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**Antecedents and predictors of aggression and violence in  
first-episode psychosis disorders - is there a relationship  
with substance use?**

**By**

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**The thesis is submitted to University College Dublin in fulfilment of the  
requirements for the degree of Doctorate in Medicine.**

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## Table of contents

	Page
1. The medical and societal importance of violence in severe mental illness	1
1.2. Epidemiology of Violence in the General Population and Individuals with Severe Mental Illness.	4
1.2.1. Community-based epidemiological studies and societal impacts	4
1.2.2. Prevalence studies of aggression and violence among individuals with severe mental illness: challenges of differing methodologies	5
1.2.3. Prevalence studies of severe mental illness in forensic settings	8
1.2.4. Prevalence studies of aggression and violence in substance use in the general population.	9
1.3 Psychopathological correlations with aggressive and violent behaviour in severe mental illness	10
1.3.1. Studies confirming an intrinsic link between severe mental illness and aggression and violence	10
1.3.2. Aggression and violence in different diagnostic groups	14
1.3.3. Psychopathological correlations of aggression and violence in severe mental illness	16

1.3.3.1.	Associations between positive negative and other relevant symptoms symptoms, and aggression and violence in clinical and forensic cohorts	17
1.3.3.2.	Lack of insight as a risk factor for aggression and violence	23
1.3.3.3.	Impulsivity as an aetiological factor for aggression and violence in severe mental illness	24
1.4.	The role of sociodemographic factors in aggression and violence among those with severe mental illness	26
1.5.	Gender Differences in Aggression and Violence	30
1.5.1.	Violence - Gender differences in the general population	30
1.5.2.	Gender differences in violence among individuals with severe mental illness	31
1.5.3.	Gender differences in substance abuse and its effect on levels of aggression	33
1.5.4.	Gender differences in victimisation in severe mental illness	34
1.6.	The impact of substance use on violence in severe mental illness	36
1.6.1.	Substance use and violence in the larger population	37
1.6.2.	The potential for violence of commonly used psychoactive substances	39
1.6.3.	Substance use as a risk factor for severe mental illness	46
1.6.4.	The impact of substance use on psychopathology and the progress of severe mental illness	49

1.6.5.	Possible links between younger age of onset of the first episode of psychosis and violence rates	51
1.7.	Discussion - Examining risk factors for aggression and violence in clinical populations is challenging.	53
1.8.	Closing remarks - Research of aggression and violence in severe mental illness raises additional questions	57
2	<b>Objectives, methods, materials, results of the thesis</b>	59
2.1.	Objectives	59
2.2.	Methods	61
2.2.1.	Sample description	61
2.2.2.	Study design	62
2.2.3.	Definition of aggression and violence	62
2.2.4.	Baseline measurements	63
2.2.5.	Materials	67
2.2.6.	Statistical analysis	75
2.2.7.	Ethics	75
2.3.	<b>Results</b>	76
2.3.1.	Sample - socio-demographic characteristics of the cohort	76
2.3.2.	Clinical factors and associations with gender and age	77
2.3.3.	Prevalence rates and gender differences of substance use	78
2.3.4.	Prevalence rates of substance use in comparison to the general population and severe mental illness cohorts	81
2.3.5.	Sociodemographic and clinical correlations of substance use	82
2.3.6.	Prevalence rate of aggression and violence	83
2.3.7.	Comparison of prevalence rates of aggression and violence with previous studies completed in the same geographic catchment area	84

2.3.8.	Statistical associations between aggression-violence and different sociodemographic and clinical variables	85
3.	<b>Discussion</b>	90
3.1.	Hypothesis A	90
	Sociodemographic factors (age, gender, education level, living status, temporal stability of patterns of aggression) show a significant link with levels of aggression	
3.2.	Hypothesis B	95
	Clinical (long duration of untreated psychosis, lack of insight into the illness) and phenomenological (higher positive symptoms of psychosis) characteristics are associated with higher levels of aggressiveness.	
3.3.	Hypothesis C	100
	Substance use significantly correlates with higher aggression and violence levels.	
3.4.	Hypothesis D	107
	A more extended observation period results in higher incident rates of aggression and violence	
4.	<b>Strengths and limitations</b>	108
5.	<b>Conclusions</b>	111
6.	<b>Closing remarks</b>	114
7.	<b>References</b>	115
8.	<b>Appendix</b>	136

## **Abstract**

Aggression and violence are becoming an increasing problem in the healthcare sector as the number of incidents reported in mental health facilities rises. There is still disagreement in the research community about the pathways to aggression and violence in the severely mentally ill. Some researchers argue that the disease plays a role, while others emphasise that different sociodemographic factors, substance use, and victimisation may contribute to this association. There is a lack of clarity about the temporal connection between violence and symptoms. Divergent study designs, setting locations, and different cultural backgrounds contribute to the high heterogeneity of the study results.

The present work aims to examine the characteristics and effects of sociodemographic factors, psychopathology, and substance abuse on aggressive and violent behaviour in a first episode of psychosis cohort, based on an extended observation period of one year consisting of six months prior and after contact with mental health services.

### **Hypotheses**

#### **Hypothesis A**

Sociodemographic factors (age, gender, level of education, marital status) show a significant relationship with the extent of aggression and violence in a cohort with the first episode of psychosis.

#### **Hypothesis B**

Clinical (long duration of untreated psychosis, lack of insight into the illness) and phenomenological (higher positive symptoms of the psychosis, depressive and manic symptoms) characteristics are associated with a higher level of aggressiveness and violence in individuals with first-episode psychosis.

#### **Hypothesis C**

Substance use has significant associations with levels of aggression and violence in individuals with first-episode psychosis.

## Hypothesis D

Levels of aggression are determined by the length of the observation period.

## Methodology

This work aims to present a retrospective examination of aggression and violence in a cohort of 264 individuals from a geographically defined catchment area, presenting with a first episode of psychosis who had detailed clinical and sociodemographic data collected prospectively throughout the study over ten years.

Systematic baseline measurements were performed during study enrolment, which served as the basis for diagnosing the first episode of psychosis.

Psychopathological factors were assessed by a set of rating scales, including positive and negative symptoms of psychosis, affective symptoms, level of insight, duration of untreated psychosis, and global assessment of functioning.

A modified version of the Overt Aggression Scale (MOAS) was used to measure aggression and violence in all retrospectively collected data, including clinical case notes and incident reports, for each study participant over a one-year period.

Statistical analysis of all clinical data collected was conducted to examine the relationship between socio-demographic and psychopathological factors, levels of substance use and the extent of aggression and violence.

## Conclusions

No gender difference in aggression and violence was observed in the first episode of the psychosis cohort.

There was a significant relationship between psychopathological determinants and violence in subjects with higher levels of positive symptoms of psychosis, higher

rates of manic symptoms, lower global functioning scores, and lower depressive scores.

A comprehensive study of different types of substances used concluded that alcohol and stimulants were associated with higher rates of aggression and violence.

An extended study period demonstrated a higher level of aggression and violence compared to previous studies conducted in the same geographically determined catchment area.

"I hereby certify that the submitted work is my own work, was completed while registered as a candidate for Doctorate in Medicine, and I have not obtained a degree elsewhere on the basis of the research presented in this submitted work"

## Acknowledgements

In this regard, I would like to thank the DETECT [Dublin and East Treatment and Early Care Team] team for allowing me to conduct this research under the supervision of Prof Mary Clarke.

DETECT is Ireland's first early intervention team for people who experience the first episode of psychosis and has produced a significant amount of research from its resources. However, the person-centered treatment approach must be recognised in addition to the centre's high-quality research work.

I also appreciate my husband's patience and support during the writing process.

When acts of violence occur, potentially leading to lethal outcomes in extreme circumstances, it is a tragic event for the individuals affected. When an offender has a severe mental illness, the media frequently sensationalises this, exacerbating the existing social stigma and heightening the vulnerability of psychiatric patients to victimisation, as well as the likelihood of aggressive and violent behaviour. Hence, I sincerely dedicate this work to the individuals who have suffered from acts of violence and to those who have been subjected to societal discrimination.

## 1. The medical and societal importance of violence in severe mental illness

The societal role of aggression and violence has been a matter of dispute since ancient times since “spiritualising” violence in ancient Greece redirected its destructive force to a competitive one in sports, philosophy, and arts, which led to our modern civilisation (More, 2010). Greek philosophers had tried to answer several phenomenological questions about aspects of human behaviour and, implicitly, the link between mental illness and violence (Ahonen, 2014).

Aggression and violence are generally considered to be significant causes of social and health challenges. However, the inadequate and unclear understanding of these phenomena creates further hurdles in research and has implications for clinical practice. For instance, the lack of agreed standardised definitions of violence (Fernandes et al., 1999, Crilly et al., 2004, Greydanus et al., 2021) results in difficulty in comparability of the studies due to diverging methodologies (Hegney et al., 2003).

Whether violence is linked to severe mental illness is still debated in the research community (Asnis et al., 1997, Van Dorn et al., 2012, Corrigan and Watson, 2005a, Friedman, 2006).

Over the last few decades, numerous studies have highlighted the elevated prevalence rates of aggression, violence, and violent crime among people with severe mental illness (Fazel et al., 2009). In fact, research suggests that violence against clinical staff is common and attacks on nursing staff affect approximately three-quarters of nursing staff in acute psychiatric units (Iozzino et al., 2015, Keane et al., 2019, Large and Nielsens, 2011).

In the case of psychosis, multiple pathways may contribute to violence, as evidenced by the large variety of reports of violence (Volavka and Citrome, 2008).

One side argues that severe mental illness can contribute to aggression and violence (Arseneault et al., 2000, Elbogen et al., 2016, Fazel et al., 2009, Modestin

and Ammann, 1996, Arboleda-Florez et al., 1998), with studies demonstrating an association between psychosis and delinquent offending (Arseneault et al., 2000).

The other side argues that most people with severe mental illness do not have higher aggression and violence rates than the general population (Appelbaum, 2000). Despite these concerning trends, only 4% of violence is perpetrated by individuals with severe mental illness in the community (Swanson et al., 1990), indicating that most psychiatric patients with a stable mental state do not pose a risk of violence (Rueve and Welton, 2008).

Furthermore, some researchers disagree on the intrinsic nature of the relationship between major mental illness and aggression or violence (Teplin, 1990) and claim that there is limited data in the research to draw any conclusions (Monahan, 1981).

In the 1990s, this debate gained prominence as concerns increased about the potential risk of aggression and violence associated with severe mental disorders. The debate over whether people with such disorders should be hospitalised or integrated into the community increasingly took on a class dimension, with politicians and the public on one side and people with severe mental disorders or their advocates on the other (Taylor and Gunn, 1999). The opinion has changed from the view that major mental illness is not a risk factor for violence (McMahon et al., 2014, Bonta et al., 1998) to a view that people with severe mental illness are more likely to be violent than the general population (Walsh et al., 2002, Whiting et al., 2021). Despite this, it is crucial to recognise that due to the low rates of severe aggression in the severe mental illness population, statistical accuracy and debates on the theoretical framework and clinical risk assessment may have been compromised, which has led to difficulties in researching this topic (Volavka, 2002).

Despite decades of research into the extent to which severe mental illness contributes to aggression and violence, the topic remains controversial, and different conclusions are drawn.

Mental health professionals are challenged to anticipate and manage aggression and violence in those under their care (Stuart, 2003). This may result in legal liability for the healthcare professional and, in some extreme cases, prosecution (Dyer, 2012).

The general population often associates mental illness with aggressive or violent behaviour and dangerousness (Taylor, 2008). Societal stigmatisation of people with mental illness or substance abuse shows no downward trend, as demonstrated in a study which showed that over 60% of US citizens believe that a hypothetical person with schizophrenia would be violent towards others (Pescosolido et al., 2010).

## 1.2 Epidemiology of violence in general versus different patient populations with severe mental illness

It is essential to assess the prevalence rates of violence in the general population and among those with severe mental illness to put the magnitude and impact of this phenomenon into perspective.

Following Resolution WHA 49.25 at the 9th World Health Assembly in 1996, the research community now recognises the importance of violence in public health. This resolution identified violence as a growing public health problem worldwide, recognising the increasing impact of violence on health services worldwide and the adverse impact on health resources and communities (World Health Organisation, 1996).

### 1.2.1 Community-based epidemiological studies and societal impacts

In a World Health Organization (WHO) public health report published in 2000, violence was a leading cause of death for people aged 15 to 44 (Krug et al., 2002).

World Health Organization statistics indicate that in 2002, 2.8% of all deaths were caused by intentional injuries (3.9% of male deaths and 1.7% of female deaths). About half of these deaths were caused by self-harm, a third by violence, and a fifth by war (WHO, 2004).

Geographical differences were highlighted in a 2008 study conducted by the WHO when a focused analysis comparing several United Nations and WHO reports between 1998 and 2008 found that the prevalence of assaults experienced by victims in middle-income countries was 9.1% and 4.1% for high-income countries, respectively in the ten studied years (Wolf et al., 2014). Alcohol use was correlated with self-reported assault rates ( $p < 0.001$ ,  $B = 0.369$ ), suggesting that interventions targeting the reduction of alcohol consumption may reduce violence (Wolf et al., 2014).

The high occurrence of violence directly and indirectly impacts health services and productivity in all sectors of the economy. Theoretical models were formulated for pathways from violent incidents to health impairments, including the impact of post-incident stress on physical and mental health and increased service utilisation (Resnick et al., 1997).

A study published in 2000 to quantify the impact of violence in society found that the cost of nonfatal injuries and deaths caused by violence in the United States alone is more than 64.8 billion dollars. Almost all the costs were attributed to lost productivity (64,4 billion). According to the WHO, it is estimated that the cost of medical care for over 2.5 million injuries resulting from interpersonal violence and self-directed violence is about \$5.6 billion annually (Corso et al., 2007).

#### 1.2.2. Prevalence of aggression and violence among individuals with a first episode of psychosis and severe mental illness: challenges of differing methodologies.

Interestingly, despite the abundance of available literature researching aggression and violence in major mental illnesses, there are few studies on the first episode of psychosis cohorts.

Further scarcity can be observed in the study of trends in the prevalence rates of aggression and violence in FEP cohorts over time.

Outstandingly, one study focused on stability over time was observed in a 15-year comparative study of the same catchment area, which found that the prevalence rates of aggression and violence did not differ significantly in a sample of South Dublin FEP cohorts (Keane et al., 2019). The aggression and violence prevalence rates in the 1995 - 1998 sample were 33 % and 29%, respectively, as measured using the Modified Overt Aggression Scale (MOAS) (Foley et al., 2005). The prevalence rates for aggression (36%) and violence (29%) were the same in the 2010-2013 cohort, based on the same methodology (Keane et al., 2019).

Aggression and violence in first-episode psychosis are characterised by factors similar to those that contribute to violent behaviour in people with chronic mental

illness and the general population (Swanson et al., 2006a). However, violent behaviour may be a symptom of first-episode psychosis, and one potentially modifiable factor, the duration of untreated psychosis, could be an intervention focus that can be adjusted to target this factor (Látalová, 2014).

Different methodological approaches and study designs may lead to variations in reported aggression rates during a first psychotic episode. This theory is supported by evidence from a systematic review and meta-analysis, which included nine studies conducted over 50 years, and found that the prevalence rates of aggression, violence, and attribution to first episodes of psychosis varied widely (Large and Nielssen, 2011). Despite using a systematic measure of violence, the studies included in this analysis had different study designs, including sampling frames [pre-contact, contact, post-contact] and follow-up periods (from 2 weeks (Foley et al., 2005) to 3 years (Milton et al., 2001)), clinical settings (inpatient, outpatient, early intervention team), and different information sources (from the patient only, collateral information, chart review) (Large and Nielssen, 2011).

A study on 168 patients with schizophrenia following their first admission investigated whether they displayed aggressive behaviour against themselves, and others based on the Modified Overt Aggression Rating Scale. It was concluded from the results of the study that 70% of the cases involved aggression, 65% of the cases involved aggression against others, and 21% of the cases involved suicide attempts over the two-year follow-up period. In the hospital setting, there was a 19% rate of violence, with threats against others at 20%, violence against persons at 23%, and violence against objects at 11% (Steinert et al., 1999).

In contrast, significantly lower prevalence rates were reported in another study examining the prevalence and correlations of aggressive behaviour in individuals with initial episodes of psychosis. In this large sample of 495 patients using psychiatric and medical history questionnaires, a prevalence rate of 39.2% for aggressive behaviour at first presentation and 20.8% for violent behaviour was found (Dean et al., 2007).

Researchers have increasingly concluded that early intervention can influence the course of the first episode of psychosis. This population's aggression rates tend to be higher earlier than in the later stages of the disease, according to a meta-analysis that included nine studies published since 1960. In 2010, rates of violence

in the first episodes of psychosis were undoubtedly high compared to the general population. There was an estimated 35% prevalence rate of violence committed by individuals with first-episode psychosis before contact with the service or during the first episode of psychosis, as shown by this analysis (Large and Nielssen, 2011).

The ability to extrapolate results to more prominent groups worldwide and other cultural contexts is limited, and most research has taken place in several developed countries (Salager-Meyer, 2008). This fact is supported by the findings that most of the first-episode studies of psychosis cohorts that analysed the prevalence and correlation of aggression and violence took place in Europe, the UK, Canada, and Australia (Winsper et al., 2013). Therefore, the data obtained may have limited applicability in other parts of the world.

Cross-sectional studies may report different levels of aggression depending on the methodology on temporality between the incident of violence and the presentation to the services in these studies: before/during or after hospitalisation.

Analysing the high rates of violence in inpatient settings is challenging, given the multitude of contextual factors that may affect prevalence results, including the interactions between the treating team and the patient (Walker and Seifert, 1994, McNiel et al., 1988). On the other hand, circular causality may be observed between violence and involuntary treatment status (Foley et al., 2005)

Across the relevant literature, considerable variability in prevalence rates of aggression and violence among individuals with schizophrenia in inpatient settings can be observed, ranging from 10% up to half of the patients (Cornaggia et al., 2011, Zhou et al., 2016, Craig, 1982). Higher prevalence rates were reported among individuals with first-episode psychosis in hospital settings (Lopez-Garcia et al., 2019).

There is also a varied picture in the post-discharge studies regarding the rates of violence among schizophrenia patients compared to the rate of violence in other disorders. According to one study, violence is lower in schizophrenia patients compared to those with other mental disorders post-discharge (Cantwell et al., 1999), a finding that has subsequently been validated in later studies (Appelbaum et al., 2000). Furthermore, it has been shown in other studies that former patients with schizophrenia seem more likely than the general population to engage in physical assault offences, both minor and severe (Soyka et al., 2007).

### 1.2.3. Prevalence studies of severe mental illness among individuals in forensic settings

The link between severe mental illness and violence has been firmly established in the criminal justice system for some time throughout human history (Hodgins, S., 2002), even dating back to ancient Greece (Dvoskin et al., 2020). The defence of “insanity” in severe mental illness is used as a mitigating or aggravating factor in sentencing decisions, which may indicate a high prevalence of the association between severe mental illness and violence (Luetttgen et al., 1998).

Evidence from several cohort studies indicates a significant association between severe mental illness and violence with legal consequences.

Based on the results of a four-month study conducted in Greater London, which involved 1241 men imprisoned for criminal offences, a high frequency of psychiatric conditions was found among the inmates (Taylor and Gunn, 1984). It was estimated that two hundred forty-six of the males (9.0%) had signs and symptoms that indicated a psychiatric disorder, and two hundred thirty-seven (8.6%) had signs and symptoms that indicated that they were in withdrawal from drugs or alcohol. It was also reported that men with schizophrenia committed 29% of nonfatal attacks and 21% of property damage. There was a much greater prevalence of schizophrenia among men convicted of homicide (five (11%) and arson (six (30%)) than would be expected among the overall population (0.1-0.4%) (Taylor and Gunn, 1984).

Similarly, a random sample of male inmates at a male correctional facility showed twice or three times the prevalence of schizophrenia and severe depressive disorders as the general population. When the prevalence rates of schizophrenia in jail inmates were adjusted for demographic variations, they were still two to three times higher prevalence rates in the prison population than their counterparts in the general population (Teplin, 1990).

Another study from another prison population found a similarly high prevalence rate; 25% of the inmates had a history of psychiatric involvement, but it was primarily attributed to substance dependence and personality disorders (Wallace et al., 1998). According to the data, despite these findings, there was an over-

representation of symptoms of severe mental disorders among those with substance abuse disorders (Wallace et al., 1998).

Case-linkage registered studies demonstrated that schizophrenia, particularly with co-morbid substance use, was overrepresented in offenders (Wallace et al., 1998), and other studies confirmed that substance use might increase the level of offending among this population (Mullen et al., 2000).

#### 1.2.4. Prevalence studies of aggression and violence in substance use in the general population.

Positive associations between substance use and violence have been demonstrated in community samples (Chermack and Blow, 2002), as well as among those in the criminal justice system (Wieczorek et al., 1990) and among those who seek treatment for intimate partner violence (Brown et al., 1999, McHugh, 2005, Teten et al., 2009).

Studies of public perceptions of alcohol as a trigger for aggression and violence suggest that most respondents believe alcohol is associated with aggression and that alcohol intoxication would not reduce the perpetrator's responsibility (Paglia and Room, 1998).

Several studies have shown a significant association between aggression and substance use disorders at two to three times the rate compared to the general public (Chermack and Blow, 2002).

Despite relevant literature supporting this positive association between substance use and violence, most alcohol or illicit substance users are not aggressive or violent (Fagan, 1990). The causality between substance use, aggression, and violence is complex, multicausal, and inconclusive (Allen et al., 1997, Fagan, 1993).

Given the complexity of the relationship between severe mental illness, substance use, and violence, there is a need for further research to understand the associations and the nature of causality that can be translated into more effective clinical interventions.

### 1.3 Psychopathological correlations of aggression and violence in severe mental illness

#### 1.3.1 Studies confirming an intrinsic link between severe mental illness and aggression and violence

Several psychiatric illnesses are associated with an increased risk of aggression and violence, according to substantive research literature and this is believed to be more relevant in severe mental illnesses (Girasek et al., 2022). The association between schizophrenia and aggressive and violent behaviour has been studied extensively and demonstrated (Hodgins, 2008, Swanson et al., 1990, Soyka et al., 2007, Cheung et al., 1997, Whiting et al., 2021). Some research groups even emphasise that severe mental illness may be a primary cause of violence (Arseneault et al., 2000, Swanson et al., 1990, Monahan, 1992, Lindqvist and Allebeck, 1990, Whiting et al., 2021).

Other studies, however, conclusively show that most patients with severe mental health problems do not act violently toward others (Appelbaum, 2013), and some studies suggest that a severe mental illness appears not to be an actual primary cause of violent behaviour (Appelbaum et al., 2000). Contrary to earlier study results (Walker and Seifert, 1994), some reports showed low violence rates in inpatient settings (Raja and Azzoni, 2005). These results point toward the importance of other psychosocial co-funding factors.

A recently published systematic review and meta-analysis examined the theoretical and experimental evidence in the literature regarding the association between severe mental illness and aggression and violence. The scale of data included in this meta-analysis is notable as studies published over a four-decade period were included. It confirmed that individuals with schizophrenia spectrum disorders are more likely to engage in violence than those in the general population, with the risk being approximately 4.5 times greater in male patients and ten times greater in female patients, based on pooled risk odds ratio estimates compared to community controls (Whiting et al., 2021). The study's strengths are apparent in its large sample size, which included 51,309 patients diagnosed with schizophrenia

spectrum disorders. To address the great level of variability within the data set, strict criteria were used to narrow the initial collection of 13,143 articles with a focus on aggression and violence in severe mental illness to a final selection of 24 articles for analysis (Whiting et al., 2021). The focus was on schizophrenia spectrum disorders in this study, with affective, drug-induced, and organic psychoses being excluded.

A definition of violence was used to include interpersonal violence ranging from physical assault to severe crimes such as homicide, sexual assault, and arson.

Subgroup data were analysed to examine factors contributing to high heterogeneity, such as substance use disorder comorbidity, geographic location, study design and quality, control group and sample size, and outcome measures. Newcastle-Ottawa Quality Assessment Scale was utilised to ensure the quality of the research was assessed using the. Only studies that scored seven or more out of nine were included.

This study included studies of different methodologies, such as outcome periods and ascertainment of violent incidents, and used registries or self-reports as sources of information. The samples demonstrated many forms of contact with services, including community and hospital samples. The study found a fundamental link between aggressive acts and people diagnosed with schizophrenia spectrum disorders, as opposed to control samples.

The limitations of this substantive meta-analysis may be attributed to the differences in methodologies of the included research studies leading to higher heterogeneity, despite an effort by the research team to address this with strict inclusion criteria. This highlights the lack of research studies conducted using consistent and similar procedures and methodologies, affecting different studies' comparability.

Likewise, existing data are unreliable and often biased due to the use of different definitions of aggressiveness and violence. Before conducting a study, a precise and consensus-based definition of aggression and violence must be established (Rippon, 2000).

The intrinsic nature of the association between severe mental illness and violence has also been shown in other studies. One study found that people with severe

mental illness engage in violence more often and earlier than people without severe mental illness or those with similar sociodemographic, age, and gender characteristics (Modestin and Ammann, 1996).

Similar results have been documented among women with severe mental illness (Lindqvist and Allebeck, 1990), raising the question of gender disparity when the associations of aggression and violence with severe mental illnesses are examined.

Recent studies show that the associations between mental illness and violence are more complex than previously thought (Adams and Yanos, 2020).

Examining the nature of the association between aggressive behaviour and psychopathological measures could help improve the prediction of aggression in mental health settings, with important implications for accurately identifying aggression (Amore et al., 2008).

At various phases of severe mental illness, numerous studies consistently document a substantial correlation between psychotic symptoms and the likelihood of aggressive or violent behaviour. Nevertheless, the nature of this association with a particular psychotic symptom remains indeterminate (Junginger, 1996).

Other studies have emphasised that nonspecific symptoms such as perceived threats to others, loss of interest, self-neglect, and attacking others may precede the onset of schizophrenia (Bhugra et al., 2000), which may underline the intimate association between aggression and the psychiatric condition.

In high-risk psychosis patients, violent thoughts and rage before psychotic symptoms may reveal underlying psychotic symptoms and predict aggression and violence (Hutton et al., 2012). However, other non-psychotic psychopathological symptoms may contribute to aggressive and violent behaviour, such as harmful cognitive content and anxiety (Marshall et al., 2016).

The link between severe mental illness and violence may be associated with distinct illness-related factors in every stage of the illness progression; however, several studies demonstrated that mainly first-episode psychosis carries a significant risk of aggressive behaviour (Humphreys et al., 1992, Large and Nielssen, 2011, Winsper et al., 2013).

In another research it has been demonstrated too that persons experiencing their initial episode of psychosis are more likely to engage in violent criminal behaviour before their first admission to a hospital and commencement of treatment (Bo et al., 2011, Large and Nielssen, 2011).

The limited literature of studies that have analysed first-episode psychosis samples has demonstrated an elevated risk of aggression and violence in patients during the pre-contact period (Foley et al., 2005, Coid et al., 2013b, Large and Nielssen, 2011).

These increased rates were demonstrated in a systematic review and meta-analysis, including multiple studies, which found that the prevalence data for perpetrated violence in first-episode psychosis was 34.5%, serious violence was 16.6%, and homicide was 0.6% (Large and Nielssen, 2011). The relevant research data also show that rates of violence do not decrease significantly after contact with services, according to a systemic review that includes fifteen studies (Winsper et al., 2013).

Follow-up studies provide insight into the correlation between aggression and violence in the latter stages of severe mental illness. A prospective observational study suggests that pharmaceutical treatment and other sociodemographic factors may reduce violence rates in advanced chronic severe mental illness, as demonstrated in a prospective study of 179 first-episode psychosis patients with a 10-year follow-up. The level of violence during the period in which 15% of patients self-reported engaging in some form of threats or physical violence was shown to decrease behaviour significantly in the extended follow-up period (Langeveld et al., 2014). This study is the first to use a long-term follow-up technique, spanning baseline, one year, two years, five years, and ten years, to explore the associations between psychopathology, aggression, and violence in a cohort of individuals experiencing their first episode of psychosis. Remarkably, the level of violence in the community has reached a point where it is comparable to the overall violence rates in the general population. This could be attributed to the treatment and interventions provided to those with severe mental illness.

Conversely, the use of illegal substances (OR = 3.70; 95% CI: 1,399.87; p = 0.009) and the presence of active psychotic symptoms (OR = 0.21; 95% CI: 0.087,632; p = 0.003) were found to be associated with aggression (Langeveld et al., 2014).

The primary constraint of this study was the reliance on self-reports for data collection on hostility and violence.

### 1.3.2 . Aggression and violence in different diagnostic groups

Aggressive behaviour has been associated with schizophrenia, mood disorders, substance use disorders, organic brain syndrome, neurocognitive disorders, and personality disorders from the perspective of diagnostic categories (Junginger and McGuire, 2004). Data from previous studies suggest that prevalence rates of violence are increasing among individuals with multiple psychiatric diagnoses (Swanson et al., 1990).

Individuals with schizophrenia, as previously hypothesised, do not form a homogeneous group (Slade and Cooper, 1979). Many clinical factors were linked with an increase in violent behaviour among individuals with schizophrenia, such as the presence of active psychotic symptoms (Taylor, 1985), angry affect (Coid et al., 2013b, Reagu et al., 2013), trauma (Bosqui et al., 2014), and untreated persecutory symptoms (Keers et al., 2014). On the other hand, a multinational study examining the Determinants of Outcomes of Severe Mental Disorders (DOSMD), which included centres from several different countries, concluded that a history of violence was strongly associated with positive symptoms of psychosis, such as excitement and auditory hallucinations, and alcohol use disorder (Volavka et al., 1997).

Based on existing theories, violence in schizophrenia may be related to at least three different aetiological associations: psychopathological factors, impulsivity, and co-morbid psychopathic personality traits (Volavka and Citrome, 2008, Large and Nielssen, 2011, Witt et al., 2013).

Mood disorders are associated with high levels of aggression (Corrigan and Watson, 2005b), particularly bipolar affective disorders during manic episodes (Yesavage, 1983) in clinical settings (Raja and Azzoni, 2005). However, a high risk of aggression and violence was also reported in those in remission (Volavka, 2013).

According to a recent study, people with schizophrenia spectrum disorder were more likely to exhibit aggressive behaviour than those with bipolar disorder. The study confirmed that schizophrenia had a higher risk of aggression and violence than people with bipolar disorder who had recently developed a manic episode and

a lower risk of aggression and violence than people with bipolar disorder who had recently had a mixed episode (Blanco et al., 2018). Self-directed aggression was primarily described as a form of aggression in depressive affective disorders (Dutton and Karakanta, 2013).

