdrawal

0 Not withdrawn, actively and frequently seeks out social contacts.
1
2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.
3
4 Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others but does not seek it.
5
6 Unrelated to others, withdrawn and isolated. Avoids contacts.

2. Peer relationships

0 Many friends, close relationships with several.
1
2 Close relationships with a few friends (one or two), casual friendships with others.
3
4 Deviant friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only.
5
6 Social isolate, no friends, not even superficial relationships.

3. Scholastic performance

0 Excellent student.
1
2 Good student.
3
4 Fair student.
5
6 Failing all classes.

4. Adaptation to school

0 Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers.
1
2 Fair adaptation, occasional discipline problem, not very interested in school, but no truancy, or rare. Has friends in school, but does not often take part in extracurricular activities.
3
4 Poor adaptation, dislikes school, frequent truancy, frequent discipline problem.
5
6 Refuses to have anything to do with school—delinquency or vandalism directed against school.

Adolescence (Early, ages 12–15)

1. Sociability and withdrawal

0 Not withdrawn.
1
2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.
3
4 Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others, but does not seek it.
5
6 Unrelated to others, withdrawn and isolated. Avoids contact.

2. Peer relationships

0 Many friends, close relationships with several.
1
2 Close relationships with a few friends (one or two), casual friendships with others.
3
4 Deviant friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only.
5
6 Social isolate, no friends, not even superficial relationships.

3. Scholastic performance

0 Excellent student.
1
2 Good student.
3
4 Fair student.
5
6 Failing all classes.

4. Adaptation to school

0 Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers.
1
2 Fair adaptation, occasional discipline problem, not very interested in school, but no truancy, or rare. Has friends in school, but does not often take part in extracurricular activities.
3
4 Poor adaptation, dislikes school, frequent truancy, frequent discipline problem.
5
6 Refuses to have anything to do with school—delinquency or vandalism directed against school.

5. Social-sexual aspects of life during early adolescence

0 Started dating, showed a "healthy interest" in the opposite sex, may have gone "steady," may include some sexual activity.
1 Attachment and interest in others, may be same-sex attachments, may be a member of a group, interested in the opposite sex, although may not have close, emotional relationship with someone of the opposite sex, "crushes" and flirtations.
2 Consistent deep interest in same-sex attachments with restricted or no interest in the opposite sex.
3 Casual same-sex attachments, with inadequate attempts at relationships with the opposite sex. Casual contacts with both sexes.
4 Casual contacts with the same sex, no interest in the opposite sex.
5 A loner, no or rare contacts with either boys or girls.
6 Antisocial, avoids and avoided by peers. (Differs from above in that an active avoidance of others rather than passive withdrawal is implied.)

Adolescence (Late, ages 16–18)

1. Sociability and withdrawal

0 Not withdrawn.
1
2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.
3
4 Moderately withdrawn, given to daydreaming and exces-

sive fantasy, may passively allow self to be drawn into contact with others, but does not seek it.

5

6 Unrelated to others, withdrawn and isolated. Avoids contact.

2. Peer relationships

0 Many friends, close relationships with several.

1

2 Close relationships with a few friends (one or two), casual friendships with others.

3

4 Deviant friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only.

5

6 Social isolate, no friends, not even superficial relationships.

3. Scholastic performance

0 Excellent student.

1

2 Good student.

3

4 Fair student.

5

6 Failing all classes.

4. Adaptation to school

0 Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers.

1

2 Fair adaptation, occasional discipline problem, not very interested in school, but no truancy, or rare. Has friends in school, but does not often take part in extracurricular activities.

3

4 Poor adaptation, dislikes school, frequent truancy, frequent discipline problem.

5

6 Refuses to have anything to do with school—delinquency or vandalism directed against school.

5. Social aspects of sexual life during adolescence and immediately beyond

0 Always showed a "healthy interest" in the opposite sex, dating, has gone "steady," engaged in some sexual activity (not necessarily intercourse).