Elevated suicidal risk had been described in the first episode of psychosis (Dutta et al., 2011) along with raised prevalence of deliberate self-harm in the period of pre-contact with the services (Harvey et al., 2008).

In non-affective psychotic disorders, it was observed that a significant portion of the violent behaviour occurred during psychotic episodes, suggesting a link between psychopathology and violent behaviour (Volavka et al., 1997). Some studies reported a four times relative risk of aggression and violence during a psychotic episode compared with the prevalence rate in the general population (Swanson et al., 1990, Steinert et al., 1999).

The findings of an extensive meta-analysis involving 110 studies on a cohort of individuals with different severe mental disorders, including a total of 45,533 participants, showed that 8,439 individuals (18.5%) exhibited violent behaviour. Among the participants, 39,995 people (87.8%) were diagnosed with schizophrenia, 209 people (0.4%) had bipolar disorder, and 5,329 people (11.8%) had other psychoses. The variables that were considered dynamic factors, or factors that can be modified, include hostile behaviour, recent substance misuse, non-adherence with psychological therapy ( $p < 0.001$ ), lower impulse control scores, recent substance abuse, recent alcohol misuse ( $p < 0.01$ ), and non-adherence with treatment ( $p$ -value 0.05). Criminal past was one of the most influential factors among the limited set of static traits. The correlations remained mostly unchanged when the outcomes were limited to serious violence (Witt et al., 2013).

In neurodevelopmental disorders, including intellectual disability, aggressive behaviour is the primary reason for referral to specialised services (Tenneij et al., 2009). It was associated with negative consequences on the quality of life for individuals with learning disabilities and their caregivers (Akker et al., 2021).

Similarly, aggressive behaviour was found to be the leading cause of hospitalisation in neurocognitive disorders, especially in moderate and severe forms (Takacs et al., 2015). One study reported that prevalence rates of aggression and violence

showed a three-fold increase in severe neurocognitive disorders due to Alzheimer's disease compared to mild neurocognitive disorders (Yu et al., 2019).

The literature provides ample evidence indicating that substance use significantly raises the rates of hostility and violence (Iro et al., 2011, Liakoni et al., 2018, Lindqvist and Allebeck, 1990, Lipsky et al., 2005, McGinty et al., 2016, Norström and Pape, 2010), which is linked with intoxication, withdrawal, or psychopathological correlations secondary to substance use (Boles and Miotto, 2003).

### 1.3.3. Psychopathological correlations of aggression and violence in severe mental illness

Overwhelmingly evidence has found that the level of aggression and violence correlates with psychopathology (Bobes et al., 2009, Markiewicz et al., 2020), and often results in more prolonged hospital treatment and a higher rehospitalisation rate (Wehring and Carpenter, 2011, Greenfield et al., 1989).

However, the process of establishing links between psychosis and violence is significantly hampered by the lack of consensus in defining these phenomena, leading to divergent research methodologies. Therefore, it seems more appropriate to focus on correlations based on psychopathological elements rather than on heterogeneously defined syndrome categories (Douglas et al., 2009, Bo et al., 2011).

Additionally, examining the relationship between psychotic symptoms and violence may be influenced by the possibility of symptoms being under-reported or not recorded. For example, examining the relationship between violent command hallucinations and violence can illustrate some critical aspects of the repeatedly found methodological difficulties in this area of research. Some researchers found that clinical staff in an inpatient forensic unit missed the occurrence of command hallucinations in nearly 50% of their sample (Rogers et al., 1990).

Comparably, a study including 141 outpatient medical records found that 27% of patients had not reported their command hallucinations to the treating physician (Zisook et al., 1995).

Likewise, it is essential to distinguish “premeditated violence” from “reactive aggression”, also known as impulsive aggression, which is a form of aggressive behaviour characterised by strong emotions and a lack of control (Stanford et al., 2003). When it comes to aggression and violence in severe mental illnesses, understanding the mechanism between psychopathology and violent acts plays an important role. Negative urgency refers to the tendency to act impulsively when experiencing intense negative emotions, whereas hostile attribution bias is the inclination to perceive others’ ambiguous actions as hostile. Both of these psychological elements are crucial in understanding reactive aggression (Gagnon and Rochat, 2017).

#### 1.3.3.1 Associations between positive, negative and other clinically significant symptoms with aggression and violence in clinical and forensic cohorts

##### 1.3.3.1.1. Associations of positive symptoms with aggression and violence

From a psychopathological perspective, positive symptoms during an acute psychotic episode have been associated with aggression and violence. In a large population-based study, it was documented that when individuals experience paranoid delusions, it typically triggers angry responses, which can subsequently escalate to aggressive and violent behaviour (Coid et al., 2013b), similar to the impact of command hallucinations on instigating aggression and aggression (Zisook et al., 1995).

Furthermore, aggression and violence may be a psychopathological feature of the phenomenology of psychosis before psychotic symptoms appear and, therefore, may play a significant role. This was demonstrated in a study in which violent behaviour and thoughts were observed in 200 people at high clinical risk who developed psychosis in the first year of their two-year longitudinal follow-up. It was found that intrusive and ego-dystonic violent thoughts and mental images were present in a third of the participants (Brucato et al., 2019). The content of these ideas was often very severe, including abuse of one’s own body or using some weapon to hurt others. Violent and suicidal ideas, similar to those experienced by

many people suffering from depression, were often associated with positive symptoms such as suspicion (Brucato et al., 2019). According to another study, individuals at high risk for psychotic symptoms showed that unusual thought content of physical violence against others was described as part of the phenomenology of psychosis (Marshall et al., 2014).

Concerning the content of delusions and their association with aggression and violence, it was found that six delusions were significantly associated with anger, including delusions of espionage, delusional misidentification, and delusions that the familiar and familiar people one should know are impersonating oneself. In addition, delusions of persecution, delusions of conspiracy, and threat control override were also significantly associated with anger after adjustment (Coid et al., 2013b). The correlation between suspicion and persecution could also be substantially related to anger, which is thought to be one of the possible routes to aggression (Coid et al., 2013b).

Several studies analysed the nature of command hallucinations in the context of aggression and violence. It has been reported that patients were more likely to agree with familiar voices than unfamiliar voices (Junginger, 1990). Similarly, others found an increased likelihood of not responding to voices that patients trusted (Shore et al., 1978).

In addition, it was found that other clinical factors determined compliance with violent commands and the consequences of obedience or disobedience, such as mood state and the pressure and persistence of the voices (Chadwick and Birchwood, 1994). In another study, patients were more likely to obey voices they described as benevolent (Beck-Sander et al., 1997). It was also shown that command hallucinations had a more aggressive and self-punitive content and that 44% of a patient sample with command hallucinations reported responding to hallucinatory commands with unquestioning obedience (Rogers et al., 1990).

In contrast, other researchers claim that command hallucinations rarely affect the behaviour of those who experience them (Hellerstein et al., 1987). Similarly, it has been noted that where significant positive associations have been shown between hallucinations and violence when associated with other psychotic symptoms, a violent-escalating interaction between delusions and hallucinations has been suggested by others (Swanson et al., 1996).

Several studies indicate that non-delusional hallucinations appear to have minimal violent effects (Taylor et al., 1998).

Nevertheless, some studies suggest that patients with violent command hallucinations are more likely than patients with other types of hallucinations to experience nonpsychotic symptoms such as self-blame (Rogers et al., 1990), depersonalization (Kasper et al., 1996), or a lack of psychomotor retardation (Rogers et al., 1990).

Similarly to clinical cohorts, significant correlations were found between positive symptoms and aggression and violence in forensic patient populations. In a study including 287 forensic patients, command hallucinations, threat control override symptoms, and Capgras syndrome persisted as independent significant risk variables that distinguished acute severe or lethal violence from less severe violence, with increased risk (OR) ranging between 2.35 and 3.58. The clinical risk variables' close temporal proximity may have been the significant factor contributing to the occurrence of such violence (Chan and Shehtman, 2019).

#### 1.3.3.1.2. Associations of negative symptoms with aggression and violence

The moderating effect of blunted affect against violence was debated in the relevant literature, implying a protective mechanism that inhibits the transition to increased intensity of positive symptoms. This theory was demonstrated in a study examining the effects of shifting positive and negative symptoms (Coid et al., 2018). All positive symptoms were associated with violence, even after controlling for demographic covariates and primary diagnosis. After removing the scores for distrust and persecution, negative scores did not appear to be a risk factor for violence (OR = 0.94, 95% CI = 0.881.00,  $p = 0.050$ ). There was a correlation between aggressiveness and shifts in the symptom profile, characterised by increased positive symptoms. The pattern of negative symptoms was relatively similar to that of positive symptoms.

Even if an increase in negative symptoms was associated with a protective effect against violence, the protective effect was only determined after the positive symptoms had been controlled. An increase in anger seemed to play a significant role in expressing violence.

According to the results, suspicion/persecution was not a major factor in explaining the link between anger and violence (Coid et al., 2018).

#### 1.3.3.1.3. Associations of clinically important phenomena with aggression and violence that are not positive or negative symptoms

Several other psychopathological risk factors were associated with aggression and violence in severe mental illness, such as hostility (Kay et al., 1989), lack of insight (Foley et al., 2005) absence of negative symptoms, impulsivity, lack of cooperation, conceptual disorganisation, and social avoidance (Cheung et al., 1997). In addition, in the first episode of psychosis, negative affect (OR = 3.52), and long duration of untreated psychosis (OR = 1.56) were associated with aggressive and violent behaviour before contact with services: (Large and Nielsen, 2011).

A model that attempted to identify predictors and mediators of trait anger across a psychotic spectrum examined the interrelationships between attachment style, paranoia, and social cognition. It was shown that attachment avoidance, paranoia, and hostile attributions all showed a significant relationship with anger, suggesting the need for interventions aimed at reducing paranoia (Darrell-Berry et al., 2017).

Several studies have suggested that social cognition and metacognition may be risk factors for aggressive, violent behaviour, as revealed by a small study that compared healthy control groups to patients with various mental health issues, including some with forensic backgrounds. Forensic patients had significantly lower cognitive and metacognitive abilities (De Jong et al., 2018).

Aside from positive symptoms and hostility, other clinical variables have been demonstrated to have positive associations with aggressive behaviour, arousal, suspiciousness, lack of attention, uncooperativeness, impulse control, preoccupation, conceptual disorganisation, and social avoidance (Cheung et al., 1997, Colasanti et al., 2010).

In forensic patients, additional clinical factors such as personality traits may contribute to aggression and violence. This issue was addressed by a study examining the potential violent pathways in schizophrenia related to antisocial traits, finding that individuals who developed the disorder early shared personality

traits similar to non-psychotic offenders (Van Dongen et al., 2015). There was a significant difference in behavioural concern in the early-onset psychosis group compared to the late-onset psychosis group. Late starters and first-time offenders were more likely to have positive psychotic symptoms after being diagnosed with psychosis. In addition, psychotic offenders who began committing offences after diagnosis were more likely to have had psychotic symptoms than non-offenders with psychosis, particularly concerning delusions of grandeur and paranoia (Van Dongen et al., 2015)

#### 1.3.3.1.4. The role of rating scales in assessing psychopathology and associations with aggression and violence

Standardised rating scales increase psychopathological symptom evaluation validity and reliability, particularly observer-rated scales (Moeller, 2009). The use of validated measurement scales is paramount in assessing the association between psychopathology and violent incidents.

Based on validated measurement scales, multiple cohort studies showed that positive symptoms related to a psychotic illness are significantly associated with aggression and violence.

In a study examining predictors of violence among acute psychiatric patients, physical assaultiveness prior to and during hospitalisation was strongly associated with higher total scores on the Brief Psychosocial Rating Scale (BPRS) and more severe positive symptoms (Amore et al., 2008). Higher BPRS scores for hostility-suspiciousness indicated worsening aggressive conduct, from verbal to physical (Amore et al., 2008).

Similarly, aggressive and violent patients reportedly had significantly more positive symptoms as measured by the Positive and Negative Syndrome Scale (PANSS), higher scores on the PANSS Psychopathology Scale overall, and less insight into the condition in another study. After logistic regression to differentiate between violent and non-violent patients, clinical characteristics were better predictors of violence on hospital admission than sociodemographic variables. Insight into psychotic symptoms was predicted to be linked with non-violence in schizophrenic patients (Arango et al., 1999).

These results are supported by evidence from a relatively recent meta-analysis that found that a higher total score on the Positive and Negative Symptom Scale (PANSS) (OR=1.5, 95% CI 1.02-2.2, z-score=2.2 ) and global symptom score (OR 1.7, 95% CI 1.12-2.6, z=2.4) were associated with aggression and violence (Witt et al., 2013). In terms of positive symptoms, violence was associated with higher levels of excitement (OR= 1.6, 95% CI 1.0-2.6, z= 2.1) and positive symptoms (OR= 1.2, 95% CI 1.0-1.5, z=1.8). Neither of the factors associated with negative symptomatology was significantly associated with violence (Witt et al., 2013).

Apart from positive symptoms, one of the strongest associations with manifestations of physical aggression is hostility. This symptom is associated with schizophrenia and is measured as one of the items of the Positive-Negative Syndrome Scale (PANSS) (Kay et al., 1989).

A hostility scale assesses the verbal and nonverbal manifestations of anger and resentment. The hostility item is scored on a scale of 1 to 7, where 1 indicates no hostility, while 7 indicates excessive hostility, defined as an excessive uncooperating attitude that limits other interactions or one or more instances of violent violence against others. When a patient appears to have a guarded or, at times, extremely distrustful attitude, but his or her ideas, interactions, and behaviours remain unaffected, a score of 3 will be given (Kay et al., 1987).

An increase in aggressive behaviour is associated with an increase in hostility rating: in the CATIE trial, every point increase on the seven-point hostility scale increased the likelihood of significant aggression by 1.65 (P = 0.001)(Swanson et al., 2006a). There is, however, a possibility that subjects may still have a clinically significant hostility rating even if they do not make use of physical violence during the assessment period.

As opposed to retrospective studies, prospective empirical studies are more likely to accurately show a temporal relationship between psychopathology and incidents of aggression and violence. A prospective, naturalistic, observational study of 183 patients with Psychotic Disorders consecutively admitted to a psychiatric ward during the relapse phase found that the symptoms of acute psychosis disorder clustered together in four distinct domains. The variables were categorised as "Excitement/Activation," "Positive symptoms," "Negative symptoms," and "Depression/Anxiety." The variable most related to the prevalence of violent

behaviour and the severity of psychopathological symptoms at discharge was excitement/activation (Colasanti et al., 2010).

Among an unselected inpatient population, a prospective study identified the following clinical risk factors for hostile or violent behaviour: lower current and prior year GAF [Global Assessment of Functioning] scores, increased hostility on BPRS [Brief Psychiatric Rating Scale], higher scores on SAPS [Scale for the Assessment of Positive Symptoms], and on CGI [Clinical Global Impression] scales, as well as a lower BPRS anxiety-depression score (Raja and Azzoni, 2005). Some factors are repeatedly associated with hostile and violent behaviour, such as a low current GAF score (aggressive behaviour is a critical criterion for assigning a low GAF score to a patient), higher BPRS hostility, and SAPS scores (some SAPS items refer to hostility and aggressive behaviour). In contrast, others (e.g., the increased levels of psychoactive drug usage) may reflect a need to manage hostility and violence (Raja and Azzoni, 2005).

#### 1.3.3.2 Lack of insight as a risk factor for aggression and violence

In schizophrenia, the assessment of insight into the condition can be complex since the patient may recognize the illness verbally but act as if he or she is unaware of the illness. For instance, the patients might be unable to distinguish between their misperceptions or not understand their narratives' validity. Accordingly, Beck's concept of "clinical insight" refers to a patient's verbal admission that they are ill, which often does not reflect exactly how they see themselves as ill. Nevertheless, by recognising the unconscious biases of the patient that may lead to biased perceptions and beliefs, Beck called this "cognitive intuition", which has proved helpful in explaining the patient's actual thinking (Beck, 2004).

A critical phenomenological construct of insight has emerged as a relevant outcome indicator. This process entails being able to recognise an illness by identifying symptoms that correspond to it and acknowledging why that illness needs to be treated. A surprising lack of research specifically examined the significance and patterns of insight impairments among individuals with schizophrenia. Some research has indicated that aggressive patients had lower

insight than non-violent patients (Arango et al., 1999, Buckley et al., 2004); however, others have not discovered this link (Lincoln and Hodgins, 2008, Yen et al., 2002). A recent meta-analysis showed that violence was strongly associated with a lack of insight (OR 2.7, 95 % CI 1.4 - 5.2,  $z = 2.9$ ) (Witt et al., 2013). Others also confirmed that apart from the role of severe mental illness the lack of insight and substance misuse further exacerbate this risk, often present before any treatment or clinical intervention is sought (Langeveld et al., 2014, Coid et al., 2013a).

#### 1.3.3.3 Impulsivity as an aetiological factor for aggression and violence in severe mental illness

Individuals who struggle to control their impulsivity find it difficult to regulate or inhibit their actions (Logan et al., 1997). Among individuals with psychosis and other severe mental illnesses, impulsivity has been a critical component of aggression and violence (Hoptman et al., 2014) (Witt et al., 2013).

Researchers began operationalising impulsivity as a multidimensional concept, including several domains, that could be better utilised to predict aggression and violence (Cyders and Smith, 2007).

It is believed that urgency, or emotionally related impulsivity, which refers to the propensity toward immediate action when strong emotions are present, contributes to aggression and violence in people with psychosis (Hoptman and Ahmed, 2016) (Whiteside and Lynam, 2001). The aggressive response that arises from negative emotions is called a negative urgency, while that which results from positive emotions is referred to as a positive urgency (Cyders and Smith, 2007, Hoptman et al., 2014). It has been estimated that 18% of aggressive incidents that cannot be explained by psychopathology resulted from negative urgency, according to a study involving 33 people with schizophrenia or schizoaffective disorders and 31 controls (Hoptman et al., 2014). Even though aggression and violence are multifactorial and have many variables influencing them, there is still a significant role that negative urgency may play when it is associated with this phenomenon (Hoptman and Ahmed, 2016) (Volavka and Citrome, 2008).

Therefore, in cases of emotion dysregulation and heightened impulsivity, negative urgency may be particularly noticeable as a symptom associated with greater aggression and violence among individuals with psychosis and other severe mental illnesses. In addition to hostile bias in attribution, there is a perception of social rejection, which has also been linked to urgency (Chester et al., 2017) (Gagnon and Rochat, 2017).

Study results showed that people with high levels of negative urgency displayed impulsive behaviour when faced with social rejection, according to research conducted with 363 people (Chester et al., 2017).

These findings are consistent with previous research (Ammerman et al., 2015) (Wilkowski and Robinson, 2008), indicating that individuals with severe mental illness may have difficulties coping effectively with increased negative affect and dysfunctional thoughts, which may result in aggression and violence (Gagnon and Rochat, 2017).

#### 1.4 The role of sociodemographic factors in aggression and violence among those with severe mental illness

Throughout the second half of the twentieth century, an approach shift emerged from the findings of new studies concerning the relationship between social problems and violence. Some researchers suggest that severe mental illness alone does not predict future violence.

Determining the role of predictors for aggression and violence in the clinical and general population is a difficult task due to the multicausality of this phenomenon. Despite a large body of literature, the potential role of mental illness in increasing the risk of aggression and violence is still debated. It tends to be associated with historical (past violence, juvenile detention, physical abuse, parental arrest record), clinical (substance abuse, perceived threats), dispositional (age, sex, income), and contextual (recent divorce, unemployment, victimisation) indicators (Elbogen and Johnson, 2009).

The role of socio-demographic risk factors of violent behaviour in severe mental illness has been demonstrated in a large body of literature (Swanson et al., 1990, Modestin and Ammann, 1996, Hodgins. S., 2002), which includes social deprivation (Swanson et al., 1990, Modestin and Ammann, 1996), single marital status (Milton et al., 2001), younger age (Modestin and Ammann, 1996, Swanson et al., 1990), and male gender (Cauffman et al., 2017).

Re-analysing data from the NESARC (National Epidemiological Survey on Alcohol and Related Conditions) in a large study concluded that mental illness and violence are mainly caused by the accumulation of risk factors of various types, including historical (previous incidents of violence, juvenile detention, physical abuse, parental arrest records), clinical (substance abuse, perceived threat), and dispositional (age, gender) factors (Van Dorn et al., 2012).

Besides the clinical and demographic determinants, social factors also may have significant associations with aggression and violence (Amore et al., 2008). While psychotic symptoms can contribute to violence, many other factors are likely to have a relevant role in triggering violence among people with severe mental illness, such as treatment adherence, medication side effect profile, adverse social

environment, adverse family history, genotype, and substance use (Lamsma and Harte, 2015).

Some authors argue that apart from individuals considered at high risk for violence, the presence of psychotic symptoms is not a predictor of aggressive and violent behaviour; thus, anger and psychosocial factors should be included in any interventions to reduce violence (Nolan et al., 2003, Adams and Yanos, 2020).

A meta-analysis of the first episode of a psychosis cohort demonstrated that young age, male gender and lower level of education proved to be significantly associated with higher rates of aggression and violence (Large and Nielssen, 2011). However, these correlations were not found in populations with attenuated psychotic symptoms (Marshall et al., 2016).

Living status may significantly predict aggressive and violent behaviour, as confirmed in a cross-sectional study of acute inpatients. In this sample, being male and living with others significantly predicted violence (Amore et al., 2008).

Several studies have also shown that substance abuse as a socio-demographic factor plays a significant role in severe mental illness and its relationship with violence (Elbogen and Johnson, 2009, Scott et al., 1998, Soyka, 1994), amplifying the existent risk of violence perpetration. A meta-analysis including 20 studies concludes that when alcohol and substance abuse are comorbid, the risk of violence is substantially augmented, with increased odds ratios between three and twenty-five on pooled data (Fazel et al., 2009).

The interlink between alcohol misuse, violent behaviour and various socio-economic factors such as lower education attainment (Boden et al., 2012) and unemployment (Smith et al., 2012) has been described. However, it remains unclear to what extent the association between co-occurring substance use and severe mental illness can be explained by the high prevalence of substance use among persons with severe mental illness (Bo et al., 2011).

It is also worth noting that gender differences in substance use and preferences for different types of substances in different age groups may add to the complexity of the association between severe mental illness and substance use, as well as violence, aggression, and aggression-related social factors.

In addition to clinical factors, stigmatisation might play an essential role since many studies have shown direct correlations between victimisation and perpetration (Choe et al., 2008).

Victimisation and perpetration of violence in severe mental illness were found to be associated in multiple studies (Albers et al., 2018, Choe et al., 2008, Labrum et al., 2018, Langeveld et al., 2018), and the impact of disproportionate media reports of violent acts on their statistical risk (Atanasova et al., 2019) may lead to the preservation of stigmatisation and repeated victimisation (De Vries et al., 2019).

The literature documented well that stigmatisation and victimisation might increase violence risk (Labrum et al., 2018). Several authors have highlighted that public perceptions of individuals with severe mental illness have been negatively distorted. Severe mental illness, particularly psychosis, has been associated with aggressive and violent behaviours and a risk of harm (Taylor, 2008, Varshney et al., 2016, Pescosolido et al., 2010, Steadman et al., 1998).

As a result of media coverage of mental illness being frequently dominated by violence and crime, the media repeatedly reinforces the negative public perception of mental illness (Wehring and Carpenter, 2011, Corrigan et al., 2005). When media reports on violent crimes committed by people with severe mental illnesses reported in mass media, it adds to the stigma and rejection of all people with severe mental illnesses.

Based on a review study of empirical studies published in the U.S. since 1990, with emphasis on the perpetration of violence and the victimisation of individuals with severe mental illness, the authors concluded that combined studies of inpatients and outpatients reported 12 - 22% of perpetrated violence and 35% victimisation of people with severe mental illness within the past 12 months. (Choe et al., 2008), which underlines the importance of victimisation.

It was found in another meta-analysis that the victimisation rates among people with severe mental illness were four to six times greater than those in the general population (De Vries et al., 2019). There is, however, a reciprocal relationship between perpetration and victimisation, as adverse impacts on social functioning, employment, and housing may increase the risk of violent behaviour (Labrum et al., 2018). Violent victimisation may have long-term adverse implications in

persons with severe mental illness (Latalova et al., 2014). An analysis of prevalence rates of violence to others, violent self-victimisation, and victimisation by others in individuals with severe mental illness found that 58% of the patients had experienced violence at least once, 28% had experienced at least two forms of violence, and 7% had experienced at least three forms of violence in the first year following discharge from hospital (Monahan et al., 2017).

Compared with the general population, the scientific community focuses more on violence perpetrated by individuals with severe mental illness rather than their victimisation, as demonstrated in a review article, which showed a 3:1 ratio between articles published on violence perpetration and victimisation (Choe et al., 2008).

A higher level of victimisation than the perpetration of violence had been reported in association with higher psychopathology scores and substance use at baseline in a patient with schizophrenia (Brekke et al., 2001). On the other hand, continued substance use and unstable housing were associated with a greater likelihood of arrest and poor treatment engagement with multiple arrests (Clark et al., 1999).

## 1.5 Gender differences in aggression and violence

In health research, the notion of gender plays an important role, as stated by the Institute of Medicine in 2001, highlighting the essential truth that "every cell has a sex" (Springer et al., 2012). An analysis of gender differences in violence among patients with severe mental illness would offer us an opportunity to understand the factors contributing to violence among people with mental illness, providing guidance for clinicians as to how to assess risk more accurately, allowing more tailored and specific treatments to be given as well as more effective harm reduction measures.

Different models had been hypothesised concerning the gender differences in the manifestation of schizophrenia (Leung and Chue, 2000) such as neurobiological [effects of the female sex hormones in the later manifestation of the illness, gender-specific vulnerability subtypes of schizophrenia](Roy et al., 2001), and clinical, sociodemographic dimensions [comorbid substance abuse [Sajatovic, 2005 #896](Preston et al., 2002), social dysfunction (Roy et al., 2001), (Simonsen et al., 2007). These models may translate into gender differences in aggression and violence levels in severe mental illness populations.

### 1.5.1 Violence - gender differences in the general population

In the field of social sciences, violence often results in the application of a traditional classification system based primarily on gender, socioeconomic class, age and ethnicity. According to some authors, violence is not evenly distributed in the community; certainly, it is more common among young men from socioeconomically disadvantaged backgrounds (Wästerfors, 2022).

For various measures of aggression, the consensus is that males are more aggressive physically when compared with females in the general population (Bjorkqvist, 2018). It has been reported that males commit far more acts of violence than females in several surveys on both selected and random samples of perpetrators

from communities or criminal justice systems (Swanson et al., 1990, Eron et al., 1994, Monahan and Steadman, 1996, Reiss Jr and Roth, 1994).

When examining the reasons for gender disparity in violence, it was found that men had a slightly increased heritability in depicting violence compared to women (Brendgen et al., 2005). There were several gene variants associated with susceptibility to violent behaviour (Craig and Halton, 2009); however, hormonal and environmental epigenetic factors have also been described (Caspi et al., 2002).

The results of a multinational study of adolescents have found that both sexes have equal rates of certain types of aggression, such as verbal aggression. In addition to gender differences, overall aggression rates also differed significantly between men and women in each group: men engaged in more physical aggression than women, but women used indirect aggression more frequently than men (Karin Österman, 1998), which was conceptualized as social aggression (Cairns et al.) or relational aggression (Crick and Grotpeter, 1995).

In a seven-year prospective study that evaluated the trajectory of violent behaviour in both genders, the results of the study showed that women were less likely to persist in violent behaviour from adolescence into adulthood (25% vs 46%); it appears that social demographics and adult accomplishments were more likely to explain offending behaviours than internal factors like impulse control development (Cauffman et al., 2017).

#### 1.5.2. Gender differences in violence among individuals with severe mental illness

Various studies suggest that severe mental illnesses are decreasing and, in some cases, eliminating the gender disparity in the prevalence of aggressive and violent behaviour among women and men (Krakowski and Czobor, 2004, Lam et al., 2000). Due to the complexity of this phenomenon, however, some authors consider it essential to distinguish between different types of aggression, such as verbal aggression or physical aggression (Krakowski and Czobor, 2004).

According to several studies, in psychiatric emergency rooms and shortly after being admitted to a hospital, statistically speaking, women commit violence at a rate nearly equal to or greater than men (Binder and McNiel, 1990, Lidz et al.,

1993, McNiel and Binder, 1995, Newhill et al., 1995). Similarly, in an unselected birth cohort study, severe mental disorders were associated with a higher likelihood of being involved in violent delinquent behaviours in both genders, but even more so for women (Hodgins, 1992).

A higher prevalence of violence among female psychiatric patients may result from methodological and environmental factors, as theorised in one study (Khalifeh and Dean, 2010). According to this theory, differential interventions in aggression in the case of each gender may lead to disproportionately higher rates reported for women, as male aggression prompted a faster response and was recorded less accurately (Khalifeh and Dean, 2010).

A prospective study examining gender differences in violent behaviour, clinical symptoms, and psychosocial factors showed that gender differences varied depending on the violence's timeframe, setting, and severity. This research also found a high predominance of verbal aggression and threatening behaviour for women in inpatient settings, which was higher in the first treatment period and was significantly reduced subsequently, as compared with men. By contrast, men who physically assaulted others had caused significantly higher injuries than women (Krakowski and Czobor, 2004).

According to another study, a more in-depth analysis of violent incidents found that male subjects experienced a higher prevalence of severe violence involving weapons in the four months before admission to the hospital. In contrast, no gender-related differences were observed when more inclusive measures of violence were used (e.g. threats and fights that did not involve weapons or injuries) (Binder and McNiel, 1990).

An analysis within the correctional institutions of the criminal justice system into motives, behaviour patterns, and gender differences in murder suspects and perpetrators who were diagnosed with psychosis or not revealed that, even though the majority of murderers or perpetrators were male, the relative risk of being diagnosed with psychosis was 2.63 times higher for a female (Hachtel et al., 2021). The higher rate of psychotic disorders among female offenders was replicated in other studies (Putkonen et al., 2001).

Using data from 24 studies that examined violence perpetration outcomes in 15 countries over four decades (N = 51 309 individuals with schizophrenia spectrum

disorders), a recent meta-analysis found significant gender differences in violence perpetration among the female and male populations. Women with schizophrenia spectrum disorders were less likely to commit violence when compared to men with schizophrenia spectrum disorders (Whiting et al., 2021).

### 1.5.3. Gender differences in substance abuse and its effect on levels of aggression in severe mental illness.

Given the data on the impact of substance use on the prevalence rates of violence in general (Schifano et al., 2020), it is critical to consider that comorbid substance use disorders may increase the prevalence rates of aggression and violence in populations with first episodes of psychosis. The health impact of various substances shows differences between the two genders. Males, for example, react differently to alcohol than females, which can be explained by differences in body composition and lower levels of the enzyme alcohol dehydrogenase, which aids in alcohol breakdown. As a result, females tend to become inebriated with less alcohol than males (Mancinelli et al., 2007).

Males report higher rates of substance abuse than females, which might influence the relationship between gender and violence (Erkiran et al., 2006).

Many agree that alcohol and drug use prevalence rates are consistently higher among males than females (Seedat et al., 2009), and this trend is most evident in psychosis samples. (Irving et al., 2021). Additionally, while various psychoactive substances may have different effects on females and males, the vast body of research on substance use remains gender blind (Greaves, 2020).

Gender differences in substance use may play a significant role in the onset of first-episode psychosis. In one sample, a similar age of first use of the substance between males and females was noted apart from cannabis use, which started earlier in males (Arranz et al., 2015a). In addition, in females, the number of substances used did not show any significant impact on the age of the onset of psychosis; however, in males, the number of substances used predicted the earlier onset of psychosis (Arranz et al., 2015a).

Despite frequent reports of substance use among males in the first episode cohort, various studies have shown that major mental illness decreases and eliminates gender disparities in the prevalence rates of violence or patterns of violence (Krakowski and Czobor, 2004).

Differences may translate into different prevalence rates of violence in the two genders, raising the possibility of substance use as an independent factor for aggressive, violent behaviour.

Substance use may further increase the likelihood of criminal victimisation, as demonstrated in a study including 1839 individuals with severe mental illness. This study showed a statistically significant correlation between the number of days these individuals were intoxicated and the number of victimisation incidents such as being a victim of physical violence, being robbed, or being threatened with a weapon (Lam and Rosenheck, 1998).

#### 1.5.4. Gender differences in victimisation in severe mental illness different

Victimisation is a significant concern for those with severe mental illness (Brekke et al., 2001). Remarkably, the literature focuses on perpetration rather than victimisation.

Those suffering from severe mental illnesses have a higher risk of becoming victims of crime than the general population. In those with a history of severe mental illness, the probability of becoming victims of violence is significantly higher than in the general population, with victimisation prevalence rates ranging from 15-45 per cent in the last year to 40-90 per cent throughout a lifetime (Maniglio, 2009) (Choe et al., 2008). According to one study, individuals with a history of severe mental illness hospitalization were three times as likely as their peers who were not assaulted to be readmitted to a hospital for their mental illness in the six months following the assault (Mlada et al., 2021). A significant association was found between criminal victimisation and the severity of symptomatology, substance abuse, homelessness, and forensic history (Maniglio, 2009).

It is important to note that, for some individuals, the roles of both perpetrator and victim are intertwined, complicating this relationship beyond what is readily understood. Professionals in mental health should be aware of all the various patterns of victimisation that occur in communities when assisting patients (Albers et al., 2018).

Concerning gender, victimisation patterns in psychiatric patients are markedly different from those observed in the general population or other patient groups. Several studies have shown that despite both genders being at increased risk of being victims of violence, the relative risk for women with severe mental illness compared to the general population is significantly higher (13-19-fold relative risk increase). In contrast, for men with severe mental illness, the relative risk is 9-11-fold (Khalifeh and Dean, 2010).

Among the general population, young men are the most likely to be victims of physical violence, although women are more likely to suffer from domestic violence and sexual assaults (Walker et al., 2009). Although severe mental illness reduces the gender difference of victimisation due to violent crime, there are limited data available to understand the nature and the background of violence and the gender-related risk factors of violence (Khalifeh and Dean, 2010).

## 1.6 The impact of comorbid substance use on violence in severe mental illness.

Aggressive behaviour, mental illness, and substance abuse may be closely linked in a triadic interaction. Violence in the context of severe mental illness is widely recognised as being significantly predicted by substance abuse (Bo et al., 2011, Erkiran et al., 2006, Soyka, 1994, Walsh et al., 2002). Licit or illicit substances may exacerbate psychiatric symptoms, and incidents of violence may increase due to impaired impulse control, hostility, grandiosity, threat perception, and dysphoria (Volavka and Citrome, 2011).

A study analysing longitudinal chart reviews of numerous patients found that the risk levels varied among different mental illnesses. Specifically, patients with organic brain disorders were found to have a fivefold increased risk of aggressive and violent behaviour and a threefold risk of psychotic episodes. In contrast, patients with substance abuse problems had a twofold increased risk compared to those with affective disorders (Edlinger et al., 2014). However, in another cohort, comorbid presentation of a schizophrenia spectrum disorder with comorbid substance misuse increased the risk of violence more than six-fold compared to the reference category (Edlinger et al., 2014).

Several studies concluded that schizophrenia patients have a high lifetime risk for violent or aggressive behaviour (Soyka, 1994, Walsh et al., 2002, Taylor, 2008); however, case of comorbid substance use may further increase the risk (Schanda et al., 2010, Walsh et al., 2002, Fazel et al., 2009).

Longitudinal studies which examined the association between specific substance abuse disorders and offending violence demonstrated a strong correlation between the three aspects of delinquency, violence and substance abuse (Pedersen and Skardhamar, 2010, Norström and Pape, 2010, Popovici et al., 2012).

It has been shown that substance abuse, when comorbid with severe mood disorders, may negatively impact those disorders, and various interventions have been developed to limit the harmful effects of substance abuse (Drake et al., 2008).

It is important to note that substance abuse can increase the risk of violent behaviour in several ways. A variety of hypotheses has explained the high

correlation between substance use and violent behaviour, some explaining it through the neurobiological effects of the substance (Norström and Pape, 2010, Sbordone et al., 1979, Scott et al., 1998, Shafi et al., 2017, Smith et al., 2012, Tobore, 2019) and others to socioeconomic factors (Swanson et al., 2006b, Popovici et al., 2012).

Furthermore, substance use combined with severe mental illnesses increases the likelihood of non-adherence to treatment, which increases the risk of violence (Volavka and Citrome, 2011).

The relationship between substance abuse and psychosis is likely complicated since there are many confounding variables, such as when the person first consumed the substance, when the psychosis began, the gender differences in substance abuse and other socio-demographic variables.

An individual's social circumstance and support network can be significantly negatively affected by substance abuse (Gregg et al., 2007). Delinquent behaviour is often the cause of the purchase and sale of illegal drugs (Hodgins, 2008). According to a recent study, individuals with schizophrenia with comorbid psychoactive substance use are more likely to engage in criminal behaviour, including homicide (Schanda et al., 2010).

#### 1.6.1. Substance use and violence in the larger population

United Nations Office on Drugs and Crime (UNODC) reports that substance abuse is a global public health concern which is evident from the number of 2.3 billion people who drink alcohol regularly (Organisation, 2018) and 271 million illicit substance users (Nations, 2019) and 1.4 billion tobacco users (Organization, 2019). Although substance use disorders are the most common mental illnesses, a small percentage of patients seek treatment (Girasek et al., 2022).

Alcohol use is one of the leading risk factors for disease burden worldwide, accounting for nearly 10% of global deaths among populations 15-49 years of age and poses severe implications for future population health (Griswold et al., 2018).

The prevalence rates of substance use and the resulting violent behaviours have been associated with multiple forms of aggressive behaviour, including self-aggression, hetero-aggression, and antisocial behaviour. It is a logical assumption that substance use has a causal effect on violence, as it has been established by several studies that have investigated the effects of substance use on violent behaviour in community-based samples. (Brown et al., 1998, Chermack et al., 2000).

Observations suggest that substance abuse is associated with increased violence rates in the general population, based on the evidence available through empirical observation (Ghossoub et al., 2019, Liakoni et al., 2018).

Based on a retrospective analysis of 2 848 768 records of deaths in the United States related to illegal substance use between 1980 - 2014, data showed a steady rise in mortality due to self-harm and interpersonal violence in the illicit drugs category (Dwyer-Lindgren et al., 2018).

Deliberate self-harm behaviours, and intentional overdoses, have been associated with mental health difficulties and substance misuse as contributing factors (WHO, 2014), with a peak prevalence rate noted among females between the ages of 14 and 17 (Whitlock, 2010).

Suicidal behaviour has also been more prevalent among substance users, with a strong correlation between substance misuse and suicidal behaviour (Kwon et al., 2013). Suicide attempt rates were reported to be six times higher in substance users than in non-users (Dragisic et al., 2015, Maloney et al., 2007), and completed suicide rates were also substantially higher in substance users irrespective of gender (Dragisic et al., 2015, Oyefeso et al., 1999, Schifano et al., 2020).

It is crucial to analyse the biopsychosocial consequences of substance abuse in the general population to understand better the impact on populations affected by severe mental illness. The link between childhood adversity, homelessness, involvement with the criminal justice system, and substance abuse is assumed to be causal (Rosenberg et al., 2007), showing the complexity when these inter-relations are examined.

### 1.6.2. The potential for violence of commonly used psychoactive substances

Alcohol, benzodiazepines, cannabis, stimulants, and novel psychoactive substances, commonly abused psychoactive substances, have all been associated with drug-related aggression (Anderson and Bokor, 2012, Moore et al., 2010, Hoaken and Stewart, 2003, Tomlinson et al., 2016). There is further evidence that concurrent polysubstance abuse increases aggression and violence in individuals (Steele and Peralta, 2020), probably due to the cumulative effects of the substances and the more significant socio-economic impacts. Delinquent behaviour is more likely associated with individuals who abuse substances (Osgood et al., 1988) and among individuals with dual diagnoses (Eggink et al., 2019).

In substance intoxication, substance withdrawal, or idiosyncratic reactions, all major neurotransmission systems (dopamine, epinephrine, norepinephrine, serotonin, acetylcholine, gamma-acetyl butyric acid systems) are associated with a potential for violent behaviour, depending on the substance receptor affinity (Hoaken and Stewart, 2003, Siever, 2008, Miller and Potter-Efron, 1990, Schifano et al., 2020).

A neurochemical mechanism associated with the dopaminergic system's abnormal salience distribution has been hypothesised to explain the aggressive nature of recreational drug users (Miyata, 2019, Miczek et al., 2002). A hypothesis suggests that hyperactivity of the dopaminergic dopamine receptors in the striatum of the midbrain causes delusions and the perception of perceptual disturbances that may lead to aggressive behaviour (Ntounas et al., 2018). Violent behaviour in animals and humans can be influenced by the dopaminergic effects of psychoactive substances, particularly those targeting the D2 family of receptors, suggesting that mesocortico-limbic dopamine plays an enabling role (Miczek et al., 2002).

"Psychotic-like experiences" have been linked with violence in a general population sample (Mojtabai, 2006), which may be associated with dopaminergic hyperactivity.

As part of its psychotropic effects, MDMA / ecstasy is also thought to affect the serotonergic system (Parrott, 2002). It is common for these patients to exhibit disinhibition, akathisia, serotonin syndrome, manic episodes, and aggressive

behaviour (Anderson and Bokor, 2012, Rouve et al., 2011). Several preclinical and clinical studies have demonstrated that serotonin modulates behaviour in many ways (Wolkers et al., 2017). Serotonin levels have been found to increase during antidepressant-induced irritability episodes and increased suicidal ideation in some studies (Gillet et al., 2001).

According to research, the glutaminergic neurotransmitter system, the third central system in the brain, plays an essential role in regulating behaviour (Miczek et al., 2015). One study showed that central GABAergic function was associated with impulsiveness and suicidal behaviour but not aggression in individuals with personality disorders (Lee et al., 2009), concluding that high dosages of benzodiazepines can cause "behavioural disinhibition" in humans.

#### 1.6.2.1. Cannabis

Cannabis has been extensively studied concerning psychosis, but its association with aggression remains unknown (Ostrowsky, 2011, Smith et al., 2013).

Meta-analytic research among teenagers, intimate partners and those with severe mental illness suggests a moderate global association between cannabis use and aggression; However, populations at risk showed higher correlations (Dellazizzo et al., 2020). According to a substantial systematic review and meta-analysis including 110 studies examining the risk factor of violence, substance misuse showed a strong association with violence (OR = 2.9, 95% CI 1.3 - 6.3,  $z = 2.6$ ); however, the association between cannabis misuse and violence was uncertain (OR = 1.3, 95% CI 0.7 - 2.4,  $z = 0.8$ ). Indeed, the adverse reaction of aggression to cannabis is infrequent, and it almost always occurs in conjunction with another substance and individuals predisposed to it (Gillet et al., 2001).

In the longer term, cannabis has robust psychotropic effects. Daily cannabis consumption during this period impairs the neural connectivity in the limbic system, prefrontal cortex, and subcortical regions, leading to an inappropriate inhibition of behaviour (Barthelemy et al., 2016, Volkow et al., 2014). Chronic cannabis usage may be linked to mild cognitive deficits in attention and executive skills (Solowij, 1998). Both simple and complex cognitive abilities altered by

marijuana in lab tests may be similar to those needed to manage interpersonal conflict, increasing violence risk effectively (Moore and Stuart, 2005). Cannabis use has been associated with a threefold risk of developing first-episode psychosis in the case of high THC content and criminal behaviour through paranoid/suspicious thinking (Barthelemy et al., 2016) and maladaptive interpersonal functioning (Martinotti et al., 2017). The potency of cannabis increased from 1995 to 2014 (Elsohly et al., 2016), as demonstrated in the surge of emergency department visits involving marijuana when used alone or in combination with other drugs between 2004 and 2011 (Substance and Mental Health Services, 2013). Dose-effect impact on the age of presentation had been documented in the case of high-potency cannabis among those who stated to use this substance at an early age and regularly (Di Forti et al., 2014); however, this may carry a risk impaired social functioning and ultimately to violence. Adolescents are particularly vulnerable to adverse long-term outcomes from marijuana use (Mechoulam and Parker, 2013). The use of cannabis during the adolescent years is important because it interferes with the neurostructural changes that are occurring in the brain during the maturing process (Di Forti et al., 2014).

Cannabis has been highlighted for its capacity to lead to polysubstance use (Dubertret et al., 2006). Using multiple substances has been associated with a ten-fold risk of violence (Witt et al., 2013).

Aggressiveness and chronic heavy cannabis consumption may be related to mood and behaviour changes during periods of intoxication and abstinence (Allsop et al., 2011, Budney and Hughes, 2006, Kouri et al., 1999).

#### 1.6.2.2. Stimulants

Stimulants are the world's second most widely used illicit psychoactive substances (Fulde and Forster, 2015). It is well known that stimulants are often associated with aggressive and impulsive behaviour, especially in alcohol consumption (Kuypers et al., 2020). It should be noted that stimulant intoxication symptoms include an increased sense of self-confidence, impaired judgment, impaired planning skills, hyperactivity, decreased inhibition, and emotional dysregulation

(Kuypers et al., 2020, Gillet et al., 2001). Studies have shown that chronic stimulant use may lead to "limbic dyscontrol syndrome" due to altered metabolism of noradrenaline and serotonin as a result of using them (Gillet et al., 2001, Davis, 1996).

Cocaine has been linked to various violent behaviours, from verbal and aggressive behaviour to physical assaults and homicides (Miller et al., 1991). Compared to other substances, amphetamine was shown to cause the most agitated and violent and aggressive behaviour (Bunting et al., 2007). The trend of methamphetamine usage in recent years is concerning due long term neurological sequelae in case of habitual misuse and the impact on health services (Fulde and Forster, 2015). However, according to a recent review paper, there was limited information in relevant literature concerning the correlation between methamphetamines and aggression (Kuypers et al., 2020). By contrast, crystalline methamphetamine ("ice") was associated with severe aggression and violence in a clinical sample among service users presenting to the emergency department with symptoms of methamphetamine intoxication (Bunting et al., 2007).

#### 1.6.2.3. Hallucinogens

Hallucinogens were not associated with aggression and violence, despite their potential to induce vivid visual perceptions and depersonalization experiences. LSD (lysergic acid diethylamide), psilocybin, and mescaline were extensively used in psychotherapy in the 1960s in individual and group psychotherapy sessions (Leuner, 1961). Few incidents of adverse reactions were reported in the context of "bad trips" that can induce panic attacks due to intense visual hallucinations (Taylor and Hulsizer, 1998). However, with the spread of novel psychoactive substances introduced in the drug markets in the recent decade, psychedelic phenethylamines have been associated with adverse reactions, including aggression and violence (Schifano et al., 2016).

#### 1.6.2.4. Opioids

It is important to acknowledge that although opioids function as central nervous system depressants, not all of their effects inevitably result in aggression and violence, even when under the influence. However, reducing inhibition may increase the likelihood of violence as one's capacity to control outburst behaviours is impaired (Schifano, 2017, Schifano et al., 2020). The withdrawal symptoms may also include increased sensitivity to pain, anxiety, mood disorders, and a lack of sleep. These may be related to aggressive behaviour and violent behaviour. Although an increase in delinquent behaviour has been described with heroin (Hayhurst et al., 2017), synthetic opioids (Schifano et al., 2019), and prescribed opioids (El-Hadidy and Helaly, 2015), psychosocial factors may be responsible for this association.

#### 1.6.2.5. Benzodiazepines

The paradoxical effects of benzodiazepines have been previously described (Tae et al., 2014) and typically manifest as agitation, irritability, aggression, and violence. Typically, individuals who abuse multiple substances (Gillet et al., 2001), are elderly (Saxon et al., 2010), or have pre-existing brain damage (Anderson and Bokor, 2012) develop these symptoms. Withdrawal from benzodiazepines may also result in aggressive and hostile behaviours (Saxon et al., 2010).

#### 1.6.2.6. Novel Psychoactive Substances: Synthetic Cannabinoids and Synthetic Cathinones

Over the past few years, there has been an increase in interest in novel psychoactive substances due to their potential for severe harm to users' mental and physical health with unpredictable effects, referred to as "spikephrenia" (Schifano et al., 2020). An analysis of data in acute mental health services found that novel psychotropic substances were significantly associated with violence during the

preadmission period (OR 14.4, 95 % CI 7.43 - 29.08) during the admission process (OR 15.98, 95 % CI 7.05 - 36.20), and with a longer length of stay (OR 15.98, 95 % CI 7.05 - 36.20) (Shafi et al., 2017).

Synthetic cannabinoids display full cannabinoid CB-1 receptor agonist activity, contributing to their ability to swiftly cross the blood-brain barrier due to their high lipophilicity (Papanti et al., 2013). A wide range of symptoms is associated with these psychoactive substances, from the intoxication of cannabis to increased anxiety, psychomotor agitation, and possibly even the emergence of psychotic symptoms (Papanti et al., 2013, Courts et al., 2016). A study conducted among university students found that cannabinoid usage is associated with increased aggressive behaviour, violent behaviour, and sexually risky behaviour. (Clayton et al., 2017).

It has been observed that synthetic cathinone has strong sympathomimetic properties, and, as a result, it has been observed that it inhibits serotonin and dopamine reuptake in a dose-dependent manner (Roberts et al., 2017). This may result in psychotic episodes and aggressive and violent behaviours (Capriola, 2013). In a large sample examining the toxic effects of mephedrone toxicity based on the National Poisons Information Services (NPIS) data, the most commonly described adverse reaction following intoxication with or without alcohol was psychomotor agitation and aggression (24% of the sample, 95% CI 18 - 33%). There is a high probability that severe agitation and violence are commonly observed when these synthetic cathinones are combined with alcohol (James et al., 2011, Schifano et al., 2011).

A recent study demonstrated that NPS abusers experienced higher levels of violence during admission and pre-admission than non-NPS substance abusers. These reports highlight the importance of these illicit substances' adverse effects on acute mental health, emergency, and public health services. (Shafi et al., 2017).

### 1.6.2.7. Alcohol

A recent systematic review found that alcohol and drug exposure was associated with violence in approximately half of the cases in emergency departments (Nikathil et al., 2017).

The psychotropic effects of alcohol are influenced by its concentration in the blood, resulting in different effects. It has been suggested that there is a statistically significant association between consumption of alcohol at any alcohol content of 0.75 g/kg and aggression in humans (Kuypers et al., 2020).

The potential of triggering aggressive behaviour of alcohol has been explained by its properties in decreasing inhibitory activity in the frontal lobe (Anderson and Bokor, 2012), regulating higher-order cognitive capacities that may increase impulsivity (Kuypers et al., 2020). Alcohol abuse and withdrawal symptoms were among the leading causes of presentation to emergency departments (Morgan, 2015).

High prevalence rates of alcohol consumption in the general population and among individuals with severe mental illness are essential given the potential of alcohol to cause aggressive or violent behaviour.

From an Irish perspective, high alcohol consumption rates were repeatedly reported along with harmful drinking habits. According to a 2014 survey, Irish consumers drank 11.0 litres of pure alcohol each (Mongan, 2016). According to a national household survey of alcohol consumption, 75% of alcohol consumption is attributable to excessive episodic use (Long and Mongan, 2014). Moreover, this trend was considered to accelerate (Manthey et al., 2019).

However, the 2019 survey completed in Ireland showed decreasing trend in alcohol consumption per capita, equating with 10.8 litres of pure alcohol consumed in the population aged 15 and over, which represents 40 bottles of vodka, 113 bottles of wine, or 436 pints of beer (Doyle, 2021). Despite this, Ireland was considered one of the countries in the European Union with one of the highest rates of alcohol consumption per capita (Manthey et al., 2019).

Based on the data collected between 2017 and 2022, Ireland has the fourteenth highest alcohol consumption per capita (over the age of 15) of the 36 countries in

the OECD, with 9.5 litres of alcohol consumed per capita (OECD online database, 2022).

With 20.6% of adults abstaining from alcohol, the remaining alcohol consumers consume even higher than average amounts.

In 2013, 37.3% of drinkers in Ireland engaged in risky single-occasion drinking (RSOD), sometimes referred to as binge drinking; 54.3% scored positively on the Audit-C screening tool; 6.9% rated for alcohol use disorder positively, suggesting that there were 149,300 to 203,897 drinkers in Ireland, who should be considered addicted. At least 75% of the alcohol was consumed binge (Mongan, 2016).

Based on a nationally representative survey of 4,338 respondents, approximately 7% of all drinkers met the DSM-IV criteria for alcohol abuse. The same survey found that 62% of all drinkers reported having a monthly or sporadic episode of excessive alcohol consumption. (O'Dwyer et al., 2019).

High rates of hazardous alcohol consumption have been reported among students compared to the general population, with similar patterns observed in both genders (Davoren et al., 2015). In addition, positive correlations were found between hazardous alcohol consumption and using other substances such as tobacco and illicit substances (Davoren et al., 2015).

### 1.6.3. Substance use as a risk factor for severe mental illness

When determining the impact of substance use on severe mental illness, one must consider comorbidity. Approximately half of the people with a history of schizophrenia have coexisting substance use problems (Kavanagh et al., 2004, Regier, 1990, Allebeck et al., 1993), with alcohol and cannabis being the most abused substances among those with psychotic disorders (Weaver et al., 2003, Kavanagh et al., 2004, Barnett et al., 2007b).

In patients with schizophrenia, there is strong evidence that the presence of a substance use disorder increases their risk of violence (Volavka, 2002).

It was found that there is a substantial prevalence of co-morbid substance use among people with severe mental illness. For instance, in the CATIE study, 60% of

individuals with schizophrenia had a substance use at baseline, and 37% met the criteria for co-morbid substance use (Swartz et al., 2006). Individuals with mental illness have a higher risk (OR = 2.7) of developing lifelong substance dependence, with the highest rates in criminal justice system populations (Regier, 1990).

Among individuals with first-episode psychosis in a population-based clinic sample, substance use was present in most cases, 51% for cannabis abuse and 43% for alcohol abuse (Barnett et al., 2007a). A variety of prevalence studies from diverse geographical locations have confirmed comparable rates of substance use among persons with first-episode psychosis (Addington and Addington, 2007, Brunette et al., 2018, Green et al., 2004).

When comparing data collected nationally on the prevalence of substance use in the general population, data collected from samples of individuals with severe mental illness demonstrated significant differences in the prevalence of substance use in one study (Barnett et al., 2007a). According to this study, 55.3% of people with severe mental illness used one or more Class A drugs, compared to 13% of the general population (Barnett et al., 2007a). Likewise, a significant difference was reported in cannabis abuse prevalence rate among individuals with first-episode psychosis compared to matched healthy control in a German sample (Hambrecht and Hafner, 2000).

The 2012 National Survey reflects the magnitude of cannabis use on Drug Use and Health reports completed in the United States, with an estimated 2.7 million people meeting the DSM-IV criteria for marijuana dependence, while 5.1 million met the DSM-IV criteria for any illicit drug dependence (National Survey on Drug Use and Health, 2010).

The most commonly used substances globally are cannabis, alcohol, and nicotine, and people with mental illnesses, particularly psychosis, are reported to use multiple substances simultaneously (Saddichha et al., 2010). It has been found that young people, who start using cannabis at a young age, are at a higher risk of developing cannabis dependence than adults who begin using cannabis at an older age (Chen et al., 2009). Furthermore, cannabis addiction may also lead to dependence on other illicit substances (Hall and Degenhardt, 2007). Numerous studies have documented polysubstance abuse patterns in patients with severe mental illness (Sevy et al., 2001, Lambert et al., 2005). While more than half of

cannabis users were reported using other substances (Arranz et al., 2015b), polysubstance use disorders were reported at higher rates (65%) among cocaine and amphetamine abusers (Ouellet-Plamondon et al., 2017).

An in-depth review and analysis describe the crucial links between violence and the history of polysubstance misuse. The relative risk (OR = 10.3) was significantly higher compared to the risk of recent alcohol misuse (OR = 2.2) or recent drug misuse (OR = 2.2). (Witt et al., 2013). Several factors contribute to the significance of polysubstance misuse, including its association with the forensic history of individuals who frequently use multiple substances simultaneously (Fraser et al., 2012).

A variety of substances have been related to substances-induced psychotic disorders (Murray et al., 2013), cannabis has been the subject of most research concerning the development of psychosis, and now there is a considerable amount of literature supporting this association (Di Forti et al., 2014, Di Forti et al., 2015, Arseneault et al., 2002, Henquet et al., 2005, Addington and Addington, 2007, Di Forti et al., 2019).

According to some prospective studies, there is increasing evidence of a moderate increase in schizophrenia risk caused by heavy cannabis use in adolescence independent of polysubstance use (Arseneault et al., 2002).

Cannabis had been hypothesized as a risk factor for schizophrenia (Allebeck et al., 1993). In addition, a relative risk of 6.0 (95% CI 4.0-8.9) has been attributed to cannabis misuse among individuals compared to non-users of the drug, resulting in the conclusion that cannabis misuse is an independent risk factor for schizophrenia (Andreasson et al., 1987). There was a three-fold adjusted odds ratio for developing a psychotic disorder (OR = 3.2, 95% CI, 2.2 - 4.1) in cannabis users versus non-users of cannabis in a study that included 11 international centres and 901 adults with a history of psychosis as their first episode of psychosis (Di Forti et al., 2019). Daily cannabis use increased this odds ratio to OR = 4.8, 95% CI, 2.5 - 6.3) (Di Forti et al., 2019). A cross-sectional study of 6722 Australian respondents between 18 and 49 also found that cannabis dependence was associated with a twofold increase in psychotic symptoms after controlling for confounding factors (Degenhardt and Hall, 2001).

Long-term stimulant use may maintain psychotic symptoms (Harro, 2015), aggression toward others, and suicidal behaviour. Alterations in the dopaminergic system (Fulde and Forster, 2015) imply the emergence of these symptoms; however, persistent reduction in automatic transmission in abstinent users has been hypothesized to contribute to increased impulsivity and aggressive behaviour (Harro, 2015).

#### 1.6.4. The impact of substance use on psychopathology and the progress of severe mental illness

The relevant literature also indicates that co-occurring substance abuse and severe mental illness increase violence risk by amplifying symptomatology, but the mechanism remains unclear (Addington and Addington, 2005, Addington and Addington, 2007, Andrade, 2016).

According to a meta-analysis, schizophrenia patients who use psychoactive substances have a fourfold increased risk of becoming violent than those who do not (Fazel et al., 2009).

Violence risk is substantial at times when psychotic symptoms are acute (Large and Nielssen, 2011, Van Dorn et al., 2012, Coid et al., 2013b) (Ullrich et al., 2014), and severe violence has been linked to prodromal phases (Nielssen and Large, 2010). On the other hand, high prevalence rates of substance use had been reported among individuals with severe mental illness both during initial psychotic episodes (Barnett et al., 2007a) and later stages of the illness (Van Dorn et al., 2012).

Diverging phenomenological aspects of the effects of concurrent substance use in psychotic illnesses have been described. Most of the research found increased positive psychotic symptoms when co-occurring substance use was present (Addington and Addington, 2007, Allebeck et al., 1993, Katz et al., 2010, Kamali et al., 2009, Swartz et al., 2006); however, other investigations could not support this interpretation (Compton, 2004).

Similarly, there are inconsistent findings for negative symptoms. Most studies indicate that substance users experience fewer negative symptoms than non-users

(Addington and Addington, 1998, Compton, 2004, Dubertret et al., 2006). However, others did not find any difference in negative symptoms between users and non-users (Addington and Addington, 2007, Kamali et al., 2009, Katz et al., 2010).

Depressive symptoms may be used to differentiate cannabis-induced psychotic disorder (CIPD) from other types of primary psychosis, according to one study using the Symptom Checklist-90-R and the Psychiatric Research Interview for Substance and Mental Disorders (Rubio et al., 2012).

Substance use following the first episode of psychosis may have significant consequences regarding the increased relapse rates in psychosis (Wade et al., 2006) and may increase the risk of violence.

According to an observational study, a relapse of psychosis was associated with changes in patterns of cannabis use that were dose-dependent, which is unlikely to be an effect of self-medication or genetic and environmental confounding factors (Schoeler et al., 2016).

Concerning other illicit substances, in a two-year follow-up study conducted in Canada of a first-episode psychosis cohort, stimulant abuse was related to higher service utilisation and worse symptomatic and functional outcomes in the first years post-contact with the services (Ouellet-Plamondon et al., 2017). The findings of this research had been confirmed by another study in the first episode of the psychosis cohort, in which previous stimulant use disorder was associated with higher readmission rates (Sara et al., 2014).

Apart from the positive and negative symptoms of schizophrenia, substance misuse has a negative impact on the quality of life in individuals with severe mental illness at the onset of first-episode psychosis (Addington and Addington, 1998), and poorer outcomes were recorded in follow-up studies on those with poor functioning at baseline (Addington and Addington, 2005) and later stage of the illness (Addington and Addington, 2007).

Similarly, poorer outcomes were reported among individuals within a first-episode psychosis cohort with co-morbid persistent substance use disorder (Cather et al., 2018). Despite these reports, there is a lack of consistency in health services in delivering interventions for individuals with dual diagnoses (Drake et al., 2008).