1 Dated regularly. Had only one friend of the opposite sex with whom the patient went "steady" for a long time. (Includes sexual aspects of a relationship, although not necessarily intercourse; implies a twosome, pairing off into couples, as distinguished from below.)

2 Always mixed closely with boys and girls. (Involves membership in a crowd, interest in and attachment to others, no couples.)

3 Consistent deep interest in same-sex attachments with restricted or no interest in the opposite sex.

4 Casual same-sex attachments with inadequate attempts at adjustment to going out with the opposite sex. Casual contacts with boys and girls.

5 Casual contacts with same sex with lack of interest in opposite sex. Occasional contacts with the opposite sex.

6 No desire to be with boys and girls, never went out with opposite sex.

Adulthood (Age 19 and above)

1. Sociability and withdrawal

0 Not withdrawn, actively and frequently seeks out social contact.

1

2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.

3

4 Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others but does not seek it.

5

6 Unrelated to others, withdrawn and isolated. Avoids contacts.

2. Peer relationships

0 Many friends, close relationships with several.

1

2 Close relationships with a few friends (one or two), casual friendships with others.

3

4 Deviant friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only.

5

6 Social isolate, no friends, not even superficial relationships.

3. Aspects of adult social-sexual life.

a. Married, presently or formerly:

0 Married, only one marriage (or remarried as a result of death

of spouse), living as a unit, adequate sexual relations.

1 Currently married with history of low sexual drive, periods of difficult sexual relations, or extramarital affair.

1 Married, more than one time, currently remarried. Adequate sexual relations during at least one marriage.

2 Married, or divorced and remarried, with chronically inadequate sex life.

2 Married, and apparently permanently separated or divorced without remarriage, but maintained a home in one marriage for at least 3 years.

3 Same as above, but: divorce occurred over 3 years ago, and, while married, maintained a home for less than 3 years.

b. Never married, over 30:

2 Has been engaged one or more times or has had a long-term relationship (at least 2 years) involving heterosexual or homosexual relations, or apparent evidence of a love affair with one person, but unable to achieve a long-term commitment such as marriage.

3 Long-term heterosexual or homosexual relationship lasting over 6 months but less than 2 years. (If stable, long-lasting homosexual relationship, over 2 years, score as "3.")

4 Brief, or short-term dating experiences (heterosexual or homosexual) with one or more partners, but no long-lasting sexual experience with a single partner.

5 Sexual and/or social relationships rare or infrequent.

6 Minimal sexual or social interest in either men or women, isolated.

c. Never married, age 20–29:

0 Has had at least one long-term love affair (minimum of 6 months) or engagement, even though religious or other prohibitions or inhibitions may have prevented actual sexual union. May have lived together.

1 Has dated actively, had several "boyfriends" or "girlfriends," some relationships have lasted a few months, but no long-term relationships. Relationships may have been "serious," but a long-term commitment such as marriage was not understood to be an eventuality.

3 Brief, short-term dating experiences or "affairs" with one or more partners, but no long-lasting sexual experiences with a single partner.

4 Casual sexual or social relationships with persons of either sex with no deep emotional bonds.

5 Sexual and/or social relationships rare or infrequent.

6 Minimal sexual or social interest in either men or women, isolated.

General

1. Education

0 Completed college and/or graduate school, or professional school (Law, for example).

1 Completed high school and some college or vocational training school or business school (such as secretarial or computer programming schools).

2 Completed high school.

3

4 Completed eighth grade.

5

6 Did not get beyond fifth grade.

2. During a period of 3 years up to 6 months before first hospitalization or onset of first episode, patient was employed for pay or functioning in school

0 All the time.

1

2 Half the time.

3

4 Briefly, about 25 percent of the time.

5

6 Never.

3. Within a period of a year up to 6 months before first hospitalization or first episode change in work or school performance occurred

0 Abruptly.

1

2 Within 3 months.

3

4 Within 6 months.

5

6 Imperceptibly, difficult or not possible to determine onset of deterioration.

4. During a period of 3 years up to 6 months before first hospitalization or first episode, frequency of job change, if working, or interruption of school attendance was

0 Same job held, or remained in school.

1

2 Job change or school interruption occurred two to three times.

3

4 Kept the same job more than 8 months but less than a year, or remained continuously in school for the same period.

5

6 Less than 2 weeks at a job or in school.

5. Establishment of independence

0 Successfully established residence away from family home, financially independent of parents.

2 Made unsuccessful attempts to establish independent residence, lives in parents' home, but pays parents room and board, otherwise financially independent.