#### 1.6.5. Possible links between comorbid substance use, younger age of onset of first episode of psychosis and violence rates

Substance use disorders and schizophrenia spectrum disorders are considered to increase the risk of violence in different ways (Arseneault et al., 2000); however, when analysing correlations between severe mental illness, violence and young age, the issue of age at which substance use was commenced should be considered.

The onset of substance use before age 15 is strongly associated with antisocial personality disorder in adulthood (Osgood et al., 1988) and was described as a robust predictor of violence in individuals with dual diagnoses (Fulwiler and Ruthazer, 1999).

Younger age of onset of the first episode of psychosis was associated with comorbid substance misuse in several studies (Addington and Addington, 1998) (Addington and Addington, 2007), particularly cannabis, as opposed to other substances (Allegri et al., 2013). In addition, a dose-dependent association was found between high potency cannabis use and the onset of first-episode psychosis (Di Forti et al., 2014) along with age of first use. Cannabis users may develop a first episode of psychosis approximately earlier than non-users (Tosato et al., 2013); however, other studies did not report the difference in age of onset between substance users and non-user groups (Kamali et al., 2009).

The younger age of onset of first-episode psychosis is an important factor concerning the longer-term progress of the illness. Younger age of onset, besides male gender, and more extended inpatient treatment at first presentation had been associated with a higher risk of transitioning from a substance-induced psychotic illness to a primary psychotic illness according to a population-based longitudinal cohort study with a relatively large cohort (n = 3486) (Alderson et al., 2017).

In another population-based study of individuals with first-episode psychosis, the peak age for the first use of cannabis and alcohol was between 12 and 14 years, which was lower than the peak age for the first use of other substances such as

amphetamine, ecstasy, hallucinogens, and cocaine (between 14 and 19 years old) (Barnett et al., 2007a).

The sociodemographic profile of a sample of first-episode psychosis cohort with concurrent substance misuse showed a positive correlation between substance abuse, positive symptom severity and male gender. At the same time, age of presentation was correlated with negative symptoms severity and lower level of functioning (Compton et al., 2017).

1.1.3 Discussion - Examining risk factors for aggression and violence in clinical populations is challenging.

The long-standing perception was that mental health problems are linked with aggression and violence (Monahan, 1992). However, studying violence in severe mental illness requires a careful approach due to the diagnostic heterogeneity of severe mental illness diagnostic groups and ambiguities concerning the causes of violence (Bo et al., 2011).

Due to the diverse and varied characteristics of the psychosis syndrome, which includes symptoms such as delusions, perceptual problems, disorganised speech, disorganised behaviours, and/or catatonia (Tandon, 2014), it is challenging to establish a consistent and standardised definition for this type of psychopathology.

Equally, despite examining it, several publications do not define aggression or violence (Adams and Yanos, 2020). Nevertheless, in other studies, there is a wide range of definitions of violence, such as violent crime (Modestin and Ammann, 1996), assault, unlawful deprivation of liberty, unlawful threats, and severe problems with the law (Lindqvist and Allebeck, 1990), violent convictions (Arseneault et al., 2000), self-reported violence against another person (Elbogen and Johnson, 2009), and diagnostic interview schedules that indicate self-reported violent behaviour (Swanson et al., 1990). The lack of agreed definitions of aggression and violence impedes systematic reviews, and meta-analyses of violence are proving difficult due to the inclusion of different types of aggression and violence in various research methodologies of studies on this topic.

Multiple measures have been devised to assess different forms of aggression and violence. These include several observation scales, such as the Modified Overt Aggression Scale (MOAS) (Kay et al., 1988), McArthur Community Violence Instrument (MCVI) (Milton et al., 2001), Disturbed Behaviour Rating (DBR) (Humphreys et al., 1992), Dynamic Appraisal of Situational Aggression - Inpatient Version (DASA - IV) (Ogloff and Daffern, 2006), Broset Violence Checklist (Almvik et al., 2000) or Staff Observation Aggression Scale-Revised (SOAR-R) (Nijman et al., 1999).

Conversely, the assessment items for aggressive and violent phenomena in these scales are various [negative attitude, sensitive perceived provocation (Ogloff and Daffern, 2006); confusion, irritability, boisterousness (Almvik et al., 2000); verbal aggression, aggression against property, self and other (Kay et al., 1988)], leading to the impracticality of comparing the results.

In addition to challenges related to psychopathology and definitions of violence, differing results and conclusions across the research field may indicate significant methodological differences. Research on aggressiveness and violence in severe mental illness comprises observational research, including cohort, cross-sectional, and case-control studies that employ various methodologies, both prospective and retrospective. Due to ethical considerations, it is not feasible to undertake experimental investigations including violence and aggression (Lamsma and Harte, 2015).

The presence of different approaches makes it challenging to compare findings. A recently published meta-analysis, which includes the most significant research conducted over a period of forty years, investigates the relationship between schizophrenia spectrum disorders and aggression.

The analysis reveals a substantial level of heterogeneity above fifty percent (Whiting et al., 2021). Commonly, only a quarter of meta-analyses have heterogeneity of over fifty percent (Higgins et al., 2003).

Furthermore, given the differences in cultural, legal, and mental health systems, generalisations from research conducted in one area may not apply to other cultural contexts (Nederlof et al., 2013). Concerning geographical differences around the world, a multinational study demonstrated that in developing countries, the prevalence rates of violence were three times higher than in developed countries based on the WHO study on Determinants of Outcomes of Severe mental illness (DOSMD) (Volavka et al., 1997). Cultural competency in research can also contribute to differences in aggression and violence, as behavioural signs of aggression can be interpreted differently and may result in selection bias.

The current discussion surrounding the cause and nature of the link between severe mental illness and violent behaviour, as well as the public's interpretation of the findings from research articles on this topic, highlights the substantial and concerning variability in the studies investigating these connections.

In addition, different risk factors may play a role in determining the severity of mental illness to varying stages of the disease, including social factors that subsequently emerge following the onset of the severe mental illness. Consequently, a more comprehensive approach to assessing associations may be required. It can be argued that “two-dimensional” or “static models” examine the connections between aggression and violence. The high variability of psychopathology and its temporal relationship to the aggressive-violent incident can lead to increased ambiguity.

According to one study hypothesising pathways of aggression and violence in psychosis without long-standing antisocial behaviour, the following pathways were identified as direct pathways of aggression and violence: psychotic symptoms - anger - aggression - violence, and factors that may influence these pathways, including victimisation, impulsivity, and cognitive contents containing harmful substances (Adams and Yanos, 2020). In another theoretical model, violence is analysed within the context of various risk factors, such as positive symptoms, demographic variables, substance abuse, mental disorders, and personality disorders; however, it has been shown that the interaction between these factors may have a significant impact on the outcome and consequently on the violence as well (Bo et al., 2011). There has been a growing emphasis on the necessity of temporal correlation for recognising these associations (Van Dorn et al., 2012, Coid et al., 2013a, Ullrich et al., 2014). Nevertheless, it can be argued that temporal proximity does not imply a chronological order of events; therefore, it is difficult to correlate the cases of aggression and violence with psychopathology.

An added layer to this complicated association of severe mental illness and aggressive behaviour is the multitude of potential risks that can reinforce aggressive behaviour. This complexity was demonstrated in a recent study that examined risk factors for aggression and violence in schizophrenia, as 41 potential pathways have been identified, highlighting the difficulties in understanding this association (Lamsma and Harte, 2015).

In light of the broader implications of the conclusions, a systemic review of violence in severe mental illness methodologies in this critical area would benefit a better understanding (Whiting et al., 2021).

This is particularly important as it is well known that perceived associations between mental illness and violence have broad implications for public perceptions and attitudes toward mental illness (Pescosolido et al., 2019, Torrey, 2011), including how people with mental illnesses are portrayed in the media (Atanasova et al., 2019, Rueve and Welton, 2008), as well as in the practice of psychiatry (Monahan et al., 2001) and how mental health legislation is formulated (Fazel et al., 2009). The public stigmatising attitude towards individuals with mental health has not shifted considerably, according to a study that examined public opinion on this subject (Pescosolido et al., 2010).

## 1.8. Closing remarks and conclusion - Research of aggression and violence in severe mental illness raises additional questions

Aggression and violence in society have been debated since ancient times. Despite being part of human existence and history in general, violence's importance has become more noticeable over the past decades. More than two decades ago, violence was declared a public health problem, showing the scale of its societal impact.

Although a minority of perpetrated violence is attributed to persons with severe mental illness, the focus on the link between mental illness and violence is widely debated and sensationalised at societal and academic levels with diverging conclusions. The effect of media reports of violence perpetrated by persons with severe mental illness contributes to further stigmatisation.

While a large body of research has examined the relationship between mental illness and violence over the past several decades, by stark contrast, limited research explores the problematic correlation between first-episode psychosis and violence, which constitutes a significant gap in academic research on such an essential topic with clinical relevance. Published studies focusing on aggression and violence in first-episode psychosis cohorts have also significantly diverged methodology.

Prevalence rates of aggression in the context of severe major mental illness may vary based on several factors, such as the type of service in which the studies were carried out, phase of mental disorder, comorbid substance use, geographical location, and cultural contexts.

Predictors of violence may change throughout the illness. Therefore, systematic reviews and meta-analyses should compare cohorts with the highest similarities from a sampling perspective, illness symptomatology, and demographic factors.

The argument about the psychopathological or sociodemographic determination of violence is yet to be answered due to the complexity of associations and several confounding factors. In addition, it is also relevant to note that a temporal relationship between the behaviour being studied and psychopathology is, in most

cases, delayed for practical reasons. The temporality between the incident and the symptom may also be reversed.

The lack of consensus around definitions of aggression and violence, divergent study designs, cohorts, methods, rating scales of violence, and cultural differences make it difficult to compare research results and lead to high heterogeneity in systematic reviews and meta-analyses.

Comparative studies on the prevalence rates of violence in the specific first-episode cohorts of psychosis from the same catchment area are scarce, as according to the current state of knowledge, one study was published to explore this subject. Likewise, a rarity of studies examined the influence of the length of observation of aggression and violence on the prevalence rates.

Although all studies examining violence in the first episode of psychosis cohorts analyse gender disparity in the prevalence rates of violence, there is a lack of data on the relationship between gender, substance use and violent behaviour in this cohort due to the scarcity of studies focusing on the first episode

In summary, given the growing number of unanswered questions in the current literature regarding aggression and violence in first-episode cohorts, as described above, the current study attempts to understand the complex relationship between clinical determinants of the first episode, sociodemographic factors, substance use, and aggression and violence by analysing these interactions in detail.

## 2. Objectives, methods, materials, results

### 2.1 Objectives

The main objective of this study is to analyse in detail the associations between sociodemographic and clinical factors and the extent of aggression and violence in a cohort with first episodes of psychosis.

A detailed analysis of incidents of aggression and violence in the first episode of psychosis cohort was based on data extracted from all electronic medical records, incident reports, supporting information, and referral documents during the observation period. This analysis provided a detailed picture of patterns of aggression and violence during the pre-contact and post-contact periods with mental health services, including the prevalence rates, the type, and the extent of aggression and violence in this cohort.

Forms of aggression and violence were quantified by the application of the Modified Overt Aggression Scale (MOAS), which stratifies aggression and violence into verbal aggression and aggression against property, self and others, utilising a well-defined methodology (Kay et al., 1988).

Previous research studies examining aggression and violence reported aggression incidents in first-episode psychosis cohorts conducted in the same geographically defined catchment area had a shorter observation period one week before and one week after an encounter with services (Foley et al., 2005, Keane et al., 2019) contrary to the majority of first episodes cohort in this area of research (Bhugra et al., 2000, Dean et al., 2007, Hodgins et al., 2011, Milton et al., 2001, Payne et al., 2006, Spidel et al., 2010, Steinert et al., 1999, Verma et al., 2005, Volavka et al., 1997).

A limited observation period of one week before and one week after contact with mental health services can find significant correlations between psychopathology and violence. However, many violent incidents in the active phase of the illness, but beyond a short observation period, may have been missed.

In addition, the influence of substance use on aggression and violence in the pre- and post-contact period can be analysed over a longer period of observation. Therefore, the systematic retrospective analysis of aggressive behaviour and

violent incidents was extended to six months before and six months after contact with services by the person with first-episode psychosis.

To assess the incidence of licit (alcohol, sedatives) and illicit (cannabis, stimulants, hallucinogens, opiates, other) substances in the first-episode cohort, data from SCID (Structured Clinical Interview for DSM-IV) - interview data, clinical records - were retrieved. The degree of substance use was measured using SCID coding standards and whether the subject met the criteria for substance use disorder. SCID and clinical records were used to obtain data on lifetime, previous years, and recent drug usage. A post-contact intervention addressing drug use was also retrieved from healthcare records retrospectively.

For each participant in this investigation, sociodemographic and clinical variables were assessed and recorded at the time of entry into the study.

Statistical analysis was conducted to analyse correlations between sociodemographic factors, clinical predictors, substance use, and aggressive and violent episodes.

Standard statistical analysis provided information about the sociodemographic characteristics of the study cohort, the prevalence rates of aggression and violence, and substance use.

Categorical variables recoded in binary forms enabled us to estimate relative risks between sociodemographic, clinical, and diagnostic variables and aggression and violence in the pre-contact and post-contact periods. In addition, the impact of a lifetime, past year and the past month of substance use were analysed concerning aggression and violence.

Chi-square and Mann-Whitney U tests were used to analyse substance use's impact on psychopathology and violence levels.

Finally, statistically significant outcomes were reviewed using binary logistic regression to determine statistically significant predictors of violence.

## 2.2 Methods

### 2.2.1. Sample description

There were two hundred sixty-five participants recruited on a prospective basis at DETECT [Dublin and East Treatment and Early Care Team], and all the case notes and incident reports for one year (six months before the first presentation and six months after the first presentation for psychosis treatment) were reviewed in retrospect.

In Ireland, DETECT [Dublin and East Treatment and Early Care Team] was the first early intervention team for the first episode of psychosis. This service is affiliated with Saint John of God's Community Mental Health Services, which specializes in providing general adult psychiatric care. This secondary psychiatric service defines the catchment area geographically in Southern Dublin, with approximately 175 000 inhabitants at the time of the study period. Consequently, the sample is regarded as urban. Over ten years, between 2006 and 2015, the recruited patients ranged from 18 to 65 years old.

To participate in the current study, all participants needed to have a diagnosis of a first-psychotic episode that met the diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition, Text Revision (DSM - IV TR). Diagnostic categories included non-affective and affective psychoses. Substance-induced psychotic episodes were included and analysed from psychopathological, aggression and violence, and sociodemographic perspectives.

In this study, the following exclusion criteria were used:

- Persons who do not reside within the catchment areas of the above-mentioned Saint John of God Community Mental Health Services
- Individuals under 18 years or over 65 years old
- Persons who have not been diagnosed with the first episode of psychosis
- Individuals with a first-episode diagnosis of psychosis with no consent to participate in the study

### 2.2.2 Study Design

The present study is a cross-sectional assessment of sociodemographic, psychopathological, and substance use characteristics of a cohort of first-episode psychological patients.

This data collection on the instances of aggression and violence was made retrospectively based on a detailed review of all clinical case notes (referral notes, daily progress notes, assessments, collateral information, discharge summaries, follow-up reports, telephone conversation reports, and incident forms) generated in each study participant's case over a year, consisting of six months before and six months after the presentation to the mental health services. Every incident was recorded and rated using the Modified Overt Aggression Scale to quantify the information for further statistical analysis.

### 2.2.3 Definition of aggression and violence

Distinguishing between aggression and violence was crucial to this study which used the definitions of the Oxford English Dictionary (Stevenson, 2010), in which aggression is defined as "Anger or antipathy manifested in hostile or violent behaviour; a readiness to attack or confront,". The Oxford English Dictionary definition of the noun 'violence' - 'the exercise of physical force so as to inflict injury on, or cause damage to, persons or property; action or conduct characterised by this; treatment or usage tending to cause bodily injury or forcibly interfering with personal freedom' (Stevenson, 2010).

Utilising the Modified Overt Aggression Scale (MOAS), an observational rating scale, aggression and violence had been stratified into four different forms: verbal aggression, aggression against property, self and others (Kay et al., 1988).

According to the MacArthur Violence Risk Assessment Study, "severe violence" is defined as assault resulting in injury, weapon use, or sexual assault (Steadman et al., 1998).

Violence against property was considered a less severe form of violence in this study, including definitions from the MOAS: “throws objects down, kicks furniture, defaces wall, breaks objects, smashes windows, sets fires, or throws objects dangerously” (Kay et al., 1988). Any form of violence causing harm to others was considered a severe form that corresponded to the following MOAS descriptions: “attacks others, causing mild injury (bruises, sprains, welts, etc.)” and more severe forms of violence comprising “attacks others, causing serious injury (fracture, loss of teeth, deep cuts, loss of consciousness, etc.)” (Kay et al., 1988).

#### 2.2.4 Baseline measurements

Relevant sociodemographic data (age, gender, employment status, living condition, education level, treatment received, and hospital) were captured for all study entrants. The information had been gathered based on the Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Patient Edition (January 2010).

##### 2.2.4.1. Age

Age groups were created using binary formats to understand better the correlations between different age groups, such as those under 35s and over 35s.

##### 2.2.4.2. Gender

Gender was captured in a binary format generating a female and male group according to the Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Patient Edition (January 2010), at the time of recruitment for this study, between 2006 and 2015. Other genders were not included in the study, given different cultural approaches to gender at the time of the study.

##### 2.2.4.3. Employment status

Employment status was recorded to all study participants within the structured interview process - current employment type (from home, at the workplace) was

asked. In the case of unemployment, the length and the reasons for unemployment were queried. They were divided into two groups based on whether they had a current job. The data collected from this part of the study was used to examine correlations with other sociodemographic and clinical variables, such as aggression and violence.

#### 2.2.4.4. Living conditions

This cohort's participants were divided into those living alone and those living with others. Binary groups were created to further analyse statistical correlations.

#### 2.2.4.5. Educational level

The highest educational achievement was recorded at the time of entry to the study. Eight education grades were distinguished based on the Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Patient Edition (January 2010). 1 - 3 groups had educational attainment from primary school to Leaving Certificate examinations. In the case of partial completion of college, educational level was rated 4. Higher educational levels were rated between 5 (graduated two-year college) to 8 (completed graduate / professional school). In order to perform further statistical analysis, it was necessary to create two groups: the first group consisted of those who had educational attainment to part college (rates between 1-4), and higher educational achievements consisted of those who graduated from a two-year college and above.

#### 2.2.4.6. Treatment status

Since community mental health services focus on outpatient and inpatient services as secondary speciality services, service users were assigned to outpatient and inpatient groups. Treatment status was rated according to Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Patient Edition (January 2010): currently

inpatient, currently outpatient, other (e.g. 12-step programme), and no current treatment.

Hospitalisation history was also recorded.

#### 2.2.4.7. Hospital treatment status

Following the Mental Health Act legislation (Mental Health Act 2001), information regarding hospital admission status has been recorded. There was a distinction made between voluntary and non-voluntary treatment statuses among inpatients.

#### 2.2.4.8. Psychopathological evaluation

Unstructured interviews are much less valid than structured ones. An interview guide of high quality is a prerequisite for structured interviews (Kici and Westhoff, 2004).

All study participants underwent the SCID-axis I interview (a structured clinical interview adapted to the Diagnostic and Statistical Manual of Mental Disorders IV-TR) as a part of the assessment process for all service users referred to DETECT [Dublin and East Treatment and Early Care Team] for early intervention. Inter-rater reliability was supported by training all clinical staff working at this service.

The semi-structured interview developed to determine whether an individual meets the criteria for any DSM disorder is called the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (SCID) (Spitzer, 1992).

The SCID rates for current and lifetime diagnoses and information on the age at which the illness onset occurred and current severity. The questions are grouped by diagnosis. The length of a SCID interview varies, depending on the patient's ability to focus during the interview; however, an average interview process takes 60 to 90 minutes (Glasofer et al., 2015a).

The SCID-IV for Axis I Disorders assesses mood disorders, psychotic disorders, substance use disorders, anxiety disorders, somatoform disorders, eating disorders, and current adjustment disorders. As part of the SCID, interviewers read mandatory probes designed to evaluate a specific diagnostic criterion. SCID is

scored in stages during the interview. The interviewer can usually complete it in a few minutes after each module (Glasofer et al., 2015b).

In addition to the SCID interview, a further detailed evaluation of psychopathology was performed utilising rating scales described in the 2.2.5 Materials section (page: 67).

#### 2.2.4.9 Information on substance use.

Data regarding alcohol and illicit substance use was gathered from SCID interviews (Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders IV-TR) and clinical notes (type, age of onset, frequency, abuse, and dependence).

Accurately diagnosing mental disorders in people who use substances can be challenging for various reasons. In the first instance, it is challenging to distinguish substance-induced symptoms (both short-term and long-term) from symptoms unrelated to substance abuse (Demarce et al., 2013). In addition, accurate diagnoses are not always available for co-occurring disorders, including psychiatric disorders (Kranzler et al., 1996, Kranzler et al., 1997).

The degree of substance use could be evaluated from the information gathered from the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders IV-TR (Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders IV-TR).

The database's secondary diagnoses section records a service user who met the criteria for a substance use disorder with this information. A distinction is made between the lifetime usage, last year's, and last month's use. Furthermore, the clinical notes also documented whether the service user continued to use the substance and whether they received substance abuse treatment.

It has been determined that different substances have been categorised: alcohol, cannabis, opiates, stimulants, hallucinogens, prescription medications, and other substance groups.

The presence of a substance-induced psychotic condition was recorded and analysed in the statistical analysis.

## 2.2.5 Materials

In addition to structured SCID interview for DSM IV-TR, all study participants were evaluated further with a set of rating scales:

- GAF - Global Assessment of Functioning,
- SAPS - Scale for the Assessment of Positive Symptoms,
- SANS - Scale for the Assessment of Negative Symptoms,
- DUP - Duration of Untreated Psychosis - based on Beiser scale,
- CDSS - Calgary Depression Scale for Schizophrenia,
- YMRS - Young Mania Rating Scale,
- Birchwood Questionnaire (to assess insight into illness),
- Modified Overt Aggression Scale (MOAS).

### 2.2.5.1. Global Assessment of Functioning (GAF)

All study participants had a GAF rating that was recorded. Global Assessment of Functioning was introduced to assess the severity of illness in psychiatry and is known worldwide as Axis V of the internationally accepted Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision (DSM-IV-TR) (Association, 2013).

The GAF is intended as a generic rather than a diagnosis-specific scoring system. It is constructed as an overall (global) measure of how patients are doing concerning their psychological, social, and occupational functioning and ranges from good mental health to severe mental illness. In international practice, GAF recorded values can be recorded as either a single score (only the most severe symptoms and functioning values are recorded) or as separate scores for symptoms (GAF-S) and functioning (GAF-F). In the GAF-F and GAF-S scales, there are 100 scoring options (1-100) (Aas, 2011).

Its comprehensiveness and simplicity have led to widespread use of the GAF in clinical practice and research; however, these same features have also been viewed as its limitations (Yamauchi et al., 2001). There were two specific limitations identified in the Global Assessment of Functioning Scale. Specifically,

the first limitation was that both symptoms and social functioning were measured on a single axis; the second limitation was that physical impairments were excluded from the rating of functioning (Goldman et al., 1992).

#### 2.2.5.2. SAPS (Scale for the Assessment of Positive Symptoms) and SANS (Scale for the Assessment of Negative Symptoms)

Many studies have classified schizophrenia into separate subtypes and associated each subtype with relevant clinical and sociodemographic factors. A division model of schizophrenia creating a distinction between positive and negative subtypes of schizophrenia was developed by Crow (1980) and Andreasen (1982) (Vázquez-Barquero et al., 1996, Andreasen, 1983, Crow, 1985).

With no standardised scale for measuring positive or negative symptoms, negative symptoms were frequently overlooked, both in clinical and research settings, while the emphasis was on positive symptoms that were occasionally exaggerated (Kumari et al., 2017).

The (SANS) and (SAPS) were developed in 1980 to address a noticeable gap in the availability of tools capable of accurately assessing the severity of negative and positive symptoms (Andreasen et al., 1991). It was followed by the widespread use of multivariable statistical tests, such as factor analysis and cluster analysis, to analyse SANS/SAPS symptom score patterns (Vázquez-Barquero et al., 1996).

A new interest in screening patients with negative symptoms and the intercorrelation of negative symptoms emerged due to Crow's observations on the significance of negative symptoms (Andreasen, 1983). The Scale for the Assessment of Negative Symptoms (SANS) was developed in response to this paradigm shift (Kumari et al., 2017).

The SANS was explicitly developed to quantify negative symptoms associated with schizophrenia. The scale contains 25 items and is subdivided into five subscales: affective flattening or blunting, alogia; apathy; asociality; and inattention

representing the concept that negative symptom structure in schizophrenia is multidimensional and distinguishable from both positive and depressive symptoms (Rabany et al., 2011). On a six-point scale, each symptom is graded (ranges from 0 to 5) according to its severity. Each subscale contains several items that address specific symptoms, such as a regular facial expression or poor eye contact. On a global scale, all subscales in a rating are combined to form a comprehensive summary (Rabany et al., 2011).

In terms of structure, there are similarities between the SAPS and the SANS. The SAPS scale was released a year after the introduction of the SANS and enabled clinicians to evaluate positive symptoms using a format and structure comparable to that of the SANS (Kumari et al., 2017).

There are four subscales under which the SAPS 34 scale items are broken down: hallucinations, delusions, bizarre behaviour, and formal thought disorder. Similarly to the SANS, each subscale includes a global rating scale designed to summarise all symptoms associated with a particular subscale category. The author provides detailed instructions on completing ratings on the SAPS and the SANS (Rabany et al., 2011, Andreasen, 1983).

The total score across specific symptoms or the global rating can summarise each component subscale for both the SANS and SAPS.

The SAPS or SANS total score can provide an overall measure of positive and negative symptoms. These total scores can be calculated by adding the scores from the global rating scales (referred to as a summary score) or adding the scores for individual symptoms (composite score). According to the author of the scales, summary scores based on global ratings are likely to be a more sensitive index than the combined score (Andreasen, 1982, Rabany et al., 2011)

Both SANS and SAPS are frequently used in clinical and research settings. Since the scales' commencement, reliability and validity have been raised, and numerous studies on the scales' validity have been conducted. Earlier research has concentrated on interrater reliability, which has been demonstrated to be consistent across multiple cross-cultural contexts (Andreasen et al., 1991) (Kumari et al., 2017).

According to one study, while the SAPS and SANS exhibit moderate temporal stability over 12 months, the apathy and bizarre behaviour subscale scores show little stability (Malla et al., 1993).

Some authors promoted a re-conceptualization of schizophrenia's structure, arguing for a multidimensional system comprising at least three groups, including hallucinations/delusions, positive thought disorder, and negative symptoms, rather than simply dividing schizophrenic symptoms into positive and positive-negative signs (Klimidis et al., 1993, Minas et al., 1992).

Separate research on the interrelationships between symptoms using SAPS and SANS resulted in a three-dimensional model comprised of psychotic, disorganised, and negative factors (Andreasen et al., 1995). Proponents of a more complex concept of schizophrenic symptomatology assert that schizophrenia cannot be neatly classified or divided as SAPS and SANS are. Based on Crow's "two syndromes," it may be essential to develop newer models incorporating additional factors and the diverse elements of schizophrenic symptoms into their structures (Kumari et al., 2017).

#### 2.2.5.3. Beiser scale - Measurement of Duration of Untreated Psychosis (DUP).

Establishing the accurate onset of psychosis is required in clinical practice and research. The Beiser scale was introduced in 1991. It is a structured interview with the individual's relatives during the first episode of psychosis that estimates the emergence of psychotic symptoms. It focuses on the first noticeable symptoms that indicate a prodromal period. In addition, it determines the emergence of first psychotic symptoms and the initiation of treatment-seeking. Reliability estimates were significant ( $p < 0.01$ ) in all three domains; the intraclass coefficient was 0.79 for the rating of first noticeable symptoms, 0.98 for the first psychotic symptoms, and 0.95 for the initiation of treatment-seeking (Fleming and Wc, 1993).

The Beiser scale was introduced to service users participating in this study and their family members as part of the assessment process.

#### 2.2.5.4. Calgary Depression Scale for Schizophrenia (CDSS)

The Calgary Depression Scale for Schizophrenia (CDSS) was developed to distinguish between negative symptoms of schizophrenia, extrapyramidal symptoms, and depressive symptoms in the presence of schizophrenia, with a high prevalence of depressive syndrome and suicidality (Addington et al., 2014, Addington et al., 1993).

Based on an interview with the individual suffering from schizophrenia spectrum disorder, the CDSS has nine items to rate zero and three points. A 0 point represents the absence of the symptom, and the intensity of the existent symptoms is assessed as mild, moderate, or severe, with one, two, or three points awarded correspondingly. The scale includes various biological indicators of depression, such as early waking and mood fluctuations throughout the day. The ranking of negative cognitions regarding oneself and one's future is also mentioned. Other cognitive symptoms, such as guilt/reference thoughts and pathological guilts, are also rated. The suicide question is similarly rated, ranging from no symptoms to a suicidal attempt with deadly intent. Item 9 is rated based on the interviewer's observations, which objectively assess depressive syndrome (Addington et al., 1993).

Excellent psychometric properties, inter-rater reliability, sensitivity and specificity, and internal consistency were demonstrated worldwide, and it has been translated into 36 languages (Addington et al., 2014).

CDSS demonstrated a potential advantage over other commonly used scales for depressive syndromes, such as the Beck Depression Inventory, as it is easier to administer in inpatient and outpatient settings (Addington et al., 1993).

#### 2.2.5.5. Young Mania Rating Scale (YMRS)

The Young Mania Rating Scale (YMRS) contains eleven items, each with five explicitly defined grades (Lukasiewicz et al., 2013). The items are selected based on the core symptomatology of a manic episode as published in relevant research

(Young et al., 1978). The scale is clinician-rated based on a clinical interview and observations 48 hours before completing the scale. All grades in every item are well anchored, improving the rating accuracy.

Four items (irritability, speech, content, disruptive-aggressive behaviour) are graded with higher points emphasising the importance of these items and compensating points in case of uncooperativeness (Young et al., 1978).

The YMRS is one of the most frequently used rating scales for assessing manic symptoms in affective and schizophrenia spectrum disorders.

The inter-rater reliability, validity and sensitivity have been examined and proved significant (Young et al., 1978).

#### 2.2.5.6. Birchwood Questionnaire (to assess insight into illness),

Insight is a multifaceted and complex concept that refers to an individual's perception of their mental illness, its impact on functioning, and the necessity of treatment. Lack of insight is a frequent co-occurring symptom of psychosis and has historically been viewed as a binary, all-or-nothing phenomenon. Insight has increasingly been recognised as a continuous, multidimensional, and modifiable phenomenon rather than a binary phenomenon (McEvoy et al., 1989).

Numerous studies, including the World Health Organization's international pilot study of schizophrenia, have discovered that most patients with schizophrenia, up to 97 %, lack insight into their condition during an acute psychotic episode (World Health, 1973, Wilson et al., 1986).

In severe mental illnesses such as schizophrenia and other psychotic disorders, Insight refers to an individual's recognition of the existence of a mental illness and a realisation that treatment will be beneficial (Cleary et al., 2014).

While insight is a poorly defined concept, it is widely used in clinical practice because it can potentially affect treatment compliance, dangerousness, suicide, risk, and prognosis (Birchwood et al., 1994).

The Birchwood Insight Scale quantifies the three dimensions of insight (awareness of the illness, need for treatment and attribution of symptoms). The

conceptualisation defined insight as a continuum representing the juxtaposition of three variables.

The Birchwood Insight Scale, which is increasingly being used in psychiatric research (particularly studies involving individuals with schizophrenia and other psychotic disorders), has several advantages: its simplicity and ease of administration.

The Birchwood Insight Scale is a self-administered questionnaire consisting of an eight-item self-report. The second and seventh questions are related to awareness of the illness, the first and eighth questions to attributions of symptoms, and the third, fourth, fifth, and sixth questions to the need for treatment. The responses "agree," "unsure," or "disagree" are scored on a three-point Likert-type scale ranging from 0 to 2. The subscale items are added together, and the Need for Treatment subscale is divided by two to account for the fact that it contains twice the number of items – these results in a total score for each subscale. Summarise the complete scores to obtain a BIS total score (range = 0-12), with higher scores indicating greater insight (Emmerson et al., 2009).

While clinician-rated instruments help assess patients' expressed attitudes and behaviours, self-report instruments provide critical information about patients' opinions and internal experiences (Cleary et al., 2014).

#### 2.2.5.7. Measurement of aggression and violence

The measurement of violence in research is based on self-report measurements and observation scales.

Self-report measurement scales published in research are difficult to administer, especially in individuals with severe mental illness as they operate with many questions and subscales. For instance, one of the oldest scales was created in 1957, the Buss-Durkee Hostility Inventory, a self-report scale consisting of 75 items and seven subscales (Buss and Perry, 1992). However, the most recently developed self-rating Aggression Questionnaire contains 34 items and three subscales (Buss and Warren, 2000). Although the advantage of the self-assessment scales lies in the

time savings and limited personnel involvement, they depend on the person's cooperation and the ability to process the information (Biggs et al., 1978).

The Modified Overt Aggression Scale (MOAS) scale was used to conduct a retrospective review of all case notes and incident reports for all study participants over one year (6 months before and after the first presentation for treatment for psychosis).

The Modified Overt Aggression Scale was introduced to quantify aggression and violence to counterbalance the lack of sophisticated assessment methods. Its purpose was also a predictive instrument to determine the likelihood of future aggressive and violent instances (Kay et al., 1988). This scale was a revision of the Overt Aggression Scale introduced earlier that used a behavioural checklist in four categories (verbal aggression, aggression towards property, self-aggression and aggression towards others) (Yudofsky et al., 1986). The modified version of the Overt Aggression Scale uses the same categories of aggression; however, it quantifies the level of aggression with a five-point rating system. The MOAS introduced a weighted total score to reflect the seriousness of aggression by multiplying the four individual aggression items by 1 in case of verbal aggression, 2 in case of aggression against property, by 3 in case of aggression against self and by 4 in case of aggression against others (Kay et al., 1988).

The validity and reliability of MOAS have been tested in several studies over the past decades (Sorgi et al., 1991, Coccaro et al., 1991, Huang et al., 2009). It was also highly valid in different cultural contexts (Chukwujekwu and Stanley, 2008, Huang et al., 2009). The reliability and effectiveness of the assessment tool and the systematized and structured way of rating aggression and violence have allowed its introduction into clinical practice for maximum security psychiatric units in some countries (Joyal et al., 2008).

### 2.2.6. Statistical analysis

Statistical analysis was conducted using SPSS version 28 (IBM Corp., Armonk, NY, USA, 2022).

Standard statistical analyses utilised in this study were used to determine the prevalence of substance use and instances of aggression and violence. In relative risk terms, one analyses the difference between the incidence of an outcome in those exposed to a specific risk factor and the incidence in those not (Freeman et al., 2006).

MOAS scores were recoded into binary forms of each category as present or absent. High MOAS scores on aggression against others with a potential to cause harm to others were considered severe violence and were recoded in binary form for further analysis. Odds Ratios were determined concerning pre-, and post-contact aggression and violence were analysed concerning substance misuse, age groups, gender, and diagnostic groups in bivariate analyses.

Statistically significant relative risk outcomes were reviewed using binary logistic regression to predict the relationship between independent variables (predictors) and dependent variables (predicted variables).

The Chi-square and Mann-Whitney U tests were used to examine the impact of substance use on continuous clinical variables and aggressive levels. Further, an in-depth analysis was conducted, deploying moderation and mediation analysis and collinearity tolerance statistics for significant correlations.

### 2.2.7. Ethics

The Research Ethics Committee of Saint John of God Hospitaller Ministries approved this study on 11th July 2017 (ID685).

## 2.3. Results

### 2.3.1. Sample - sociodemographic characteristics of the cohort

#### 2.3.1.1. Age

This study included two hundred sixty-five people with a first episode psychosis. The mean age of the patients was 32.48 years (SD = 11.273), and the median age was 30.0 years (SD = 11.273). There was a significant difference between the mean ages of men and women. The mean age for males was 30.61 years (SD = 11.174), while the mean age for females was 35.23 years (SD = 10.897),  $p < 0.001$ ).

Two age groups were formed to investigate the associations between age and other clinical factors: those under 35 and those over 35. A percentage of 62.3% in this sample were under 35 years old, while a rate of 37.7% were over 35 years old.

Gender distribution in different age subgroups is visualised in Graphic No 1 (Appendix section, page: 136), and the relationship map between age groups and gender is presented in Graphic No. 2 (Appendix section, page: 136).

#### 2.3.1.2 Gender

59.5% of this sample were male, while 40.8% were female. There was an association between the male gender and the under 35 age group (OR = 2.413, 95% CI 1.449 - 4.020,  $p < 0.001$ ).

#### 2.3.1.3 Sociodemographic factors

As part of the initial contact, various sociodemographic characteristics were collected from each research participant and recoded into a binary format for statistical analysis.

Concerning educational background, there were two categories: non-graduates and secondary school graduates. According to this sample, 67 per cent of service users passed their high school exams. Females were significantly more likely than males to graduate high school (OR = 2.786, 95% CI = 1.629 - 4.765,  $p < 0.001$ ).

Most cohort members (78.5%) were not married, and males were more likely to be single than females (OR = 3.570, 95% CI = 1.930 - 6.602,  $p = 0.001$ ). However, there is a possibility that age plays a role in this association, as the mean age for males was significantly lower in comparison to females.

Regarding employment, 66.4% of study participants were not employed at the time of enrolment. Based on professional status, this cohort had no significant gender differences ( $p = 0.083$ ).

Concerning living status, the proportion of people living alone in this cohort was 46.5%. No statistically significant difference ( $p = 0.163$ ) between genders concerning living status.

### 2.3.2 . Clinical factors and associations with gender and age

Based on the available data, the vast majority (76.9%) of this patient cohort was classified as having schizophrenia spectrum disorders when they had their first episode of psychosis. Sixty-eight participants were diagnosed with schizophrenia, accounting for 25.8% of the sample. There were 26 patients with delusional disorder (9.8% of the sample), 25 patients with schizophreniform disorder (9.5%), 20 patients with transient psychosis (7.6%), 33 patients with substance-induced psychosis (12.5% ), eight patients with psychotic disorder resulting from general medical procedures, and 13 patients with diagnosed psychotic disorder not otherwise specified (4.9%). The minority of this patient group had a mood disorder with psychotic features, 26 (9.8%) individuals with bipolar disorder, 23 (8.7%) people with major depression with psychotic features, and 12 (4.5%) people with a substance-induced mood disorder.

There were sporadic presentations of Bipolar II Affective Disorder in this sample, with one case accounting for less than 0.4% and schizoaffective disorder representing two cases accounting for more than 0.8% of this sample.

Gender differences were observed concerning diagnostic categories. Males had a 2.38-fold higher chance (CI 95%: 1.297 - 4.364,  $p = 0.004$ ) of receiving a diagnosis of schizophrenia and a relative risk of 4.428 (CI 95% 1.651 - 11.873,  $p < 0.001$ ) to

develop substance-induced psychosis than females. No gender differences were observed in the case of affective psychoses (OR = 1.727, CI 95% 0.970 - 3.074,  $p = 0.74$ ). Diagnostic categories in both genders are presented in Graph No 3 (Appendix, page:137).

Mann-Whitney U test was performed to compare differences between two independent variables on several continuous dependent variables, including global assessment of functioning (GAF), duration of untreated psychosis (DUP), positive and negative symptoms (SAPS, SANS), depressive symptoms (CDSS), manic symptoms (YMRS), and insight into the condition (Birchwood).

No gender differences were observed in the global level of functioning, duration of untreated psychosis, positive, depressive, and manic symptoms, and insight into the condition. Negative symptoms were the only clinical variables that showed statistically significant gender difference, as males ranked significantly higher than females (mean rank: males 137.83, females 112.77; Mann-Whitney U: 6227,000,  $p = 0.008$ ) (Table Nr 1, Appendix, page: 137).

Younger age showed no significant correlation with clinical variables, including positive and negative symptoms of psychosis, depressive symptoms, manic symptoms, and insight into condition (Table Nr 2, Appendix, page: 138).

### 2.3.3. Prevalence rates and gender differences of substance use

In studies including first-episode psychosis cohorts, gender and age differences concerning the prevalence of substance use were frequently reported in the literature (Arranz et al., 2015b, Tosato et al., 2013, Stone et al., 2014, Schimmelmann et al., 2011, Compton et al., 2017, Allegri et al., 2013), as cannabis use and gender can have an independent effect on the age of onset of the first episode of psychosis (Barnes et al., 2006).

The information on substance use in this sample was extracted from the SCID interview. Lifetime, past year, use in the past month, and SCID dependence diagnoses were recorded.

## Alcohol

A total of 20.2% of patients in the present study had used alcohol in the month prior to their first episode of psychosis, and 15.6% of alcohol users continued to use alcohol after contact with services. The prevalence of alcohol use disorder was 31.4%, with no significant gender difference ( $p = 0.064$ ).

## Illicit substance use

There was a significant difference in illicit substance use among men in this cohort (OR = 2.025, 95% CI 1.489 2.754,  $p = 0.001$ ). In addition, males are more likely to continue using illicit drugs after being diagnosed with psychosis (OR = 2.708, 95% CI 1.448 3.678,  $p = 0.001$ ).

## Cannabis

There was a lifetime prevalence of cannabis use of 44.5%. 35.4% of the cohort used cannabis in the past year and 28.5% in the last month before a diagnosis of first psychosis.

A significant association was found between cannabis use and the male gender (OR=2.146, CI 95% 1.518-3.193,  $p=0.001$ ) and stimulant use (OR=2.084, CI 95% 1.229-3.533,  $p=0.003$ ).

Age below 35 years showed a statistically significant association with illicit substance use (OR = 2.348, CI 95% 1.668 3.303,  $p = 0.001$ ); continued substance use after contact with services (OR = 2.188, CI 1.359 3.524,  $p = 0.000$ ); cannabis use (OR=2.760, CI 95% 1.858 4.120,  $p=0.001$ ); and for stimulant use (OR = 3.959, CI 95% 1.966 7.972,  $p = 0.001$ ).

## Stimulants

23.3% of this cohort had used stimulants at some point in their lives, 9.9% in the last year and 5.7% in the last month.

## Other substances

On average, 12.2% of this cohort had used hallucinogens over their lifetime, 5.3% in the last year and 3.4% in the previous month. Prevalence rates for opiates were lower than for cannabis and stimulant use, showing lifetime use of 7.3%, 4.2% in the prior year and 3.1% for last month's use.

In the sample, sedatives, prescription drug abuse, and other drug usage were infrequent.

In the absence of sufficient statistical power, in this cohort, it was impossible to quantitatively analyse the relationship between gender, the young age group, and the use of other substances (hallucinogens, tranquillisers, and other substances).

## Polysubstance use

According to this sample, poly-substance use was observed in 31.1% of participants. Alcohol use disorder with concomitant illicit substance use was detected in 20.5% of participants. Combinations of several illegal substances use also accounted for 21.2%.

64.1% of those with a lifetime of cannabis use used multiple substances, including 40.5% with an alcohol use disorder and 47.9% who used other illicit substances but did not meet the criteria for alcohol dependence.

Lifetime cannabis users were more likely to use other substances (OR = 35.204, 95% CI 15.075 82.210,  $p < 0.001$ ). Similarly, lifetime cannabis use was significantly associated with alcohol use disorder (OR = 13.49, 95% CI 5.768 31.261,  $p < 0.001$ ).

## Access to addiction services

Despite the high prevalence rates of alcohol use disorders and cannabis use recorded in this sample, only 4.9% were referred to an addiction counselling centre for further intervention, and 46.8% received psychoeducation on the effects of substance use.

#### 2.3.4. Prevalence rates of substance use in comparison to the general population and severe mental illness cohorts

Study participants in the current study were recruited between 2006 and 2015 inclusive. A comparison was made to the data on drug and alcohol use in the general population of the same geographically defined catchment area. The information was extracted from the Human Research Board online databases covering the same period.

A 2018 report from the National Drug Treatment Reporting System (NDTRS) on treated alcohol use disorders found that 53,763 patients were treated for alcohol as a primary concern over these seven years in Ireland, from 2010 to 2016 (Board, 2018). Almost two-thirds of all cases (64.9 %) were alcohol dependent. Three out of every five (60.2 %) new patients (those who had not previously been treated for problem alcohol consumption) were classed as alcohol dependent.

The number of individuals seeking treatment for alcohol use disorder in the same catchment area (Community Health Organisation 6 (CHO6) - comprising 398,000 inhabitants in 2017) fluctuated from 245 (in 2016) to 345 (in 2014). By contrast, 31.5% of the current study's cohort, representing 82 individuals, had a lifetime alcohol use disorder diagnosis based on a SCID interview.

The findings of this study were compared clearly to those of a study analysing clinical and demographic associations with comorbid substance use in psychotic patients, where the lifetime diagnosis of alcohol dependence or abuse was identified in 27.6% (Kavanagh et al., 2004).

Regarding the general population, 17.4 % of individuals treated for problem alcohol use also reported polydrug use in the National Drug Treatment Reporting System (NDTRS). Cannabis was the most often utilised as a second substance (57.7%), followed by cocaine (35.4 %)(Board, 2018).

In the current study cohort, past-year cannabis use was found in 43.9% of individuals diagnosed with alcohol use disorder, and past-year stimulant use was 12.5%. Lifetime illicit substance use data among the first episode of psychosis cohort with co-morbid alcohol use disorder showed 54.9% for cannabis and 38.3% for stimulants, comparable to the general population's results in the same period.

According to All Ireland Prevalence Survey results published in 2015, the most significant increase in drug usage tends to be among those under 35. In the age group between 35 and 64, however, past-year and current use of any illegal substance, cannabis, and ecstasy increased modestly between 2011 and 2015 (Bates, 2017).

### 2.3.5. Sociodemographic and clinical correlations of substance use

A significant difference was shown in the age of onset of psychosis among individuals who used illicit substances and those who did not use them (mean age: nonusers 37.04, SD = 11.892; users 28.07, SD = 8.678,  $p = 0.001$ ).

Further analysis showed significant age difference in presentation with first-episode psychosis was significant only in case of cannabis users (mean age: nonusers 36.68, SD = 11.750; users 27.36, SD = 8.235,  $p = 0.000$ ), stimulant users (mean age: nonusers 33.99, SD = 11.772; users 27.41, SD = 7.606,  $p = 0.000$ ), hallucinogen users (mean age: non users 33.61, SD = 11.364; users 24.19, SD = 24.19,  $p = 0.001$ ).

There were no significant differences in age between those who used sedatives or other illicit substances and those diagnosed with alcohol use disorder.

Gender differences in substance use were presented in the previous section 2.3.3.

Other sociodemographic variables analysed in multivariate tests (marital status, living alone or with others, employment status, level of education attained) showed no significant associations with substance use, except for marital status in the case of illicit substance users; however, age proved to be a confounding factor in this case.

Statistically, no significant associations were found between lifetime illicit substance use and clinical presentation in the following categories: SAPS, SANS, CDSS, YMRS, DUP, insight, and GAF (Table Nr 3, Appendix, page:138).

An analysis of various psychoactive substances, the presence or absence of alcohol use disorder (Table Nr 4, 5, Appendix, pages: 138, 139), and the use of illicit or

legal substances before and after contact did not reveal any significant associations with clinical indicators (Table Nr 6, 7, 8, Appendix, pages: 139, 140).

#### 2.3.6. Prevalence rate of aggression and violence

Incidents of aggression and violence were recorded retrospectively by evaluating all medical records six months before and six months after the diagnosis of the first episode of psychosis.

Each aggressive and violent episode was rated and weighted using the Modified Overt Aggression Scale (MOAS) according to the guidelines of the scale's original author (Kay et al., 1988).

The sample showed that 44.7% of the cohort had perpetrated aggression and violence in the six months before contacting services, and 28.4% demonstrated such behaviour after that. One in five individuals from this cohort showed aggression and violence during pre- and post-contact phases. A total of 25.6% of the cohort demonstrated verbal aggression prior to contact, while 20.5% demonstrated verbal aggression after contact with the services.

The percentage of any violence recorded in the post-contact period (17.4%) reduced to nearly half of the rate of violent incidents during the pre-contact period (31.1%). The minority of study participants (8.7%) showed signs of violence before and after the contact. In this cohort, there was a relatively low prevalence of violence against property at 8.7% before contact and 9.8% after contact with the services.

Regarding violence against others, there was a significant difference between the pre-contact (16.4%) and post-contact (8.8%) period.

For suicide attempts, there were significantly higher rates in the pre-contact period (13.4%) than in the post-contact period (5.7%,  $z = 3$ ,  $p = 0.0026$ ).

### 2.3.7. Comparison of prevalence rates of aggression and violence with previous studies completed in the same geographic catchment area

Previous studies conducted in 1995 - 1998 (Foley et al., 2005) and 2010 - 2013 (Keane et al., 2019) assessed aggression and violence one week before and one week after the contact with services.

The results of a much more extended observation period reveal an increase of three times the level of aggressive behaviour (44.7%) in this cohort compared to the cohort from 1995 to 1998 (16%) and two times the rate when compared to the cohort from 2010 to 2013 (21%,  $z = 4.6$ ,  $p = 0.0001$ ).

It is also worth noting that post-contact aggression rates have been significantly higher in the extended period of data collection within the same catchment area (28.4%) than in the 1995 - 1998 cohort (7.3%,  $z = 5.2$ ,  $p = 0.0001$ ) or the 2010 - 2013 cohort (5.6%,  $z = 5.4$ ,  $p = 0.0001$ ).

In both the pre-contact period and the post-contact period, aggression rates for both cohorts were significantly higher than those for the cohort from 1995 - 1998 (10%,  $z = 2.7$ ,  $p = 0.0067$ ), but not significant in comparison to those of the 2010 - 2013 cohort (11%,  $z = 2.3$ ,  $p = 0.0233$ ).

This cohort had a significant increase in the rate of pre-contact violence (31.1%) as compared to the cohort for the 1995 - 1998 years (13.0%,  $z = 4.2$ ,  $p < 0.0001$ ), but not significantly compared to the cohort for the 2010-2013 years (22%,  $z = 1.9$ ,  $p = 0.575$ ).

There was a significant increase in the rate of post-contact violence (17.4%) during the current cohort when compared to the 1995 - 1998 cohort (8%,  $z = 2.7$ ,  $p = 0.007$ ), and to the 2010 - 2013 cohort (7%,  $z = 2.8$ ,  $p = 0.0048$ ).

During both, pre- and post-contact periods, violence rate was 8% in current cohort, as compared to 8% in 1995 - 1998 cohort ( $z = 0.2$ ,  $p = 0.807$ ), and significantly higher than 0% in 2010 - 2013 cohort ( $z = 3.5$ ,  $p = 0.0005$ ).

### 2.3.8. Statistical associations between aggression - violence and different sociodemographic and clinical variables

The intricate nature of the relationship between gender, age and aggression and violence is visualised in Graphic No: 4 (Appendix, page: 141) and Graphic No: 5 (Appendix, page: 141), which is further complicated when substance use is introduced as an additional factor Graphic No: 6, 7 (Appendix, page: 143).

#### 2.3.8.1. Statistical associations between gender - aggression and violence

The cases of aggression or violence before and after the contact showed no significant gender patterns. It is essential to acknowledge that verbal aggression and physical violence (against property, self and others) were analysed separately, but neither was statistically related to gender (Table Nr: 9, Appendix, page: 142). Further binary logistic regression analysis did not show any significant associations between gender and aggression (Table Nr: 10 Appendix, page: 142) or gender and violence Table Nr: 11, Appendix, page: 143).

#### 2.3.8.2. Statistical associations between age - aggression and violence

There was no significant difference between the age groups under 35 and over 35 after an independent analysis of pre-contact and post-contact aggression and violence (Table Nr 12, Appendix, page: 143). No significant correlation was found in the linear regression model ( $R = 0.008$ ,  $p = 0.152$ ).

Age did not significantly correlate with severe violent behaviour (Mann- Whitney U 3378.00,  $p = 0.154$ ).

#### 2.3.8.3. Statistical associations between social factors - aggression and violence

From all sociodemographic variables analysed in this study, only lower educational levels showed a statistically significant correlation with aggression (OR = 2.362, CI 95% 1.386 - 4.025,  $p = 0.002$ ), that remained statistically significant in logistic regression analysis (Table No: 10, page: 142).

#### 2.3.8.4. Statistical associations between diagnosis / psychopathology - Aggression and Violence

There was no statistically significant difference in aggression and violence incidents between affective and non-affective psychosis groups, despite statistical differences in the duration of untreated psychosis, negative symptoms, and manic symptoms (Table No: 13, Appendix, page: 145).

When compared to primary psychoses, individuals with substance-induced psychotic episodes showed an increased risk of self-harm in the post-contact period (OR=4.913, CI 95% 1.777 - 13.585,  $p = 0.004$ ), as well as an increased risk of post-contact violence against others (OR=4.544, CI 95% 1.752 - 11.783,  $p = 0.003$ ). Using binary logistic regression analysis, the significance of auto-aggression post-contact remained the same (B 0.131, S.E. 0.052, Wald 6.463,  $p=0.01$ , Exp(B) 1.140 CI 95% 1.031 - 1.262).

Despite substantial correlations between substance-induced psychosis and aggression, there were no significant differences between those with and without substance-induced psychosis in terms of psychopathology, age, duration of untreated psychosis, or level of insight Table Nr: 14, Appendix, page: 145).

Any aggression during the pre-contact and post-contact periods was significantly correlated with reduced GAF scores (Table Nr 15, Appendix, page:145). Detailed analysis showed that aggression in pre-contact period was associated with lower level of functioning and positive symptoms (Table Nr 16 Appendix, page: 145). In the post-contact period, aggression was statistically significantly associated with lower depressive symptoms (Table Nr 17, Appendix, page:146).

Violence was associated with positive symptoms in the pre-and post-contact period (Table Nr: 18, Appendix, page:146). A lower level of GAF scores and higher rates of positive symptoms were associated significantly with pre-contact violence (Table Nr:19, Appendix, page:147). Still, no significant associations were observed between post-contact violence and psychopathology (Table Nr:20, Appendix, page: 147).

A significant correlation was observed between severe violence and the SAPS global rate, manic symptoms, lack of depressive symptoms and lower GAF scores (Table Nr: 21, Appendix, page: 148). However, manic symptoms and lower depressive symptoms may be inter-correlated.

A detailed analysis of positive symptoms and severe violence showed statistically significant associations with delusions of persecution (Mann - Whitney U 2615,  $p = 0.007$ ), delusions of guilt (Mann -Whitney U 2944  $p = 0.008$ ), delusions of grandeur (Mann -Whitney U 2816.000  $p = 0.007$ ); bizarre behaviour [social (Mann -Whitney U 2775.500,  $p = 0.006$ ); agitated behaviour (Mann - Whitney U 1629.000  $p < 0.001$ )]; and thought disorders [derailment (Mann - Whitney U 2331.000  $< 0.001$ ), tangential (Mann - Whitney U 2381.500  $p < 0.001$ ), pressured speech (Mann - Whitney U 2387.000  $p < 0.001$ )].

#### 2.3.8.5. Statistical associations between substance use - aggression and violence

A substantial increase in the risk of aggression was associated with alcohol use disorder following post-contact with services (OR = 2.139, 95% CI = 1.216 - 3.761,  $p = 0.01$ ).

It was also noted that alcohol use in the last month prior to contact was significantly associated with aggression (OR = 2.671, 95% CI 1.345 - 5.305,  $p = 0.007$ ), specifically with verbal aggression (OR = 2.689, 95% CI 1.387 - 5.936,  $p = 0.006$ ).

Violence towards others causing harm was associated with alcohol use disorder (OR = 2.664, CI 95% 1.292 - 5.491,  $p = 0.007$ ), alcohol use in the month preceding contact with services (OR = 2.748, CI 95% 1.277 - 5.911,  $p = 0.01$ ), and alcohol use following the contact with services (OR = 3.562, CI 95% 1.602- 7.934,  $p = 0.003$ ).

These results were replicated in the degree of aggression and violence: a significant association between alcohol use disorders and post-contact violence (Table No:22, Appendix, page: 148) and a significant correlation between alcohol consumption in the post-contact period and verbal aggression (Mann-Whitney U 3627.500,  $p = 0.004$ ) and violence against others (Mann- Whitney U 3818.000  $p = 0.001$ ).

Illicit substance use in general was associated with aggression and violence showing a two-fold relative risk (OR 2.103, CI 95% 1.283 - 3.447,  $p = 0.003$ ) attributed to both pre-contact violence (OR = 2.193, CI 95% 1.276 - 3.769,  $p = 0.003$ ) and post-contact violence (OR = 2.437, CI 95% 1.225 - 4.848,  $p = 0.007$ ).

Those who used substances following contact with services had twice the odds of engaging in aggressive or violent behaviour in the post-contact period (OR = 2.114, CI 95% 1.200-3.722,  $p = 0.007$ ) compared to those who stopped using substances after contact with services.

Among all the incidents of aggression and violence that were assessed, violence against property and violence against others were associated with illicit substance use in the post-contact period (Table No: 23, Appendix, page:149).

Lifetime cannabis use was not associated with aggressive or violent behaviour during pre- or post-contact periods (Table No:24, Appendix, page:149). However, the recent use of cannabis was associated with verbal aggression during the post-contact period (Table No: 25, Appendix, page:150).

As compared with lifetime stimulant use, recent stimulant use was significantly associated with post-contact aggression (OR = 5.710, CI 95% 1.913 - 17.646,  $p = 0.002$ ), as well as post-contact violence (OR = 2.476, CI 95% 1.240 - 4.942,  $p = 0.009$ ).

A more detailed analysis showed that lifetime stimulant use was significantly associated with self-directed violence and violence against property in the post-contact period (Table No: 26, Appendix, page: 151); however, past month stimulant use did show any correlation with any aggression (Table No: 27, Appendix, page: 152).

According to a detailed analysis, there was no statistically significant correlation between substance use and suicide attempts.

As a result of the low statistical power, further analyses of relative risks related to other licit or illicit substances were not performed, including sedatives, other substance groups and prescription medications.

#### 2.3.8.6. Substance use as possible moderating factor in aggression and violence in first-episode cohort

The study examined the role of alcohol use, particularly alcohol use disorder and past month alcohol use, in violence-related positive symptoms. A link between violence and positive symptoms has been demonstrated. However, the study found no statistically significant evidence that alcohol use disorder plays a moderating role in this context. The analysis revealed that the SAPS composite scores were a statistically significant predictor ( $p = 0.036$ ) with the highest standardised coefficient ( $\beta = 0.146$ ), suggesting that it played a critical role in predicting precontact violence. In contrast, alcohol and the moderating variable were not statistically significant ( $p > .05$ ), suggesting that their effects on precontact violence were not significant in this model. Although there were no serious multicollinearity issues, the moderately elevated VIF (Variance Inflation Factor) scores for alcohol use disorder and moderating factor suggest possible multicollinearity that requires further attention. (Table No:28, page 153).

Polysubstance use had significant correlations with pre-contact violence on the linear regression model. Post-contact verbal aggression (Mann–Whitney U 6361.500,  $p = 0.01$ ) and post-contact violence against property (Mann–Whitney U 6535,  $p = 0.003$ ) were positively associated with polysubstance use. However, the moderating role of polysubstance use did not show statistical significance. The variables representing polysubstance use and the SAPS composite score were statistically significant predictors of the dependent variable, as indicated by their low  $p$  values (0.030 and 0.042, respectively). In contrast, the moderating factor had no statistically significant impact on the dependent variable ( $p = 0.383$ ) and showed some multicollinearity (VIF = 6.151), suggesting that it contributed only limited value to the model. Among the predictors, the SAPS composite score had the most substantial positive effect, as reflected in its standardised coefficient ( $\beta = 0.241$ ), closely followed by multiple substance use ( $\beta = 0.237$ ). (Table No: 29, page 153).

### 3. Discussion

3.1 Hypothesis A - Sociodemographic factors (age, gender, education level, and living conditions) show a significant relationship with levels of aggression. Levels of aggression show temporal stability in a geographically determined catchment area.

#### 3.1.1. Gender correlations with aggression and violence in first-episode psychosis and severe mental illness cohorts

The current study did not find any significant correlation between gender and levels of aggression and violence in the studied first-episode psychosis cohort, which is in contrast with the general perception and with most of the first-episode psychosis studies.

The first-episode psychosis studies showed divergent results regarding gender differences in the broader literature concerning the associations between severe mental illness and aggressive and violent behaviour.

Unlike several studies in first-episode psychosis cohorts (Dean et al., 2007, Foley et al., 2005, Milton et al., 2001, Steinert et al., 1999), in the current study, there was no significant association between male gender and aggressive and violent behaviour.

Nevertheless, other studies (Harris et al., 2010, Humphreys et al., 1992, Spidel et al., 2010, Verma et al., 2005, Volavka et al., 1997) in the first-episode psychosis, cohort did not find gender disparity concerning aggression and violence.