4 Lives in parents' home, receiving an allowance from parents which patient budgets to pay for entertainment, clothes, etc.

6 Made no attempt to leave home or be financially independent.

6. Global assessment of highest level of functioning achieved in patient's life

0 Fully able to function successfully in and take pleasure from (1) school or job; (2) friends; (3) intimate sexual relationships; (4) church, hobbies, etc. Enjoys life and copes with it well.

2 Able to function well in and enjoys some spheres of life, but has a definite lack of success in at least one area.

4 Minimum success and pleasure in three areas of life.

6 Unable to function in or enjoy any aspect of life.

7. Social-personal adjustment

0 A leader or officer in formally designated groups, clubs, organizations, or athletic teams in senior high school, vocational school, college, or young adulthood. Involved in intimate, close relationship with others.

1 An active and interested participant, but did not play a leading role in groups of friends, clubs, organizations, or athletic teams, but was involved in close relationships with others also.

2 A nominal member, but had no involvement in or commitment to, groups of friends, clubs, organizations, etc. Had close relationships with a few friends.

3 From adolescence through early adulthood had a few casual friends.

4 From adolescence through early adulthood had no real friends, only superficial relationships.

5 From adolescence through early adulthood (i.e., after childhood), quiet, seclusive, preferred to be by self, minimal efforts to maintain any contact at all with others.

6 No desire to be with peers or others. Either asocial or antisocial.

8. Degree of interest in life

0 Keen, ambitious interest in some of the following: home, family, friends, work, sports, art, pets, gardening, social activities, music, and drama.

2 Moderate degree of interest in several activities including social gatherings, sports, music, and opposite sex.

4 Mild interest in a few things such as job, family, quiet social gatherings. The interest is barely sustaining.

6 Withdrawn and indifferent toward life interests of average individual. No deep interests of any sort.

9. Energy level

0 Strong drive, keen, active, alert interest in life. Liked life and had energy enough to enjoy it. Outgoing and adequate in meeting life.

2 Moderately adequate drive, energy, interest, as described above.

4 Moderately inadequate energy level. Tended toward submissive, passive reactions. Showed some potential to face life's problems, but would rather avoid them than expend the necessary energy.

6 Submissive, inadequate, passive reactions. Weak grasp on life, does not go out to meet life's problems, does not participate actively, but passively accepts his lot without having the energy to help self.

Taken from: Cannon-Spoor HE, Potkin SG, Wyatt RJ. Measurement of Premorbid Adjustment in Chronic Schizophrenia. Schizophr Bull [Internet]. 1982 Jan 1;8(3):470–84. Available from: http://schizophreniabulletin.oxfordjournals.org/content/8/3/470.long

ANNEX 7: CASE REPORT FORM

CASE REPORT FORM

Participant number: _____

BASELINE DATA

SOCIODEMOGRAPHIC FEATURES:

- **Birth date: _____ /_____ /_____**
- **Gender:** Male ☐ Female ☐
- **Maximum education grade finished: _____**
- **Labour situation:**

Student ☐ Unemployed ☐ Employed ☐
Pensioner ☐ Work absence for illness ☐

FAMILY HISTORY: *(first/second degree)*

☐ Psychosis ☐ Depression
☐ Bipolar disorder ☐ Completed suicide

PERSONAL PAST PSYCHIATRIC HISTORY:

☐ Attention deficit-hyperactivity disorder
☐ Post-traumatic stress disorder
☐ Depression
☐ Anxiety
☐ Alcohol misuse (abuse or dependence)
☐ Substance misuse (abuse or dependence)
  - Type of substance: _____

FIRST EPISODE OF PSYCHOSIS - CLINICAL FEATURES:

- **Intelligence quotient: _____**
- **Age at psychosis onset:_____**
- **Duration of untreated psychosis:_____**
- **Premorbid functioning (PAS score):_____**
- **PANSS score: _____**
- **HDRS score: _____**
- **Provisional diagnosis: _____**

COMORBIDITIES:

☐ Attention deficit-hyperactivity disorder
☐ Post-traumatic stress disorder

- ☐ Depression
- ☐ Anxiety
- ☐ Alcohol misuse (abuse or dependence)
- ☐ Substance misuse (abuse or dependence)
  - Type of substance: _____
- ☐ Bipolar disorder

SUICIDAL BEHAVIOUR PRIOR TO PSYCHOSIS ONSET: Yes ☐ No ☐

- **MINI (section C) score: _____**

HISTORY OF CHILDHOOD TRAUMA: Yes ☐ No ☐

- **Type of childhood trauma experienced:**

  Physical abuse ☐ Emotional abuse ☐ Sexual abuse ☐

  Physical neglect ☐ Emotional neglect ☐

  Other :_____

- **CTQ-SF score: _____**

FOLLOW-UP DATA

DIAGNOSTIC OUTCOME ACCORDING TO THE DSM-V CRITERIA: ***(one year after psychosis onset)***

PSYCHOTIC DISORDERS	AFFECTIVE PSYCHOSES
☐ **Schizophrenia** ☐ **Schizotypal (personality) disorder** ☐ **Delusional disorder** ☐ **Brief psychotic disorder** ☐ **Schizophreniform disorder** ☐ **Schizoaffective disorder** ☐ **Substance-induced psychotic disorder** ☐ **Other specified schizophrenia spectrum and other psychotic disorder** ☐ **Unspecified schizophrenia spectrum and other psychotic disorder**	☐ **Major depressive disorder** ☐ **Bipolar disorder**

OTHER FOLLOW-UP DATA:

HISTORY OF CHILDHOOD TRAUMA

Yes ☐ No ☐

- **Type of childhood trauma experienced:**
  - ☐ Physical abuse
  - ☐ Emotional abuse
  - ☐ Sexual abuse
  - ☐ Physical neglect
  - ☐ Emotional neglect

  Other:_____
- **CTQ-SF score: _____**

1st year	
2nd year	
3rd year	
4th year	
5th year	

SUICIDALITY

- ☐ None
- ☐ Passive ideation
- ☐ Planning
- ☐ Attempts
- ☐ Completed suicide

MINI (section C) score: _____
HDRS (item 3) score: _____

1st year	
2nd year	
3rd year	
4th year	
5th year	

ALCOHOL MISUSE

- ☐ Absent
- ☐ Abuse
- ☐ Dependence

1st year	
2nd year	
3rd year	
4th year	
5th year	

SUBSTANCE MISUSE

- ☐ Absent
- ☐ Abuse
- ☐ Dependence

Type of substance: _____

1st year	
2nd year	
3rd year	
4th year	
5th year	

DEPRESSION

☐ Yes ☐ No

HDRS score: _____

1st year	
2nd year	
3rd year	
4th year	
5th year	

POST-TRAUMATIC STRESS DISORDER

☐ Yes ☐ No

1st year	
2nd year	
3rd year	
4th year	
5th year	

ANXIETY

☐ Yes ☐ No

1st year	
2nd year	
3rd year	
4th year	
5th year	

ATTENTION DEFICIT-HYPERACTIVITY DISORDER ☐ Yes ☐ No	**1st year**	
	2nd year	
	3rd year	
	4th year	
	5th year	
COMPLIANCE TO TREATMENT ☐ Yes ☐ No	**1st year**	
	2nd year	
	3rd year	
	4th year	
	5th year	