There has been debate in the literature on how severe mental illness can reduce gender disparity or change the patterns of violence (Lam et al., 2000, Krakowski and Czobor, 2004). By contrast, several decades-long surveys concluded that females are more likely to become victims of intimate partner violence (Field and Caetano, 2005).

A recent systematic review and meta-analysis including 24 studies over four decades, corresponding to 51309 individuals with severe mental illness, showed an absolute risk for males is less than one in four and for females is less than one in twenty perpetrate violence when compared to the general population (Whiting et al., 2021). This meta-analysis examined the two genders' prevalence rates and other correlating factors separately.

A national study, which included 1410 individuals with severe mental illness, analysed gender effects concerning aggression and violence and found no significant gender difference in severe violence (Swanson et al., 2006a). Interestingly, females were more likely to engage in minor violence, and the gender effect was explained by sociodemographic correlations, such as living with family, that gave more opportunities for physical fights with social network members (Swanson et al., 1998, Swanson et al., 2006a). In another sample of patients with severe mental illness, the male gender was associated with violence; however, after controlling several confounding factors in multivariate analysis, gender difference remained significant only in conjunction with substance misuse (Hiday et al., 1998).

Similar results were reproduced in another study, where no gender differences were observed in acts of aggression and violence in a hospital setting. Females tended to engage in verbal assaults throughout the observation period and physical violence at the beginning of hospitalisation. However, males were more likely to engage in violence in the community, associated with substance use and delinquent behaviour (Krakowski and Czobor, 2004). This gender discrepancy in association with other factors, such as treatment in community or inpatient settings and the phase of the treatment, was also highlighted in other studies (Hodgins and Riaz, 2011).

As confirmed by current research, the gender disparity in aggression amongst people with severe mental illnesses is insignificant, contrary to the aggression and violence described in the larger population. According to the current research study, there was no gender difference observed in verbal aggression and violence of any kind. This is contrary to other studies completed on gender disparity, which found different patterns of aggression in males and females (Krakowski and Czobor, 2004)

### 3.1.2 Age correlations with aggression and violence in the first episode of psychosis cohorts and among those with severe mental illness

In the current study, significant gender disparities in median age were found, with males presenting approximately five years earlier than females with an episode of first-episode psychosis. This is consistent with the relevant literature, as, in the case of schizophrenia, the peak age of onset is between 10 - 25 years for men and 25 - 35 years for women (Kaplan, 2015). However, one study of a first-episode psychosis cohort showed no significant difference in the age of presentation but a statistically significant longer duration of psychosis in women (Køster et al., 2008).

When different age groups under and over 35 were analysed, aggression and violence were not substantially related to a younger age. Further subdividing the population into four age groups revealed no significant connections between younger age and aggressive and violent behaviour, similar to the previous studies (Foley et al., 2005, Keane et al., 2019) completed in the same catchment area.

In contrast, several studies examining aggressiveness and violence in the first episode of psychosis revealed a significant link between young age and aggression (Dean et al., 2007, Harris et al., 2010, Milton et al., 2001, Volavka et al., 1997).

Significantly younger age at presentation with the first episode of psychosis in males did not translate into higher aggression levels in the younger population, which may be linked with the absence of gender difference in aggression and violence in this sample.

### 3.1.3 Social factors and aggression and violence

After controlling for age and gender as confounding factors, the current study identified no significant associations between socioeconomic indicators and violence. However, lower educational attainment showed a statistically significant correlation with aggression with more than two-fold relative risk and statistical significance in binary logistic regression analysis.

A review of relevant literature examining social predictors of aggression and violence in first episode cohorts shows a mixed picture.

The minority of these reports show a significant association between living alone (Milton et al., 2001, Verma et al., 2005), being single (Verma et al., 2005, Milton et al., 2001), or being unemployed (Milton et al., 2001, Foley et al., 2005, Verma et al., 2005).

There have also been descriptions in studies with first-episode psychosis cohorts of other social factors contributing to aggression, such as lower education levels (Volavka et al., 1997) and living conditions (Milton et al., 2001, Verma et al., 2005).

The current study's results are concordant with a conclusion meta-analysis (Large and Nielssen, 2011), which found that lower educational attainment predicts aggression and violence in the first-episode cohort.

#### 3.1.4. Comparison to prevalence rates of aggression and violence in other first-episode psychosis cohorts

A rate of any aggression of 42.4% in this cohort was comparable to several studies with a similarly systematic, structured measurement of violence (Verma et al., 2005, Spidel et al., 2010, Dean et al., 2007) regardless of variable periods of recording violent incidents from contact with services only (Dean et al., 2007) up to two years follow-up post-diagnosis of first-episode psychosis (Spidel et al., 2010).

However, one research (Harris et al., 2010) found a higher but not statistically different prevalence rate of violence compared to the current study over a pre-contact period with services of 3 months (56 %,  $z = 2.2$ ,  $p = 0.0285$ ). In contrast, other research found that aggression rates were 17 % lower ( $z = 5.5$ ,  $p = 0.0001$ ) before contact with services and during the first episode of psychosis (Milton et al., 2001).

The prevalence rate (13%) of severe violence that caused mild or severe injury to others was comparable to the majority of first-episode psychosis cohort studies,

apart from two studies that showed significantly higher rates of 20.7% ( $z = 2.7$ ,  $p = 0.0065$ ) (Humphreys et al., 1992) to 27% ( $z = 3$ ,  $p = 0.0024$ ) (Harris et al., 2010). Different study methodologies or geographical locations may explain these differences. It is generally recognized that the initial episode of psychosis is associated with an increased risk of aggressive behaviour.

A systematic review and meta-analysis of fifteen studies involving 3294 patients with first-episode psychosis showed that pre-contact aggression rates were 28% (CI 95% 22-34), but post-contact aggression rates remained high at 31% (CI 95% 20-42). During the pre-contact and post-contact periods, this meta-analysis's pooled prevalence rates of violence were 16% (CI 95% 11-20). During the post-contact period, the prevalence rate was 13% (CI 95% 6-20). These results indicated that contact with mental health services did not significantly impact reducing the prevalence rates of aggression and violence. However, as the authors of this metanalysis stated, the high heterogeneity of the studies included and the retrospective data collection may explain these results (Winsper et al., 2013).

Suicidality and stigma in severe mental illness have a reciprocal interrelation (Carpiniello and Pinna, 2017). Perpetrated violence against others usually gets more attention than self-directed violence among individuals with severe mental illness. In individuals with schizophrenia, suicide is the leading cause of premature death, and suicide attempts are also common (Hor and Taylor, 2010). The prevalence of suicidal behaviour is high in FEP cohorts also, and substance abuse may further increase this risk (Addington et al., 2004).

The wide variability in violence rates found across studies examining rates of violence in first-episode psychosis cohorts can be attributed to different methodologies in the observation period, rating scale, and definition of aggression and violence (Table No: 30, Appendix, pages: 154). Nonetheless, the present study's findings are comparable with most of the research conducted on this specific cohort and mainly pertain to the prevalence rates of severe violence (Table No 31, Appendix, page 155).

## 3.2 Hypothesis B

Clinical (long duration of untreated psychosis, lack of insight into the illness) and phenomenological (higher positive symptoms of psychosis) characteristics are associated with higher levels of aggressiveness.

### 3.2.1 Phenomenological and clinical correlations with aggressive and violent behaviour

This study found no statistically significant associations between negative symptoms, manic symptoms, duration of untreated psychosis and depressive symptoms, insight level and aggression, and less severe violence. Significant correlations existed between severe violence and higher SAPS, YMRS, CDSS, and GAF scores.

The relevant literature on psychopathological predictors of aggression and violence paints a mixed picture on this topic.

This result is consistent with the results of a meta-analysis and a systematic review of violence in initial episodes of psychosis, which concluded that measures of the severity of psychotic symptoms were not significantly associated with less severe forms of violence but with more severe forms of violence (Large and Niessen, 2011).

A detailed analysis of positive symptoms and severe violence showed statistically significant associations with delusions (delusions of persecution, guilt, delusions of grandeur), bizarre behaviour (social, agitated behaviour, and global values), and thought disorders (rambling, tangential, forced speech). In contrast, a study of a first-episode psychosis cohort found that delusions, hallucinations, and passivity phenomena, while commonly observed, were not explicitly associated with aggression (Milton et al., 2001). However, another cohort study of first-episode psychosis found no correlation between the severity of aggression and violence and global Positive and Negative Syndrome Scale (PANSS) scores, but analysing subscales, were analysed mainly in the general psychopathology scores, hostility and poor impulse control were significantly associated with aggression (Verma et al., 2005).

A study of the association between four delusional beliefs and violent behaviour in the year prior to initial contact in patients with a first episode of psychosis in East London examined the associations between violent behaviour and delusional beliefs within a large and representative sample of patients with the first episode of psychosis. For mild violence, there was significant but only partial mediation by anger ( $z=2.10$ ,  $p=0.04$ ). In their analysis, severe violence associated with paranoid delusions of being spied on ( $z=3.03$ ,  $p=0.002$ ), persecution ( $z=3.09$ ,  $p=0.002$ ), and conspiracy ( $z=2.98$ ,  $p = 0.002$ ) were strongly mediated by anger resulting from emotional distress. A strong association has been found between severe violence and delusions (particularly those associated with severe violence), and the high attributable risk of anger caused by delusions has implications for prevention and therapy (Coid et al., 2013b).

Some studies focusing on first-episode psychosis cohorts and aggression found significant associations with manic symptoms (Dean et al., 2007, Harris et al., 2010), absence of depression (Dean et al., 2007), auditory hallucinations (Volavka et al., 1997), hostility (Volavka et al., 1997, Verma et al., 2005), poor impulse control (Verma et al., 2005), excitement (Volavka et al., 1997), lack of insight (Verma et al., 2005) and long duration of untreated psychosis (Humphreys et al., 1992, Verma et al., 2005).

However, most of the relevant literature on the first episode of psychosis cohorts showed more consistency in association with substance use, some sociodemographic variables (younger age, male gender) and aggressive and violence rather than clinical factors (Dean et al., 2007, Foley et al., 2005, Harris et al., 2010, Humphreys et al., 1992, Milton et al., 2001, Spidel et al., 2010, Steinert et al., 1999, Verma et al., 2005, Volavka et al., 1997).

In severe mental illness, aggressiveness and violence have been shown to be related to various phenomenological traits, similar to first-episode psychosis cohorts.

Some authors found that schizophrenia was significantly linked with violence in those with an early history of violence and psychotic symptoms had a limited influence on aggression and violence (Hodgins, 2008).

By contrast, others argue that schizophrenia contributes to violence in those without a history of violence (Volavka and Citrome, 2008). Research suggests that a history of violence, combined with substance abuse, may increase the risk of aggression and violence among those with schizophrenia (Erkiran et al., 2006). Several studies have shown that clinical factors rather than sociodemographic characteristics are more likely to predict violence during hospitalization (Arango et al., 1999). Most consistently positive symptoms of schizophrenia demonstrated significant links with aggression and violence (Amore et al., 2008).

Higher hostility - suspiciousness rates on BPRS predicted a transformation from verbal to physical aggression in a study of an inpatient cohort (Amore et al., 2008). In a study that was conducted using a cohort of forensic patients with severe mental illness, it was demonstrated that command hallucinations (OR = 2.35, 95% CI = 1.05 - 5.24), threat/control-override symptoms (OR = 3.10, 95% CI = 1.51 - 6.35), and Capgras syndrome (OR = 3.58, 95% CI = 1.06 - 12.15) were all independently significant risk factors for acute severe and fatal violence (Chan and Shehtman, 2019). Interestingly, gender, current alcohol use, and recent drug use were statistically not correlated with acute severe or extreme violence (Chan and Shehtman, 2019).

The results of a study that examined the relationship between changes in positive and negative symptomatology and violence suggested that the stronger the shift in positive symptoms, the greater the likelihood of incidents of violence. Despite this, increases in anger affect were the primary factor responsible for the positive symptom changes linked with violence. Although co-occurring fluctuations in negative symptoms were positive and protective, the effects of co-occurring shifts in anger outweighed those of fluctuating negative symptoms. The correlation between severe but stable delusions and aggression was also independent (Coid et al., 2018). Another study examined the impact of state versus trait factors on aggression in a small sample of individuals with schizophrenia and found that affective responses to hallucinations or delusions were significantly linked to aggression (Cheung et al., 1997).

In a prospective, naturalistic, observational study of persons experiencing a psychotic episode, excitement/activation was shown to be the component most linked with violent behaviours and the severity of psychopathological symptoms upon discharge. Additionally, the dimension of negative symptoms predicted the

extent of symptoms at discharge. Both positive and negative symptom categories were significant predictors of hospitalisation length. Only self-aggression was strongly linked with the depressed component (Colasanti et al., 2010).

Involuntary treatment was significantly associated with pre-contact and post-contact aggression and violence. This association was in line with several studies examining aggression and violence in the first episode of the psychosis cohort (Foley et al., 2005, Milton et al., 2001, Dean et al., 2007).

The relationship between involuntary treatment and violence may be considered circular causation in the pre- and post-contact periods. Aggression and, in particular, violence may be a reason for the application for involuntary treatment. Involuntary treatment status may present a risk of aggression and violence during treatment.

### 3.2.2 Aggression and violence in different diagnostic categories

As a result of the analysis of diagnostic categories, the current study did not detect any significant association between affective and non-affective psychotic disorders and aggression and violence in the pre- and post-contact periods. Similarly, significant correlations were not found when severe violence was analysed.

Several studies confirmed a significant association between schizophrenia and violence (Lindqvist and Allebeck, 1990, Modestin and Ammann, 1996, Soyka et al., 2007), theorising an intrinsic link between the two entities (Whiting et al., 2021). However, others argued that this association is mediated by comorbid substance use (Fazel et al., 2009).

A previous study that included individuals with first episodes of psychosis found that schizophrenia alone did not confer any particular risk of aggression, independent of the type or severity of aggression (Milton et al., 2001).

Compared with relevant literature on only first-episode psychosis cohorts, schizophrenia was a significant predictor of aggression and violence in one study (Dean et al., 2007). Nevertheless, the majority did not find any significant associations between schizophrenia and aggression (Foley et al., 2005, Harris et al., 2010, Milton et al., 2001, Steinert et al., 1999); however, diagnostic

ambiguities between primary and secondary psychoses at the first presentation may be the explanation.

A similar conclusion was reached in a study that included a large representative sample to examine the relationship between severe mental illness and aggression and violence. Bivariate analyses revealed that persons with severe mental illness had increased violence, but only significantly more than those with co-occurring drug misuse and dependency (Elbogen and Johnson, 2009). Multivariate analyses revealed that severe mental illness did not predict future violence on its own. It was associated with a variety of factors, including historical (past violence, juvenile detention, physical abuse, parental arrest record), clinical (substance abuse, perceived threats), dispositional (age, sex, income), and contextual (recent divorce, unemployment, victimisation). Most of these variables were more frequently noted by those with severe mental illness (Elbogen and Johnson, 2009).

Similarly, when compared to affective disorders, schizophrenia spectrum disorders showed a more significant association with violence than bipolar affective disorders in an empirical study, including 3322 patients in an emergency department setting (Blanco et al., 2018). Interestingly, further analyses revealed that mixed episodes in bipolar affective disorders had a greater relative risk for aggression and violence than schizophrenia spectrum disorders, but recent manic episodes had lower odds for violence (Blanco et al., 2018).

Substance-induced psychosis in the current study, on the other hand, showed a significant correlation with post-contact behaviours of self-harming behaviours despite no statistically significant difference in psychopathology between primary and substance-induced psychosis.

Research relating substance-induced psychosis to aggressive and violent behaviour is relatively scarce, and among the few studies with first-episode cohorts, none examined it separately (Dean et al., 2007, Foley et al., 2005, Harris et al., 2010, Humphreys et al., 1992, Milton et al., 2001, Spidel et al., 2010, Steinert et al., 1999, Verma et al., 2005, Volavka et al., 1997). A multicentred, first-episode psychosis cohort found no correlation between substance use and history of violence (Volavka et al., 1997). They claim that research with first-episode

psychosis cohorts may not be comparable to those studies that suggest this significant link (Volavka et al., 1997).

However, substance-induced psychoses in first-episode psychosis cohorts have a significant relevance concerning the high prevalence rates in first-episode psychosis cohorts (Lambert et al., 2005) and from a differential diagnosis perspective between primary and secondary psychoses (Fraser et al., 2012).

### 3.3 Hypothesis C

Substance use significantly correlates with higher aggression and violence levels

#### 3.3.1 Prevalence rates of substance use in current and other first-episode psychosis cohorts

Different levels of accessibility of illicit substances in each community may explain the difference in illicit substance use rates but also can point towards differences in data collection.

A significant increase in the prevalence of history of alcohol abuse was observed in the current study as compared to the 1995 - 1998 cohort of first episode psychosis patients in the same geographically determined catchment area ( $z = 5.4$ , CI 95% 0.0452 - 1.34,  $p < 0.0001$ )(Foley et al., 2005).

These results contrast with another study in the first episode of psychosis cohort there was twice as much substance abuse among people with first-episode psychosis as among the general population, and it was more prevalent among men than among women. In 51 % of patients ( $n=62$ ), cannabis abuse was reported, as was alcohol abuse in 43 % of patients ( $n=53$ ) in the 30 days prior to contact with services. More than half (68, 55%) had used Class A drugs, and 38% ( $n = 43$ ) had abused multiple substances in the same period (Barnett et al., 2007a).

Similarly, the past month's substance use prevalence rates in the current sample were significantly lower concerning illicit substances compared to the results of another first-episode psychosis cohort study examining aggression and violence (Spidel et al., 2010). Additionally, that study demonstrated that stimulant use

over the past month was fourfold greater, whereas cannabis use was almost twofold higher. In contrast, alcohol use was not significantly different in either sample over the past month. Data for the current study were collected using SCID interview data and clinical records, whereas, for the reference study, the Addiction Severity Index was used (Spidel et al., 2010).

According to the results of the Epidemiologic Catchment Area (ECA) report, substance use disorders were significantly more prevalent among individuals with severe mental illness. The relative risk of comorbid substance misuse was 2.7, with a lifetime prevalence of 29%, 22% with alcohol and 15% with other drugs (Regier, 1990). Similarly, a meta-analysis including forty-four unique studies concluded a 25% prevalence rate of comorbid alcohol use disorder and cannabis use disorder among individuals with first-episode psychosis (Wisdom and Manuel, 2011).

The impact of substance use among individuals with severe mental illness is demonstrated by the high prevalence rates and the lack of interventions for dual diagnosis. Following a clinical survey completed in England, 44% of community mental health services patients (95 % CI: 38.1-49.9) reported past-year problem drug use and harmful alcohol use; 75% reported past-year problem drug use and harmful alcohol use. According to the study, 75% of drug treatment patients (95% CI 68.2-80.2) and 85% of alcohol treatment patients (95% CI 74.2-93.1) had a psychiatric disorder in the previous year. Most patients with comorbidity did not qualify for cross-referral between services. In this case study, a large percentage of people were not identified by service providers, so they received no specialist interventions (Weaver et al., 2003).

Estimation in the current study found that 5% of patients with the first episode of psychosis and coexisting substance use were referred to addiction services, which was significantly lower than the results of the National Household Survey, which found that 12% of people with coexisting mental health and substance use disorders received treatment for both issues (Epstein, 2004). However, for approximately half of the service users, psychoeducational support about substance use had been provided.

### 3.3.2 Correlations between different substance groups and aggressive and violent behaviour

In this first episode psychosis cohort, detailed statistical analyses revealed that substance misuse had significant associations with aggression and violence despite no significant impact on clinical variables. According to these associations, it is critical to consider the impact of substance use on the behaviour of patients. In addition, it is essential to assess the impact of different substances on aggression and violence.

#### Alcohol

This study demonstrated that alcohol use disorder was associated with a two-fold relative risk of post-contact violence. The use of alcohol in the month preceding contact with services also showed a correlation with significant aggression in the period following contact with services. Alcohol consumption following contact with services seems to be associated with aggressive verbal behaviour and violence against others.

Compared to studies that examined aggression and violence in the first episode of the psychosis cohort, alcohol use was only significantly associated with aggression and violence in the minority of studies (Spidel et al., 2010, Foley et al., 2005).

Since the emphasis on alcohol's adverse effects has led to more research in the past decades on this issue, it has been suggested that alcohol may contribute to aggressive behaviour (Kuypers et al., 2020). Alcohol dependence had been associated with violence in the context of psychotic-like experiences reported by 5.1 % of adults in the community in a large community sample comprising 38,132 individuals (Mojtabai, 2006). These experiences were associated with an increased risk of attacking someone with the intent of hurting that person (Odds Ratio [OR] = 5.72), intimate partner violence (OR = 4.97), arrests for aggravated assault (OR = 5.12), and arrests for other assault (OR = 3.65). The risk of violence increased with the number of psychotic-like experiences. Unusual perceptual experiences and paranoid ideations were more consistently associated with violence (Mojtabai, 2006).

As alcohol and drug misuse may have forensic implications, it is important to consider studies conducted within the criminal justice system. A study (Modestin and Ammann, 1996) compared male patients with schizophrenia with and without criminal records indicated that those with criminal records were younger, had shorter illness durations, and spent less time in psychiatric hospitals. Moreover, they were more likely to have histories of alcohol and drug abuse, and their social circumstances at the index admission were less favourable. If the same type of comparison is conducted, but chronic patients are excluded, then the age differences, duration of illness, total time spent in psychiatric hospitals, and average duration of psychiatric hospitalization become insignificant. Drug abuse was correlated with violations of drug laws ( $r = 0.4$ ,  $p < 0.0001$ ) and crime against property ( $r = 0.3$ ,  $p < 0.0001$ ), but not with violent crimes ( $r = -0.06$ , not significant) or other crimes (Modestin and Ammann, 1996).

Similarly, in another sample, including individuals with severe mental illness, there was a significant difference between those reporting psychosis only and those with dual diagnoses concerning any history of committing an offence ( $p=0.001$ ) or recent hostile activity ( $p=0.001$ ). Significant differences remained when confounding factors such as demographics and clinical characteristics were examined using logistic regression (Scott et al., 1998).

Alcohol has been shown in several studies to cause aggressive behaviour in samples without severe mental illness. A study reported higher rates of physical violence (32%) in a sample of 250 individuals who had a history of substance abuse of alcohol and cocaine three months before they enrolled in a treatment program for their addiction. In addition to some socio-demographic variables (race, age, education), alcohol and cocaine consumption was significantly related to severe violence. Subsequent analyses revealed that higher levels of alcohol consumption were associated with higher levels of violence (Chermack and Blow, 2002).

The effect of alcohol in a 30-year longitudinal study showed significant bivariate associations between alcohol abuse and dependence symptoms and different violence outcomes ( $p < .001$ ). No gender differences were observed in the findings related to these associations (Boden et al., 2012).

There is evidence that alcohol increases aggression by decreasing the inhibitory ability of the frontal lobe region (Anderson and Bokor, 2012) and dysregulating higher-order cognitive functions, leading to increased impulsive behaviour and overreaction (Kuypers et al., 2020).

## Cannabis

According to the current study, there was no statistically significant relationship between cannabis use and violent behaviour.

Consumption of cannabis during the past month was associated with verbal aggression after contacting services, which may be explained by agitation in the context of withdrawal; however, withdrawal symptoms are often underreported.

These results contrast with the findings of other research studies conducted with first-episode cohorts that have found a significant association between the regular use of cannabis and more violent severe behaviour (Harris et al., 2010).

Despite the large body of related research, the strength of the association between marijuana use and aggression is still unclear (Ostrowsky, 2011). There has been evidence from other studies that shows cannabis use has the potential to be an independent predictor of violence on a community level (Arseneault et al., 2000). In the severe mental illness cohort, cannabis use had been associated with violent behaviour (Koen et al., 2004).

Due to prevalence levels of polysubstance use, including alcohol use disorder, it is unclear whether cannabis or other substances may contribute to aggression and violence among polysubstance users. However, the data on polysubstance use among cannabis users highlights the role of cannabis as a “gateway drug”, especially among early users (Hall and Lynskey, 2005).

Cannabis has been the subject of a growing body of evidence indicating that regular usage is strongly associated with the early onset of psychosis, providing further evidence that schizophrenia may be precipitated by marijuana use (Barnes et al., 2006).

Even if cannabis has the potential to have a calming effect and reduce violent behaviour (Reiss Jr and Roth, 1994), it is disputed that it may have these effects. Aggressive behaviour and chronic/heavy marijuana consumption may well be associated due to changes in mood and behaviour during periods of both intoxication (Allsop et al., 2011) and cannabis withdrawal (Smith et al., 2013), but

this was only associated with intimate partner violence and not with violence in social context in people who had a history of violence.

A study examining the impact of cannabis use among young people who presented to emergency departments in connection with cannabis use found an association between longer-term and substantial cannabis use among males in urban communities in co-determination with both positive and negative peer influences (Walton et al., 2017). Early cannabis use has been implicated in criminal behaviour and linked to paranoid/suspicious ideation (Barthelemy et al., 2016) and maladaptive interpersonal functioning (Martinotti et al., 2017).

Daily marijuana use during adolescence, may result in the occurrence of neurologic impairment levels, coupled together with a reduction of connectivity and inappropriate behaviour inhibition activity of the prefrontal cortex and subcortical areas in the prefrontal cortex and the subcortical areas of the brain (Volkow et al., 2014, Barthelemy et al., 2016).

### Stimulants

The use of stimulants did not show any significant relationship with psychopathology. However, recent stimulant use was significantly associated with post-contact aggression and post-contact violence. A more detailed analysis found that lifetime stimulant use was significantly associated with self-directed violence (but not suicide attempts) and violence against property. In the area of agitation and aggression, several studies have shown that stimulants influence behaviour. In particular, some of these studies have explored the topic in depth.

### Hallucinogens

Due to low statistical power, detailed statistical analysis could not be completed. Relevant literature conforms to the general knowledge that aggressive and violent behaviour is rarely associated with hallucinogens (Schifano et al., 2020)

### Other substances

Other substance groups included licit and illicit substances, such as prescription medications, sedatives, NPS, and inhalers; however, no further analyses were conducted due to low statistical power. (Schifano et al., 2016)

In the case of novel psychoactive substances, growing evidence suggests in research that the emergence of novel psychoactive substances poses a public health concern (Schifano et al., 2016) and may significantly impact the prevalence of aggression and violence (Schifano et al., 2020). Relevant literature highlights the potential of these substances to induce aggression and violence in intoxication, especially in the case of NPS and withdrawal syndromes (Schifano et al., 2020). Benzodiazepines, in the context of psychotropic effects, had been associated with aggression due to disinhibiting effects (Gillet et al., 2001).

#### Polysubstance use

This study demonstrated significant correlations between post-contact verbal aggression and post-contact violence against property and poly-substance use. However, there was no significant association between polysubstance use and severe violence, defined as violence against others resulting in injuries. A detailed analysis was conducted in the case of polysubstance use, including alcohol or just illicit substances; however, no further significant correlations were found with psychopathology, aggression, or violence.

Cannabis abuse in patients with schizophrenia was strongly associated with abuse of other substances (including alcohol and opiates) (OR = 4.95; 95% CI = 2.47-9.93). This result was in line with a study indicating the importance of considering other substance abuse when the individual with severe mental illness endorses cannabis use (Dubertret et al., 2006). Polysubstance abuse is strongly correlated with aggression and violence among individuals with severe mental illness (OR = 10.3, 95% CI 2.5 - 42.5,  $p < 0.01$ ,  $z = 3.3$ ) (Witt et al., 2013).

Polysubstance use may result in multiple psychopharmacologic interactions that are still unclear how they may impact aggressive and violent behaviour (Gillet et al., 2001).

From a clinical perspective, it is imperative to pay close attention to early substance use interventions as about a third of first-episode psychosis patients may have a history of polydrug use (Barnett et al., 2007a).

The separation of addiction services in Ireland led to fragmented care for individuals with dual diagnoses, highlighting the need for more integrated care.

### 3.4. Hypothesis D

A more extended observation study period results in higher incident rates of aggression and violence

As expected, expanding the period of study over one year showed a higher level of aggression and violence compared to previous studies (Foley et al., 2005), (Keane et al., 2019) conducted in the same catchment area and using the same methodology apart from the significantly extended pre- and post-contact periods.

These results were based on a one-year period which comprises six months before and six months after the contact with services and the diagnosis of first-episode psychosis.

Comparison of this study's results with previous studies conducted in the same geographically defined catchment area demonstrated the value of the analysis period of cases of aggression and violence, despite mixed results in violence rates across the three cohorts. However, there is a significant increase in aggression in both the pre-and post-contact and post-contact violence, contributing to prolonged observation periods.

An interesting finding of a systematic review and meta-regression analysis of aggression during the first episode of psychosis was the inverse correlation between more extended observation periods and aggression prevalence rates (Winsper et al., 2013). This had been attributed to the difference in study methodologies by the authors, stating that studies with shorter observational periods use structured assessment tools while others rely on clinical and forensic records (Winsper et al., 2013).

Nevertheless, the current study used the same rating scale, the Modified Overt Aggression Scale, for a more extended observation period than previous studies.

#### 4. Strengths and Limitations

There is a perpetual concern in both clinical and scientific correlations between severe mental illness and aggression and violence - whether there is an intrinsic link between these two phenomena or if other factors, such as co-morbid substance abuse, play a role. Selection bias could be mitigated as a result of the retrospective observational study design.

As far as is known, the present thesis is the first study conducted in Ireland that examined the relationship between substance use and aggressive and violent behaviour among individuals with a first episode of psychosis for one year.

Research on this subject in the same geographically defined area has previously examined clinical and sociodemographic correlations for two weeks - one week before and one week after the contact with services. In the current study, this observational period was expanded to six months before and six months after the contact, thus providing an extended window for investigating the impact of substance use on psychopathology and aggressive or violent behaviour. Observations during a prolonged period revealed significantly different aggressive and violent behaviour occurrences.

A further aspect of the current study is the addition of several rating scales to a structured interview for diagnostic formulation based on the DSM - IV-TR. Psychotic symptomatology, including positive, negative, and disorganisation symptoms, depressive symptoms, manic symptoms, level of insight, global assessment of functioning, and the duration of untreated psychosis, were included in a detailed analysis to explore their relationship with aggression, violence, and substance abuse.

The findings of this study demonstrate that comprehensive analyses of different substances provide more significant benefits than incorporating them into a single group of illicit substance use.

In addition, this study examined the impact of substance-induced psychotic disorder on phenomenology and aggressive and violent behaviour. Other studies with first-episode psychosis cohorts that examined aggression or violence did not include this diagnostic category, despite its relative frequency. A limited amount of

relevant literature examines the correlations between phenomenology and aggressive and violent behaviours in primary and secondary psychoses.

As a result of the long observation period among individuals referred to secondary services for first-episode psychosis, it was also possible to examine the rates of referral to addiction services of those with a co-morbid substance use disorder. A low number of referrals to such services highlighted a need for better coordination between addiction and psychiatric services in Ireland.

Studying the gender disparity from multiple perspectives (sociodemographic, clinical, substance use, aggression and violence) reveals that contrary to the general belief that males are likely to be more violent than females in general society, the gender gap disappears in all aspects of aggression and violence among individuals with a first-psychotic episode. In addition to reviewing gender differences in alcohol and substance misuse patterns, this study noted no significant gender variation in alcohol misuse. However, there were significant differences in the use of illicit substances.

Several limitations were identified in the present study that are similar to those in the current literature. However, most are related to the retrospective nature of recording cases of aggression violence and substance use.

The primary limitation of this study is the absence of a non-psychosis comparison group representative of the population from which the cohort was drawn. This limitation similarly extends to the data on substance use. Due to the retrospective design of the study, it was not feasible to recruit a control group of substance users for comparison of aggression and violence levels.

Furthermore, reports of pre-contact aggression may be underestimated, as these instances were derived from entries in the patients' electronic health records. The retrospective nature of the study precluded the clarification of clinical and contextual variables at the exact time of each aggressive act, making it impossible to accurately determine these factors after the fact. The information on pre-contact aggression and violence was gathered from patient accounts, collateral histories, or other documentation available in the records.

In addition, the extensive review of all clinical documentation generated within the six months before and after the contract with the services, certain information may be lost due to the lack of recording of all incidents of aggression and violence. As milder forms of aggression, verbal attacks, and shouting may not be recorded in clinical case notes, it is possible that prevalence data on milder forms of aggression do not reflect actual clinical experience. Considering that violence, particularly severe violence, is recorded on multiple platforms, including incident reports, the data may indicate more accurate prevalence rates.

Another limitation of this study is the temporal relationship between the phenomenological aspect and the occurrence of aggression or violence. An explanation for this can be found in the retrospective nature of the systematic review of aggression and violence. On the other hand, there is also a time delay between the time of the aggressive incident and the assessment of the current psychopathology that cannot be corrected by a prospective study design. Generally, a SCID assessment occurs when the individual is in a relatively stable mental state. From a practical perspective, it would be difficult to envision a semi-structured interview with an individual who displays aggression and violence. In all study designs, the relationship between psychopathology and aggression and violence is relative. Prospective recording of violent incidents can't be designed due to ethical concerns.

Furthermore, the sample under examination consisted of individuals with both affective and non-affective, primary and secondary psychoses syndromes, resulting in a significant range of heterogeneity in psychopathology. This constraint was addressed by using a wide range of scales and analysing the relationships between aggression, violence and psychopathology at the symptom level.

Conducting a structured baseline interview aimed at collecting information about substance use only provides a limited amount of information, which was a limitation in this study. Furthermore, the lack of information regarding baseline drug tests from urine or hair samples could also contribute to lower prevalence rates of substance abuse. Despite this, due to the extended observation period, substance use was possible to record in clinical notes, and a detailed assessment based on SCID data collection on substance use was conducted in a structured manner.

Routine administration of the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders Research Version [SCID - RV], used to assess patients with first-episode psychosis, did not include the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders for Personality Disorder [SCID-PD], therefore there are potential confounders for certain personality disorders reported to be associated with aggression and violence that could not be assessed.

## 5. Conclusions

The interrelationships between clinical and nonclinical predictors of aggression and violence proved complex and multifactorial. The research community is divided on whether there is an intrinsic link between severe mental illness and violence or whether sociodemographic factors play a role in this association. Several studies in first-episode psychosis cohorts demonstrated high prevalence rates of aggression and violence. However, systematic reviews and meta-analyses are challenging due to the heterogeneity of radically different study methodologies.

The main objectives of this study of first-episode psychosis cohorts were to determine the relationship between aggression and violence and sociodemographic factors (age, gender, level of education, marital status), clinical factors (long duration of untreated psychosis, lack of insight into the illness, higher positive symptoms of the psychosis, depressive and manic symptoms), and different patterns and types of substance use.

An additional aim of the study was to determine whether an extended observation period may result in higher prevalence rates of aggression and violence.

Contrary to the expectations of this study, young age and male gender did not demonstrate a significant relationship with aggression and violence, despite statistically significant levels of the younger age of presentation among males and higher prevalence rates of illicit substance use among males, contrary to the results of several first episode studies.

Unequivocally statistically significant associations couldn't be demonstrated in this study between psychopathology and aggression despite the effort to reduce the psychopathological variability through symptom-level research.

From a psychopathological perspective, there were no significant associations between psychopathological factors and aggression and less severe violence. However, as expected, severe violence, defined as violence causing injury to others, was significantly associated with several clinical variables.

Using the data collected through the SCID interview, the prevalence of substance misuse was similar to the general population in the given geographically defined catchment area.

As opposed to cannabis, alcohol misuse and recent alcohol intake were significantly associated with aggression and violence in the post-contact period. From illicit substances, stimulant use and polysubstance use proved to have a statistically significant correlation with aggression and violence in the pre-and post-contact periods.

Given the high interest in the search for cannabis in first-episode psychosis and chronic mental illness, an in-depth study has been conducted to evaluate its potential ability to alter psychopathology and trigger aggression and violence.

Nevertheless, a statistically significant association was not found between cannabis use and aggression or violence, except for recently consumed cannabis, which was significantly associated with verbal aggression after contact. A withdrawal syndrome may explain this phenomenon.

However, the role of cannabis as a “gate drug” had been demonstrated in this study as most cannabis users had a history of misuse of other substances. This is particularly concerning, as cannabis is used as a licit substance in the world. From a clinical perspective, the extent of polysubstance use raises the difficulty in assessing the impact of cannabis on clinical presentation and, ultimately, on behaviour.

The extended observation period resulted in higher rates of aggression and violence when results were compared to two previous results conducted in the same catchment area utilising a similar methodology apart from a short, two weeks observation period. This demonstrates that detailed analysis over a more extended period may capture instances of aggression in pre-contact, particularly in the post-contact period when the psychotic episode is considered to be in an active phase.

The intricate relationship between sociodemographic, clinical variables, substance use, aggression, and violence prove challenging to disentangle. However, this study demonstrated that alcohol and stimulant use is associated with aggressive and violent behaviour in an individual with first-episode psychosis. Gender disparities in substance use did not translate into gender differences in prevalence rates of aggression and violence.

## 6. Closing remarks

Violence and aggression have been studied in various populations, including the general population, those who use substances, and those with severe mental illness, as research shows that aggressive and violent incidents are not uncommon in these populations.

Unfortunately, due to high levels of victimisation and stigma associated with mental health, the focus of attention has shifted to individuals with severe mental illnesses. Criminal acts by seriously ill people continue to enjoy sensational publicity, while aggression and violence are commonplace in the general population, sub-forms of domestic violence, inter-communal violence, and international conflict.

The value of early interventions in the first episode of psychosis is significant as they aim to reduce symptoms, provide psychoeducation regarding illness and substance use, and prevent higher rates of aggression and violence in mental health settings.

Although several publications document a high prevalence of substance and polysubstance misuse among individuals with severe mental illness, only a modest proportion of individuals are referred to multiple services to address their mental health and addiction problems. As a result, there is a significant need to improve access to various services and to narrow the gap between addiction and mental health services. This has a significant relevance as psychopathology and substance abuse are potentially modifiable factors in reducing violence in this community.

As reiterated on several occasions in this work, research of aggression and violence in connection with severe mental illness is a highly complex task due to the multifaceted relationship between multiple variables and confounding factors. This leads to a multitude of diverse research methodologies that hinder the attainment of clarity on this subject, thereby necessitating further research to be conducted to examine violence in severe mental illness in a more unified manner.

Therefore, the connection between severe mental disorders and violence is still unclear and cannot be unequivocally explained at this time.

## 7. References

- AAS, I. M. 2011. Guidelines for rating Global Assessment of Functioning (GAF). *Annals of General Psychiatry*, 10, 2.
- ADAMS, S. W. & YANOS, P. T. 2020. Pathways to aggression and violence in psychosis without longstanding antisocial behavior: A review and proposed psychosocial model for integrative clinical interventions. *Psychiatry Res*, 293, 113427.
- ADDINGTON, D., ADDINGTON, J. & MATICKA-TYNDAL, E. 1993. Assessing Depression in Schizophrenia: The Calgary Depression Scale. *The British Journal of Psychiatry*, 163, 39-44.
- ADDINGTON, J. & ADDINGTON, D. 1998. Effect of substance misuse in early psychosis. *Br J Psychiatry Suppl*, 172, 134-6.
- ADDINGTON, J. & ADDINGTON, D. 2005. Patterns of premorbid functioning in first episode psychosis: relationship to 2-year outcome. *Acta Psychiatr Scand*, 112, 40-6.
- ADDINGTON, J. & ADDINGTON, D. 2007. Patterns, predictors and impact of substance use in early psychosis: a longitudinal study. *Acta Psychiatr Scand*, 115, 304-9.
- ADDINGTON, J., SHAH, H., LIU, L. & ADDINGTON, D. 2014. Reliability and validity of the Calgary Depression Scale for Schizophrenia (CDSS) in youth at clinical high risk for psychosis. *Schizophrenia Research*, 153, 64-67.
- ADDINGTON, J., WILLIAMS, J., YOUNG, J. & ADDINGTON, D. 2004. Suicidal behaviour in early psychosis. *Acta Psychiatr Scand*, 109, 116-20.
- AHONEN, M. 2014. *Mental disorders in ancient philosophy*, Springer Science & Business Media.
- AKKER, N., KROEZEN, M., WIELAND, J., PASMA, A. & WOLKORTE, R. 2021. Behavioural, psychiatric and psychosocial factors associated with aggressive behaviour in adults with intellectual disabilities: A systematic review and narrative analysis. *Journal of Applied Research in Intellectual Disabilities*, 34, 327-389.
- ALBERS, W. M. M., ROEG, D. P. K., NIJSSEN, Y., VAN WEEGHEL, J. & BONGERS, I. M. B. 2018. Profiling of victimization, perpetration, and participation: A latent class analysis among people with severe mental illness. *PLOS ONE*, 13, e0208457.
- ALDERSON, H. L., SEMPLE, D. M., BLAYNEY, C., QUEIRAZZA, F., CHEKURI, V. & LAWRIE, S. M. 2017. Risk of transition to schizophrenia following first admission with substance-induced psychotic disorder: a population-based longitudinal cohort study. *Psychol Med*, 47, 2548-2555.
- ALLEBECK, P., ADAMSSON, C. & ENGSTRÖM, A. 1993. Cannabis and schizophrenia: a longitudinal study of cases treated in Stockholm County. *Acta Psychiatrica Scandinavica*, 88, 21-24.
- ALLEGRI, F., BELVEDERI MURRI, M., PAPARELLI, A., MARCACCI, T., BRACA, M., MENCHETTI, M., MICHETTI, R., BERARDI, D. & TARRICONE, I. 2013. Current cannabis use and age of psychosis onset: a gender-mediated relationship? Results from an 8-year FEP incidence study in Bologna. *Psychiatry Res*, 210, 368-70.
- ALLEN, T. J., GERARD MOELLER, F., M. RHOADES, H. & CHEREK, D. R. 1997. Subjects with a history of drug dependence are more aggressive than subjects with no drug use history. *Drug and Alcohol Dependence*, 46, 95-103.
- ALLSOP, D. J., NORBERG, M. M., COPELAND, J., FU, S. & BUDNEY, A. J. 2011. The Cannabis Withdrawal Scale development: patterns and predictors of cannabis withdrawal and distress. *Drug Alcohol Depend*, 119, 123-9.
- ALMVIK, R., WOODS, P. & RASMUSSEN, K. 2000. The Brøset Violence Checklist. *Journal of Interpersonal Violence*, 15, 1284-1296.
- AMMERMAN, B. A., KLEIMAN, E. M., UYEJI, L. L., KNORR, A. C. & MCCLOSKEY, M. S. 2015. Suicidal and violent behavior: The role of anger, emotion dysregulation, and impulsivity. *Personality and Individual Differences*, 79, 57-62.
- AMORE, M., MENCHETTI, M., TONTI, C., SCARLATTI, F., LUNDGREN, E., ESPOSITO, W. & BERARDI, D. 2008. Predictors of violent behavior among acute psychiatric patients: clinical study. *Psychiatry Clin Neurosci*, 62, 247-55.
- ANDERSON, P. D. & BOKOR, G. 2012. Forensic aspects of drug-induced violence. *J Pharm Pract*, 25, 41-9.

- ANDRADE, C. 2016. Cannabis and Neuropsychiatry, 2: The Longitudinal Risk of Psychosis as an Adverse Outcome. *J Clin Psychiatry*, 77, e739-42.
- ANDREASEN, N. C. 1982. Negative symptoms in schizophrenia: definition and reliability. *Archives of general psychiatry*, 39, 784-788.
- ANDREASEN, N. C. 1983. The scale for the assessment of negative symptoms (SANS) Iowa City. IA: University of Iowa.
- ANDREASEN, N. C., ARNDT, S., DEL MILLER, D., FLAUM, M. & NAPOULOS, P. 1995. Correlational studies of the Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms: an overview and update. *Psychopathology*, 28, 7-17.
- ANDREASEN, N. C., FLAUM, M., ARNDT, S., ALLIGER, R. & SWAYZE, V. W. 1991. Positive and negative symptoms: assessment and validity. *Negative versus positive schizophrenia*. Springer.
- ANDREASSON, S., ALLEBECK, P., ENGSTROM, A. & RYDBERG, U. 1987. Cannabis and schizophrenia. A longitudinal study of Swedish conscripts. *Lancet*, 2, 1483-6.
- APPELBAUM, P. S. 2000. Violence and Delusions: Data From the MacArthur Violence Risk Assessment Study. *American Journal of Psychiatry*, 157, 566-572.
- APPELBAUM, P. S. 2013. Public safety, mental disorders, and guns. *JAMA Psychiatry*, 70, 565-6.
- APPELBAUM, P. S., ROBBINS, P. C. & MONAHAN, J. 2000. Violence and delusions: data from the MacArthur Violence Risk Assessment Study. *Am J Psychiatry*, 157, 566-72.
- ARANGO, C., BARBA, A. C., GONZALEZ-SALVADOR, T. & ORDONEZ, A. C. 1999. Violence in Inpatients With Schizophrenia: A Prospective Study. *Schizophrenia Bulletin*, 25, 493-503.
- ARBOLEDA-FLOREZ, J., HOLLEY, H. & CRISANTI, A. 1998. Understanding causal paths between mental illness and violence. *Soc Psychiatry Psychiatr Epidemiol*, 33 Suppl 1, S38-46.
- ARRANZ, B., SAFONT, G., CORRIPIO, I., RAMIREZ, N., DUENAS, R. M., PEREZ, V., ALVAREZ, E. & SAN, L. 2015a. Substance Use in Patients With First-Episode Psychosis: Is Gender Relevant? *J Dual Diagn*, 11, 153-60.
- ARRANZ, B., SAFONT, G., CORRIPIO, I., RAMIREZ, N., DUEÑAS, R. M., PEREZ, V., ALVAREZ, E. & SAN, L. 2015b. Substance Use in Patients With First-Episode Psychosis: Is Gender Relevant? *Journal of Dual Diagnosis*, 11, 153-160.
- ARSENEAULT, L., CANNON, M., POULTON, R., MURRAY, R., CASPI, A. & MOFFITT, T. E. 2002. Cannabis use in adolescence and risk for adult psychosis: Longitudinal prospective study. *British Medical Journal*, 325, 1212-1213.
- ARSENEAULT, L., MOFFITT, T. E., CASPI, A., TAYLOR, P. J. & SILVA, P. A. 2000. Mental Disorders and Violence in a Total Birth Cohort. *Archives of General Psychiatry*, 57, 979.
- ASNIS, G. M., KAPLAN, M. L., HUNDORFEAN, G. & SAEED, W. 1997. Violence and homicidal behaviors in psychiatric disorders. *Psychiatr Clin North Am*, 20, 405-25.
- ASSOCIATION, A. P. 2013. *Diagnostic and statistical manual of mental disorders*, American Psychiatric Publishing.
- ATANASOVA, D., KOTEYKO, N., BROWN, B. & CRAWFORD, P. 2019. Mental health and the media: From illness to wellbeing. *Sociology Compass*, 13, e12678.
- BARNES, T. R., MUTSATSA, S. H., HUTTON, S. B., WATT, H. C. & JOYCE, E. M. 2006. Comorbid substance use and age at onset of schizophrenia. *Br J Psychiatry*, 188, 237-42.
- BARNETT, J. H., WERNERS, U., SECHER, S. M., HILL, K. E., BRAZIL, R., MASSON, K., PERNET, D. E., KIRKBRIDE, J. B., MURRAY, G. K., BULLMORE, E. T. & JONES, P. B. 2007a. Substance use in a population-based clinic sample of people with first-episode psychosis. *Br J Psychiatry*, 190, 515-20.
- BARNETT, J. H., WERNERS, U., SECHER, S. M., HILL, K. E., BRAZIL, R., MASSON, K., PERNET, D. E., KIRKBRIDE, J. B., MURRAY, G. K., BULLMORE, E. T. & JONES, P. B. 2007b. Substance use in a population-based clinic sample of people with first-episode psychosis. *British Journal of Psychiatry*, 190, 515-520.
- BARTHELEMY, O. J., RICHARDSON, M. A., CABRAL, H. J. & FRANK, D. A. 2016. Prenatal, perinatal, and adolescent exposure to marijuana: Relationships with aggressive behavior. *Neurotoxicol Teratol*, 58, 60-77.
- BATES, G. 2017. The drugs situation in Ireland: an overview of trends from 2005 to 2015.

- BECK-SANDER, A., BIRCHWOOD, M. & CHADWICK, P. 1997. Acting on command hallucinations: a cognitive approach. *British Journal of Clinical Psychology*, 36, 139-148.
- BECK, A. 2004. A new instrument for measuring insight: the Beck Cognitive Insight Scale. *Schizophrenia Research*, 68, 319-329.
- BHUGRA, D., HILWIG, M., MALLETT, R., CORRIDAN, B., LEFF, J., NEEHALL, J. & RUDGE, S. 2000. Factors in the onset of schizophrenia: a comparison between London and Trinidad samples. *Acta Psychiatrica Scandinavica*, 101, 135-141.
- BIGGS, J. T., WYLIE, L. T. & ZIEGLER, V. E. 1978. Validity of the Zung Self-rating Depression Scale. *British Journal of Psychiatry*, 132, 381-385.
- BINDER, R. L. & MCNIEL, D. E. 1990. The relationship of gender to violent behavior in acutely disturbed psychiatric patients. *The Journal of clinical psychiatry*.
- BIRCHWOOD, M., SMITH, J., DRURY, V., HEALY, J., MACMILLAN, F. & SLADE, M. 1994. A self-report Insight Scale for psychosis: reliability, validity and sensitivity to change. *Acta Psychiatrica Scandinavica*, 89, 62-67.
- BJORKQVIST, K. 2018. Gender differences in aggression. *Curr Opin Psychol*, 19, 39-42.
- BLANCO, E. A., DUQUE, L. M., RACHAMALLU, V., YUEN, E., KANE, J. M. & GALLEGU, J. A. 2018. Predictors of aggression in 3,322 patients with affective disorders and schizophrenia spectrum disorders evaluated in an emergency department setting. *Schizophrenia Research*, 195, 136-141.
- BO, S., ABU-AKEL, A., KONGERSLEV, M., HAAHR, U. H. & SIMONSEN, E. 2011. Risk factors for violence among patients with schizophrenia. *Clinical Psychology Review*, 31, 711-726.
- BOARD, H. R. 2018. National Drug Treatment Reporting System 2010 to 2016 - Alcohol Treatment Health Research Board
- BOBES, J., FILLAT, O. & ARANGO, C. 2009. Violence among schizophrenia out-patients compliant with medication: prevalence and associated factors. *Acta Psychiatrica Scandinavica*, 119, 218-225.
- BODEN, J. M., FERGUSSON, D. M. & HORWOOD, L. J. 2012. Alcohol misuse and violent behavior: Findings from a 30-year longitudinal study. *Drug and Alcohol Dependence*, 122, 135-141.
- BOLES, S. M. & MIOTTO, K. 2003. Substance abuse and violence: A review of the literature. *Aggression and Violent Behavior*, 8, 155-174.
- BONTA, J., LAW, M. & HANSON, K. 1998. The prediction of criminal and violent recidivism among mentally disordered offenders: A meta-analysis. *Psychological Bulletin*, 123, 123-142.
- BOSQUI, T. J., SHANNON, C., TIERNAN, B., BEATTIE, N., FERGUSON, J. & MULHOLLAND, C. 2014. Childhood trauma and the risk of violence in adulthood in a population with a psychotic illness. *Journal of Psychiatric Research*, 54, 121-125.
- BREKKE, J. S., PRINDLE, C., BAE, S. W. & LONG, J. D. 2001. Risks for Individuals With Schizophrenia Who Are Living in the Community. *Psychiatric Services*, 52, 1358-1366.
- BRENDGEN, M., DIONNE, G., GIRARD, A., BOIVIN, M., VITARO, F. & PÉRUSSE, D. 2005. Examining genetic and environmental effects on social aggression: A study of 6-year-old twins. *Child development*, 76, 930-946.
- BROWN, T. G., WERK, A., CAPLAN, T. & SERAGANIAN, P. 1999. Violent substance abusers in domestic violence treatment. *Violence and Victims*, 14, 179-190.
- BROWN, T. G., WERK, A., CAPLAN, T., SHIELDS, N. & SERAGANIAN, P. 1998. The incidence and characteristics of violent men in substance abuse treatment. *Addictive Behaviors*, 23, 573-586.
- BRUCATO, G., APPELBAUM, P. S., MASUCCI, M. D., ROLIN, S., WALL, M. M., LEVIN, M., ALTSCHULER, R., FIRST, M. B., LIEBERMAN, J. A. & GIRGIS, R. R. 2019. Prevalence and phenomenology of violent ideation and behavior among 200 young people at clinical high-risk for psychosis: an emerging model of violence and psychotic illness. *Neuropsychopharmacology*, 44, 907-914.
- BRUNETTE, M. F., MUESER, K. T., BABBIN, S., MEYER-KALOS, P., ROSENHECK, R., CORRELL, C. U., CATHER, C., ROBINSON, D. G., SCHOOLER, N. R., PENN, D. L., ADDINGTON, J., ESTROFF, S. E., GOTTLIEB, J., GLYNN, S. M., MARCY, P., ROBINSON, J. & KANE, J. M. 2018. Demographic and clinical correlates of substance use disorders in first episode psychosis. *Schizophr Res*, 194, 4-12.

- BUCKLEY, P. F., HROUDA, D. R., FRIEDMAN, L., NOFFSINGER, S. G., RESNICK, P. J. & CAMLIN-SHINGLER, K. 2004. Insight and Its Relationship to Violent Behavior in Patients With Schizophrenia. *American Journal of Psychiatry*, 161, 1712-1714.
- BUDNEY, A. J. & HUGHES, J. R. 2006. The cannabis withdrawal syndrome. *Curr Opin Psychiatry*, 19, 233-8.
- BUNTING, P. J., FULDE, G. W. & FORSTER, S. L. 2007. Comparison of crystalline methamphetamine ("ice") users and other patients with toxicology-related problems presenting to a hospital emergency department. *Med J Aust*, 187, 564-6.
- BUSS, A. H. & PERRY, M. 1992. The aggression questionnaire. *Journal of personality and social psychology*, 63, 452.
- BUSS, A. H. & WARREN, W. L. 2000. *Aggression questionnaire:(AQ)*, Western Psychological Services Torrance, CA.
- CAIRNS, R. B., CAIRNS, B. D., NECKERMAN, H. J., FERGUSON, L. L. & GARIÉPY, J.-L. 1989. Growth and aggression: I. Childhood to early adolescence. *Developmental Psychology*, 25, 320-330.
- CANTWELL, R., BREWIN, J., GLAZEBROOK, C., DALKIN, T., FOX, R., MEDLEY, I. & HARRISON, G. 1999. Prevalence of substance misuse in first-episode psychosis. *Br J Psychiatry*, 174, 150-3.
- CAPRIOLA, M. 2013. Synthetic cathinone abuse. *Clin Pharmacol*, 5, 109-15.
- CARPINIELLO, B. & PINNA, F. 2017. The Reciprocal Relationship between Suicidality and Stigma. *Frontiers in Psychiatry*, 8.
- CASPI, A., MCCLAY, J., MOFFITT, T. E., MILL, J., MARTIN, J., CRAIG, I. W., TAYLOR, A. & POULTON, R. 2002. Role of genotype in the cycle of violence in maltreated children. *Science*, 297, 851-854.
- CATHER, C., BRUNETTE, M. F., MUESER, K. T., BABBIN, S. F., ROSENHECK, R., CORRELL, C. U. & KALOSMEYER, P. 2018. Impact of comprehensive treatment for first episode psychosis on substance use outcomes: A randomized controlled trial. *Psychiatry Res*, 268, 303-311.
- CAUFFMAN, E., FINE, A., THOMAS, A. G. & MONAHAN, K. C. 2017. Trajectories of Violent Behavior Among Females and Males. *Child Development*, 88, 41-54.
- CHADWICK, P. & BIRCHWOOD, M. 1994. The omnipotence of voices: A cognitive approach to auditory hallucinations. *The British Journal of Psychiatry*, 164, 190-201.
- CHAN, B. & SHEHTMAN, M. 2019. Clinical risk factors of acute severe or fatal violence among forensic mental health patients. *Psychiatry Research*, 275, 20-26.
- CHEN, C.-Y., STORR, C. L. & ANTHONY, J. C. 2009. Early-onset drug use and risk for drug dependence problems. *Addictive Behaviors*, 34, 319-322.
- CHERMACK, S. T. & BLOW, F. C. 2002. Violence among individuals in substance abuse treatment: the role of alcohol and cocaine consumption. *Drug and Alcohol Dependence*, 66, 29-37.
- CHERMACK, S. T., FULLER, B. E. & BLOW, F. C. 2000. Predictors of expressed partner and non-partner violence among patients in substance abuse treatment. *Drug and Alcohol Dependence*, 58, 43-54.
- CHESTER, D. S., LYNAM, D. R., MILICH, R. & DEWALL, C. N. 2017. Social rejection magnifies impulsive behavior among individuals with greater negative urgency: An experimental test of urgency theory. American Psychological Association.
- CHEUNG, P., SCHWEITZER, I., CROWLEY, K. & TUCKWELL, V. 1997. Aggressive behaviour in schizophrenia: role of state versus trait factors. *Psychiatry Res*, 72, 41-50.
- CHOE, J. Y., TEPLIN, L. A. & ABRAM, K. M. 2008. Perpetration of Violence, Violent Victimization, and Severe Mental Illness: Balancing Public Health Concerns. *Psychiatric Services*, 59, 153-164.
- CHUKWUJEKWU, D. C. & STANLEY, P. C. 2008. The Modified Overt Aggression Scale: how valid in this environment? *Niger J Med*, 17, 153-5.
- CLARK, R. E., RICKETTS, S. K. & MCHUGO, G. J. 1999. Legal System Involvement and Costs for Persons in Treatment for Severe Mental Illness and Substance Use Disorders. *Psychiatric Services*, 50, 641-647.
- CLAYTON, H. B., LOWRY, R., ASHLEY, C., WOLKIN, A. & GRANT, A. M. 2017. Health Risk Behaviors With Synthetic Cannabinoids Versus Marijuana. *Pediatrics*, 139.
- CLEARY, S. D., BHATTY, S., BROUSSARD, B., CRISTOFARO, S. L., WAN, C. R. & COMPTON, M. T. 2014. Measuring insight through patient self-report: An in-depth analysis of the factor structure of the Birchwood Insight Scale. *Psychiatry Research*, 216, 263-268.

- COCCARO, E. F., HARVEY, P. D., KUPSAW-LAWRENCE, E., HERBERT, J. L. & BERNSTEIN, D. P. 1991. Development of neuropharmacologically based behavioral assessments of impulsive aggressive behavior. *The Journal of Neuropsychiatry and Clinical Neurosciences*.
- COID, J. W., KALLIS, C., DOYLE, M., SHAW, J. & ULLRICH, S. 2018. Shifts in positive and negative psychotic symptoms and anger: effects on violence. *Psychological Medicine*, 48, 2428-2438.
- COID, J. W., ULLRICH, S. & KALLIS, C. 2013a. Predicting future violence among individuals with psychopathy. *British Journal of Psychiatry*, 203, 387-388.
- COID, J. W., ULLRICH, S., KALLIS, C., KEERS, R., BARKER, D., COWDEN, F. & STAMPS, R. 2013b. The Relationship Between Delusions and Violence. *JAMA Psychiatry*, 70, 465.
- COLASANTI, A., PALETTA, S., MOLITERNO, D., MAZZOCCHI, A., MAURI, M. C. & ALTAMURA, A. C. 2010. Symptom dimensions as predictors of clinical outcome, duration of hospitalization, and aggressive behaviours in acutely hospitalized patients with psychotic exacerbation. *Clin Pract Epidemiol Ment Health*, 6, 72-8.
- COMPTON, M. 2004. Lower negative symptom scores among cannabis-dependent patients with schizophrenia-spectrum disorders: preliminary evidence from an African American first-episode sample. *Schizophrenia Research*, 71, 61-64.
- COMPTON, M. T., BEREZ, C. & WALKER, E. F. 2017. The Relative Importance of Family History, Gender, Mode of Onset, and Age at Onset in Predicting Clinical Features of First-Episode Psychotic Disorders. *Clin Schizophr Relat Psychoses*, 11, 143-150.
- CORNAGGIA, C. M., BEGHI, M., PAVONE, F. & BARALE, F. 2011. Aggression in psychiatry wards: A systematic review. *Psychiatry Research*, 189, 10-20.
- CORRIGAN, P. W. & WATSON, A. C. 2005a. Findings from the National Comorbidity Survey on the frequency of violent behavior in individuals with psychiatric disorders. *Psychiatry Res*, 136, 153-62.
- CORRIGAN, P. W. & WATSON, A. C. 2005b. Findings from the National Comorbidity Survey on the frequency of violent behavior in individuals with psychiatric disorders. *Psychiatry Research*, 136, 153-162.
- CORRIGAN, P. W., WATSON, A. C., GRACIA, G., SLOPEN, N., RASINSKI, K. & HALL, L. L. 2005. Newspaper stories as measures of structural stigma. *Psychiatr Serv*, 56, 551-6.
- CORSO, P. S., MERCY, J. A., SIMON, T. R., FINKELSTEIN, E. A. & MILLER, T. R. 2007. Medical costs and productivity losses due to interpersonal and self-directed violence in the United States. *Am J Prev Med*, 32, 474-482.
- COURTS, J., MASKILL, V., GRAY, A. & GLUE, P. 2016. Signs and symptoms associated with synthetic cannabinoid toxicity: systematic review. *Australas Psychiatry*, 24, 598-601.
- CRAIG, I. W. & HALTON, K. E. 2009. Genetics of human aggressive behaviour. *Human genetics*, 126, 101-113.
- CRAIG, T. J. 1982. An epidemiologic study of problems associated with violence among psychiatric inpatients. *The American Journal of Psychiatry*.
- CRICK, N. R. & GROTPETER, J. K. 1995. Relational Aggression, Gender, and Social-Psychological Adjustment. *Child Development*, 66, 710-722.
- CRILLY, J., CHABOYER, W. & CREEDY, D. 2004. Violence towards emergency department nurses by patients. *Accid Emerg Nurs*, 12, 67-73.
- CROW, T. J. 1985. The Two-syndrome Concept: Origins and Current Status. *Schizophrenia Bulletin*, 11, 471-488.
- CYDERS, M. A. & SMITH, G. T. 2007. Mood-based rash action and its components: Positive and negative urgency. *Personality and Individual Differences*, 43, 839-850.
- DARRELL-BERRY, H., BUCCI, S., PALMIER-CLAUS, J., EMSLEY, R., DRAKE, R. & BERRY, K. 2017. Predictors and mediators of trait anger across the psychosis continuum: The role of attachment style, paranoia and social cognition. *Psychiatry Research*, 249, 132-138.
- DAVIS, W. M. 1996. Psychopharmacologic violence associated with cocaine abuse: kindling of a limbic dyscontrol syndrome? *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 20, 1273-1300.
- DAVOREN, M. P., SHIELY, F., BYRNE, M. & PERRY, I. J. 2015. Hazardous alcohol consumption among university students in Ireland: a cross-sectional study. *BMJ open*, 5, e006045.

- DE JONG, S., VAN DONKERSGOED, R., RENARD, S., CARTER, S., BOKERN, H., LYSAKER, P., VAN DER GAAG, M., ALEMAN, A. & PIJNENBORG, G. H. M. 2018. Social-cognitive risk factors for violence in psychosis: A discriminant function analysis. *Psychiatry Research*, 265, 93-99.
- DE VRIES, B., VAN BUSSCHBACH, J. T., VAN DER STOUWE, E. C. D., ALEMAN, A., VAN DIJK, J. J. M., LYSAKER, P. H., ARENDS, J., NIJMAN, S. A. & PIJNENBORG, G. H. M. 2019. Prevalence Rate and Risk Factors of Victimization in Adult Patients With a Psychotic Disorder: A Systematic Review and Meta-analysis. *Schizophrenia Bulletin*, 45, 114-126.
- DEAN, K., WALSH, E., MORGAN, C., DEMJAHIA, A., DAZZAN, P., MORGAN, K., LLOYD, T., FEARON, P., JONES, P. B. & MURRAY, R. M. 2007. Aggressive behaviour at first contact with services: findings from the AESOP First Episode Psychosis Study. *Psychological Medicine*, 37, 547-557.
- DEGENHARDT, L. & HALL, W. 2001. The association between psychosis and problematical drug use among Australian adults: findings from the National Survey of Mental Health and Well-Being. *Psychol Med*, 31, 659-68.
- DELLAZIZZO, L., POTVIN, S., ATHANASSIOU, M. & DUMAIS, A. 2020. Violence and cannabis use: a focused review of a forgotten aspect in the era of liberalizing cannabis. *Frontiers in psychiatry*, 11, 567887.
- DEMARCE, J. M., LASH, S. J., PARKER, J. D., BURKE, R. S. & GRAMBOW, S. C. 2013. Validity of the Structured Clinical Interview for DSM-IV Among Veterans Seeking Treatment for Substance Use Disorders. *International Journal of Mental Health and Addiction*, 11, 546-556.
- DI FORTI, M., MARCONI, A., CARRA, E., FRAIETTA, S., TROTTA, A., BONOMO, M., BIANCONI, F., GARDNER-SOOD, P., O'CONNOR, J., RUSSO, M., STILO, S. A., MARQUES, T. R., MONDELLI, V., DAZZAN, P., PARIANTE, C., DAVID, A. S., GAUGHRAN, F., ATAKAN, Z., IYEGBE, C., POWELL, J., MORGAN, C., LYNSKEY, M. & MURRAY, R. M. 2015. Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study. *Lancet Psychiatry*, 2, 233-8.
- DI FORTI, M., QUATTRONE, D., FREEMAN, T. P., TRIPOLI, G., GAYER-ANDERSON, C., QUIGLEY, H., RODRIGUEZ, V., JONGSMA, H. E., FERRARO, L., LA CASCIA, C., LA BARBERA, D., TARRICONE, I., BERARDI, D., SZOKE, A., ARANGO, C., TORTELLI, A., VELTHORST, E., BERNARDO, M., DEL-BEN, C. M., MENEZES, P. R., SELTEN, J. P., JONES, P. B., KIRKBRIDE, J. B., RUTTEN, B. P., DE HAAN, L., SHAM, P. C., VAN OS, J., LEWIS, C. M., LYNSKEY, M., MORGAN, C., MURRAY, R. M. & GROUP, E.-G. W. 2019. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. *Lancet Psychiatry*, 6, 427-436.
- DI FORTI, M., SALLIS, H., ALLEGRI, F., TROTTA, A., FERRARO, L., STILO, S. A., MARCONI, A., LA CASCIA, C., REIS MARQUES, T., PARIANTE, C., DAZZAN, P., MONDELLI, V., PAPARELLI, A., KOLLIAKOU, A., PRATA, D., GAUGHRAN, F., DAVID, A. S., MORGAN, C., STAHL, D., KHONDOKER, M., MACCABE, J. H. & MURRAY, R. M. 2014. Daily use, especially of high-potency cannabis, drives the earlier onset of psychosis in cannabis users. *Schizophr Bull*, 40, 1509-17.
- DOUGLAS, K. S., GUY, L. S. & HART, S. D. 2009. Psychosis as a Risk Factor for Violence to Others: A Meta-Analysis. *Psychological bulletin*, 135, 679-706.
- DOYLE, A. 2021. Alcohol consumption, alcohol-related harm, and alcohol policy in Ireland. *Drugnet Ireland*, 1-8.
- DRAGISIC, T., DICKOV, A., DICKOV, V. & MIJATOVIC, V. 2015. Drug Addiction as Risk for Suicide Attempts. *Materia Socio Medica*, 27, 188.
- DRAKE, R. E., O'NEAL, E. L. & WALLACH, M. A. 2008. A systematic review of psychosocial research on psychosocial interventions for people with co-occurring severe mental and substance use disorders. *Journal of Substance Abuse Treatment*, 34, 123-138.
- DUBERTRET, C., BIDARD, I., ADES, J. & GORWOOD, P. 2006. Lifetime positive symptoms in patients with schizophrenia and cannabis abuse are partially explained by co-morbid addiction. *Schizophr Res*, 86, 284-90.
- DUTTA, R., MURRAY, R. M., ALLARDYCE, J., JONES, P. B. & BOYDELL, J. 2011. Early risk factors for suicide in an epidemiological first episode psychosis cohort. *Schizophrenia Research*, 126, 11-19.

- DUTTON, D. G. & KARAKANTA, C. 2013. Depression as a risk marker for aggression: A critical review. *Aggression and Violent Behavior*, 18, 310-319.
- DVOSKIN, J. A., KNOLL, J. L. & SILVA, M. 2020. A brief history of the criminalization of mental illness. *CNS Spectrums*, 25, 638-650.
- DWYER-LINDGREN, L., BERTOZZI-VILLA, A., STUBBS, R. W., MOROZOFF, C., SHIRUDE, S., UNÜTZER, J., NAGHAVI, M., MOKDAD, A. H. & MURRAY, C. J. L. 2018. Trends and Patterns of Geographic Variation in Mortality From Substance Use Disorders and Intentional Injuries Among US Counties, 1980-2014. *JAMA*, 319, 1013-1023.
- DYER, C. 2012. French psychiatrist is convicted of manslaughter after her patient kills an elderly man. *BMJ: British Medical Journal (Online)*, 345.
- EDLINGER, M., RAUCH, A.-S., KEMMLER, G., YALCIN-SIEDENTOPF, N., WOLFGANG FLEISCHHACKER, W. & HOFER, A. 2014. Risk of violence of inpatients with severe mental illness – Do patients with schizophrenia pose harm to others? *Psychiatry Research*, 219, 450-456.
- EGGINK, E., DE WAAL, M. M. & GOUDRIAAN, A. E. 2019. Criminal offending and associated factors in dual diagnosis patients. *Psychiatry Research*, 273, 355-362.
- EL-HADIDY, M. A. & HELALY, A. M. N. 2015. Medical and Psychiatric Effects of Long-Term Dependence on High Dose of tramadol. *Substance Use & Misuse*, 50, 582-589.
- ELBOGEN, E. B., DENNIS, P. A. & JOHNSON, S. C. 2016. Beyond Mental Illness. *Clinical Psychological Science*, 4, 747-759.
- ELBOGEN, E. B. & JOHNSON, S. C. 2009. The Intricate Link Between Violence and Mental Disorder. *Archives of General Psychiatry*, 66, 152.
- ELSOHLY, M. A., MEHMEDIC, Z., FOSTER, S., GON, C., CHANDRA, S. & CHURCH, J. C. 2016. Changes in Cannabis Potency Over the Last 2 Decades (1995–2014): Analysis of Current Data in the United States. *Biological Psychiatry*, 79, 613-619.
- EMMERSON, L. C., GRANHOLM, E., LINK, P. C., MCQUAID, J. R. & JESTE, D. V. 2009. Insight and treatment outcome with cognitive-behavioral social skills training for older people with schizophrenia. *J Rehabil Res Dev*, 46, 1053-1058.
- EPSTEIN, J. 2004. *Serious mental illness and its co-occurrence with substance use disorders, 2002*, Department of Health and Human Services, Substance Abuse and Mental Health ....
- ERKIRAN, M., OZUNALAN, H., EVREN, C., AYTAÇLAR, S., KIRISCI, L. & TARTER, R. 2006. Substance abuse amplifies the risk for violence in schizophrenia spectrum disorder. *Addict Behav*, 31, 1797-805.
- ERON, L. D., GENTRY, J. H. & SCHLEGEL, P. 1994. Reason to hope: A psychosocial perspective on violence & youth. American Psychological Association.
- FAGAN, J. 1990. Intoxication and Aggression. *Crime and Justice*, 13, 241-320.
- FAGAN, J. 1993. Interactions Among Drugs, Alcohol, and Violence. *Health Affairs*, 12, 65-79.
- FAZEL, S., GULATI, G., LINSELL, L., GEDDES, J. R. & GRANN, M. 2009. Schizophrenia and Violence: Systematic Review and Meta-Analysis. *PLoS Medicine*, 6, e1000120.
- FERNANDES, C. M., BOUTHILLETTE, F., RABOUD, J. M., BULLOCK, L., MOORE, C. F., CHRISTENSON, J. M., GRAFSTEIN, E., RAE, S., OUELLET, L., GILLRIE, C. & WAY, M. 1999. Violence in the emergency department: a survey of health care workers. *CMAJ*, 161, 1245-8.
- FIELD, C. A. & CAETANO, R. 2005. Intimate Partner Violence in the U.S. General Population. *Journal of Interpersonal Violence*, 20, 463-469.
- FLEMING, I. B. M. E. D. & WC, J. A. F. I. 1993. Establishing the onset of psychotic illness. *Am J Psychiatry*, 150, 1349-13.
- FOLEY, S. R., KELLY, B. D., CLARKE, M., MCTIGUE, O., GERVIN, M., KAMALI, M., LARKIN, C., O'CALLAGHAN, E. & BROWNE, S. 2005. Incidence and clinical correlates of aggression and violence at presentation in patients with first episode psychosis. *Schizophrenia Research*, 72, 161-168.
- FRASER, S., HIDES, L., PHILIPS, L., PROCTOR, D. & LUBMAN, D. I. 2012. Differentiating first episode substance induced and primary psychotic disorders with concurrent substance use in young people. *Schizophrenia Research*, 136, 110-115.
- FREEMAN, C., TYRER, P. J. & TYRER, P. 2006. Research methods in psychiatry.

- FRIEDMAN, R. A. 2006. Violence and mental illness--how strong is the link? *N Engl J Med*, 355, 2064-6.
- FULDE, G. W. & FORSTER, S. L. 2015. The impact of amphetamine-type stimulants on emergency services. *Curr Opin Psychiatry*, 28, 275-9.
- FULWILER, C. & RUTHAZER, R. 1999. Premorbid risk factors for violence in adult mental illness. *Compr Psychiatry*, 40, 96-100.
- GAGNON, J. & ROCHAT, L. 2017. Relationships Between Hostile Attribution Bias, Negative Urgency, and Reactive Aggression. *Journal of Individual Differences*, 38, 211-219.
- GHOSSOUB, E., ADIB, S. M., MAALOUF, F. T., FULEIHAN, G. E. H., TAMIM, H., NAHAS, Z. & FULEIHAN, G. E. H. 2019. Association between substance use disorders and self- and other-directed aggression: An integrated model approach. *Aggressive Behavior*, 45, 652-661.
- GILLET, C., POLARD, E., MAUDUIT, N. & ALLAIN, H. 2001. [Acting out and psychoactive substances: alcohol, drugs, illicit substances]. *Encephale*, 27, 351-9.
- GIRASEK, H., NAGY, V. A., FEKETE, S., UNGVARI, G. S. & GAZDAG, G. 2022. Prevalence and correlates of aggressive behavior in psychiatric inpatient populations. *World Journal of Psychiatry*, 12, 1-23.
- GLASOFER, D. R., BROWN, A. J. & RIEGEL, M. 2015a. Structured Clinical Interview for DSM-IV (SCID). In: WADE, T. (ed.) *Encyclopedia of Feeding and Eating Disorders*. Singapore: Springer Singapore.
- GLASOFER, D. R., BROWN, A. J., RIEGEL, M. & WADE, T. 2015b. Structured clinical interview for DSM-IV (SCID). *Encyclopedia of feeding and eating disorders*, 1-4.
- GOLDMAN, H. H., SKODOL, A. E. & LAVE, T. R. 1992. Revising axis V for DSM-IV: a review of measures of social functioning. *Am J Psychiatry*, 149, 9.
- GREAVES, L. 2020. Missing in Action: Sex and Gender in Substance Use Research. *Int J Environ Res Public Health*, 17.
- GREEN, A. I., TOHEN, M. F., HAMER, R. M., STRAKOWSKI, S. M., LIEBERMAN, J. A., GLICK, I., CLARK, W. S. & GROUP, H. R. 2004. First episode schizophrenia-related psychosis and substance use disorders: acute response to olanzapine and haloperidol. *Schizophr Res*, 66, 125-35.
- GREENFIELD, T. K., MCNIEL, D. E. & BINDER, R. L. 1989. Violent Behavior and Length of Psychiatric Hospitalization. *Psychiatric Services*, 40, 809-814.
- GREGG, L., BARROWCLOUGH, C. & HADDOCK, G. 2007. Reasons for increased substance use in psychosis. *Clin Psychol Rev*, 27, 494-510.
- GREYDANUS, D. E., HAWVER, J. R. & ROWLAND, D. C. 2021. Concepts of aggression: Perspectives in the 21st century. *Journal of alternative medicine research*, 13, 361-385.
- GRISWOLD, M. G., FULLMAN, N., HAWLEY, C., ARIAN, N., ZIMSEN, S. R. M., TYMESON, H. D., VENKATESWARAN, V., TAPP, A. D., FOROUZANFAR, M. H., SALAMA, J. S., ABATE, K. H., ABATE, D., ABAY, S. M., ABBAFATI, C., ABDULKADER, R. S., ABEBE, Z., ABOYANS, V., ABRAR, M. M., ACHARYA, P., ADETOKUNBOH, O. O., ADHIKARI, T. B., ADSUAR, J. C., AFARIDEH, M., AGARDH, E. E., AGARWAL, G., AGHAYAN, S. A., AGRAWAL, S., AHMED, M. B., AKIBU, M., AKINYEMIJU, T., AKSEER, N., ASFOOR, D. H. A., AL-ALY, Z., ALAHDAB, F., ALAM, K., ALBUJEER, A., ALENE, K. A., ALI, R., ALI, S. D., ALIJANZADEH, M., ALJUNID, S. M., ALKERWI, A. A., ALLEBECK, P., ALVIS-GUZMAN, N., AMARE, A. T., AMINDE, L. N., AMMAR, W., AMOAKO, Y. A., AMUL, G. G. H., ANDREI, C. L., ANGUS, C., ANSHA, M. G., ANTONIO, C. A. T., AREMU, O., ÄRNLÖV, J., ARTAMAN, A., ARYAL, K. K., ASSADI, R., AUSLOOS, M., AVILA-BURGOS, L., AVOKPAHO, E. F., AWASTHI, A., AYELE, H. T., AYER, R., AYUK, T. B., AZZOPARDI, P. S., BADALI, H., BADAWI, A., BANACH, M., BARKER-COLLO, S. L., BARRERO, L. H., BASALEEM, H., BAYE, E., BAZARGAN-HEJAZI, S., BEDI, N., BÉJOT, Y., BELACHEW, A. B., BELAY, S. A., BENNETT, D. A., BENSENOR, I. M., BERNABE, E., BERNSTEIN, R. S., BEYENE, A. S., BEYRANVAND, T., BHAUMIK, S., BHUTTA, Z. A., BIADGO, B., BIJANI, A., BILILIGN, N., BIRLIK, S. M., BIRUNGI, C., BIZUNEH, H., BJERREGAARD, P., BJØRGE, T., BORGES, G., BOSETTI, C., BOUFOUS, S., BRAGAZZI, N. L., BRENNER, H., BUTT, Z. A., et al. 2018. Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*, 392, 1015-1035.

- HACHTEL, H., NIXON, M., BENNETT, D., MULLEN, P. & OGLOFF, J. 2021. Motives, Offending Behavior, and Gender Differences in Murder Perpetrators With or Without Psychosis. *Journal of Interpersonal Violence*, 36, 3168-3190.
- HALL, W. & DEGENHARDT, L. 2007. Prevalence and correlates of cannabis use in developed and developing countries. *Current opinion in Psychiatry*, 20, 393-397.
- HALL, W. D. & LYNSKEY, M. 2005. Is cannabis a gateway drug? Testing hypotheses about the relationship between cannabis use and the use of other illicit drugs. *Drug and Alcohol Review*, 24, 39-48.
- HAMBRECHT, M. & HAFNER, H. 2000. Cannabis, vulnerability, and the onset of schizophrenia: an epidemiological perspective. *Aust N Z J Psychiatry*, 34, 468-75.
- HARRIS, A. W. F., LARGE, M. M., REDOBLADO-HODGE, A., NIELSSEN, O., ANDERSON, J. & BRENNAN, J. 2010. Clinical and Cognitive Associations with Aggression in the First Episode of Psychosis. *Australian & New Zealand Journal of Psychiatry*, 44, 85-93.
- HARRO, J. 2015. Neuropsychiatric Adverse Effects of Amphetamine and Methamphetamine. *Int Rev Neurobiol*, 120, 179-204.
- HARVEY, S. B., DEAN, K., MORGAN, C., WALSH, E., DEMJAHA, A., DAZZAN, P., MORGAN, K., LLOYD, T., FEARON, P., JONES, P. B. & MURRAY, R. M. 2008. Self-harm in first-episode psychosis. *British Journal of Psychiatry*, 192, 178-184.
- HAYHURST, K. P., PIERCE, M., HICKMAN, M., SEDDON, T., DUNN, G., KEANE, J. & MILLAR, T. 2017. Pathways through opiate use and offending: A systematic review. *Int J Drug Policy*, 39, 1-13.
- HEGNEY, D., PLANK, A. & PARKER, V. 2003. Workplace violence in nursing in Queensland, Australia: a self-reported study. *Int J Nurs Pract*, 9, 261-8.
- HELLERSTEIN, D., FROSCH, W. & KOENIGSBERG, H. W. 1987. The clinical significance of command hallucinations. *The American journal of psychiatry*.
- HENQUET, C., KRABBENDAM, L., SPAUWEN, J., KAPLAN, C., LIEB, R., WITTCHEN, H.-U. & VAN OS, J. 2005. Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. *BMJ*, 330, 11.
- HIDAY, V. A., SWARTZ, M. S., SWANSON, J. W., BORUM, R. & WAGNER, H. R. 1998. Male-female differences in the setting and construction of violence among people with severe mental illness. *Social Psychiatry and Psychiatric Epidemiology*, 33, S68-S74.
- HIGGINS, J. P. T., THOMPSON, S. G., DEEKS, J. J. & ALTMAN, D. G. 2003. Measuring inconsistency in meta-analyses. *BMJ*, 327, 557.
- HOAKEN, P. N. S. & STEWART, S. H. 2003. Drugs of abuse and the elicitation of human aggressive behavior. *Addictive behaviors*, 28, 1533-1554.
- HODGINS, S. 1992. Mental disorder, intellectual deficiency, and crime: evidence from a birth cohort. *Archives of general psychiatry*, 49, 476-483.
- HODGINS, S. 2008. Violent behaviour among people with schizophrenia: a framework for investigations of causes, and effective treatment, and prevention. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 363, 2505-2518.
- HODGINS, S., CALEM, M., SHIMEL, R., WILLIAMS, A., HARLESTON, D., MORGAN, C., DAZZAN, P., FEARON, P., MORGAN, K., LAPPIN, J., ZANELLI, J., REICHENBERG, A. & JONES, P. 2011. Criminal offending and distinguishing features of offenders among persons experiencing a first episode of psychosis. *Early Intervention in Psychiatry*, 5, 15-23.
- HODGINS, S. & RIAZ, M. 2011. Violence and phases of illness: Differential risk and predictors. *European Psychiatry*, 26, 518-524.
- HODGINS, S., J. C. G. 2002. *Criminality and violence among mentally disordered: The Stockholm Project Metropolitan*, New York, Cambridge University Press.
- HOPTMAN, M. J. & AHMED, A. O. 2016. Neural Foundations of Mood-Induced Impulsivity and Impulsive Aggression in Schizophrenia. *Current Behavioral Neuroscience Reports*, 3, 248-255.
- HOPTMAN, M. J., ANTONIUS, D., MAURO, C. J., PARKER, E. M. & JAVITT, D. C. 2014. Cortical Thinning, Functional Connectivity, and Mood-Related Impulsivity in Schizophrenia: Relationship to Aggressive Attitudes and Behavior. *American Journal of Psychiatry*, 171, 939-948.
- HOR, K. & TAYLOR, M. 2010. Suicide and schizophrenia: a systematic review of rates and risk factors. *Journal of psychopharmacology*, 24, 81-90.

- HUANG, H. C., WANG, Y. T., CHEN, K. C., YEH, T. L., LEE, I. H., CHEN, P. S., YANG, Y. K. & LU, R. B. 2009. The reliability and validity of the Chinese version of the Modified Overt Aggression Scale. *Int J Psychiatry Clin Pract*, 13, 303-6.
- HUMPHREYS, M. S., JOHNSTONE, E. C., MACMILLAN, J. F. & TAYLOR, P. J. 1992. Dangerous Behaviour Preceding First Admissions for Schizophrenia. *British Journal of Psychiatry*, 161, 501-505.
- HUTTON, P., PARKER, S., BOWE, S. & FORD, S. 2012. Prevalence of violence risk factors in people at ultra-high risk of developing psychosis: a service audit. *Early Intervention in Psychiatry*, 6, 91-96.
- IOZZINO, L., FERRARI, C., LARGE, M., NIELSSEN, O. & DE GIROLAMO, G. 2015. Prevalence and Risk Factors of Violence by Psychiatric Acute Inpatients: A Systematic Review and Meta-Analysis. *PLOS ONE*, 10, e0128536.
- IRO, C. J., NKIRE, N. & O'CONNOR, J. 2011. Violence and aggression at a substance misuse treatment clinic in Ireland. *The Psychiatrist*, 35, 216-219.
- IRVING, J., COLLING, C., SHETTY, H., PRITCHARD, M., STEWART, R., FUSAR-POLI, P., MCGUIRE, P. & PATEL, R. 2021. Gender differences in clinical presentation and illicit substance use during first episode psychosis: a natural language processing, electronic case register study. *BMJ Open*, 11, e042949.
- JAMES, D., ADAMS, R. D., SPEARS, R., COOPER, G., LUPTON, D. J., THOMPSON, J. P. & THOMAS, S. H. 2011. Clinical characteristics of mephedrone toxicity reported to the U.K. National Poisons Information Service. *Emerg Med J*, 28, 686-9.
- JOYAL, C. C., GENDRON, C. & COTE, G. 2008. Nature and frequency of aggressive behaviours among long-term inpatients with schizophrenia: a 6-month report using the modified overt aggression scale. *Can J Psychiatry*, 53, 478-81.
- JUNGINGER, J. 1990. Predicting compliance with command hallucinations. *The American journal of psychiatry*.
- JUNGINGER, J. 1996. Psychosis and Violence: The Case for a Content Analysis of Psychotic Experience. *Schizophrenia Bulletin*, 22, 91-103.
- JUNGINGER, J. & MCGUIRE, L. 2004. Psychotic Motivation and the Paradox of Current Research on Serious Mental Illness and Rates of Violence. *Schizophrenia Bulletin*, 30, 21-30.
- KAMALI, M., MCTIGUE, O., WHITTY, P., GERVIN, M., CLARKE, M., BROWNE, S., LARKIN, C. & O'CALLAGHAN, E. 2009. Lifetime history of substance misuse in first-episode psychosis: prevalence and its influence on psychopathology and onset of psychotic symptoms. *Early Interv Psychiatry*, 3, 198-203.
- KAPLAN, H. 2015. Kaplan & Sadock's synopsis of psychiatry. Philadelphia: Wolter Kluwer. Lippincott Williams & Wilkins.
- KARIN ÖSTERMAN, K. B., KIRSTI M. J. LAGERSPETZ,ARI KAUKIAINEN,SIMHA F. LANDAU,ADAM FRĄCZEK,GIAN VITTORIO CAPRARA 1998. Cross-cultural evidence of female indirect aggression. *Aggressive Behaviour*, 24, 1-8.
- KASPER, M. E., ROGERS, R. & ADAMS, P. A. 1996. Dangerousness and command hallucinations: an investigation of psychotic inpatients. *Journal of the American Academy of Psychiatry and the Law Online*, 24, 219-224.
- KATZ, G., DURST, R., SHUFMAN, E., BAR-HAMBURGER, R. & GRUNHAUS, L. 2010. Cannabis abuse and severity of psychotic and affective disorders in Israeli psychiatric inpatients. *Compr Psychiatry*, 51, 37-41.
- KAVANAGH, D. J., WAGHORN, G., JENNER, L., CHANT, D. C., CARR, V., EVANS, M., HERRMAN, H., JABLENSKY, A. & MCGRATH, J. J. 2004. Demographic and clinical correlates of comorbid substance use disorders in psychosis: multivariate analyses from an epidemiological sample. *Schizophrenia Research*, 66, 115-124.
- KAY, S. R., FISZBEIN, A. & OPLER, L. A. 1987. The Positive and Negative Syndrome Scale (PANSS) for Schizophrenia. *Schizophrenia Bulletin*, 13, 261-276.
- KAY, S. R., OPLER, L. A. & LINDENMAYER, J.-P. 1989. The Positive and Negative Syndrome Scale (PANSS): Rationale and Standardisation. *British Journal of Psychiatry*, 155, 59-65.
- KAY, S. R., WOLKENFELD, F. & MURRILL, L. M. 1988. Profiles of aggression among psychiatric patients. I. Nature and prevalence. *J Nerv Ment Dis*, 176, 539-46.

- KEANE, S., SZIGETI, A., FANNING, F. & CLARKE, M. 2019. Are patterns of violence and aggression at presentation in patients with first-episode psychosis temporally stable? A comparison of 2 cohorts. *Early Intervention in Psychiatry*, 13, 888-894.
- KEERS, R., ULLRICH, S., DESTAVOLA, B. L. & COID, J. W. 2014. Association of Violence With Emergence of Persecutory Delusions in Untreated Schizophrenia. *American Journal of Psychiatry*, 171, 332-339.
- KHALIFEH, H. & DEAN, K. 2010. Gender and violence against people with severe mental illness. *International Review of Psychiatry*, 22, 535-546.
- KICI, G. & WESTHOFF, K. 2004. Evaluation of requirements for the assessment and construction of interview guides in psychological assessment. *European Journal of Psychological Assessment*, 20, 83-98.
- KLIMIDIS, S., STUART, G. W., MINAS, I. H., COPOLOV, D. L. & SINGH, B. S. 1993. Positive and negative symptoms in the psychoses: re-analysis of published SAPS and SANS global ratings. *Schizophrenia research*, 9, 11-18.
- KOEN, L., KINNEAR, C. J., CORFIELD, V. A., EMSLEY, R. A., JORDAAN, E., KEYTER, N., MOOLMAN-SMOOK, J. C., STEIN, D. J. & NIEHAUS, D. J. H. 2004. Violence in male patients with schizophrenia: risk markers in a South African population. *Australian & New Zealand Journal of Psychiatry*, 38, 254-259.
- KØSTER, A., LAJER, M., LINDHARDT, A. & ROSENBAUM, B. 2008. Gender differences in first episode psychosis. *Social Psychiatry and Psychiatric Epidemiology*, 43, 940-946.
- KOURI, E. M., POPE JR, H. G. & LUKAS, S. E. 1999. Changes in aggressive behavior during withdrawal from long-term marijuana use. *Psychopharmacology*, 143, 302-308.
- KRAKOWSKI, M. & CZOBOR, P. 2004. Gender Differences in Violent Behaviors: Relationship to Clinical Symptoms and Psychosocial Factors. *American Journal of Psychiatry*, 161, 459-465.
- KRANZLER, H. R., KADDEN, R. M., BABOR, T. F., TENNEN, H. & ROUNSAVILLE, B. J. 1996. Validity of the SCID in substance abuse patients. *Addiction*, 91, 859-868.
- KRANZLER, H. R., TENNEN, H., BABOR, T. F., KADDEN, R. M. & ROUNSAVILLE, B. J. 1997. Validity of the longitudinal, expert, all data procedure for psychiatric diagnosis in patients with psychoactive substance use disorders. *Drug and alcohol dependence*, 45, 93-104.
- KRUG, E. G., MERCY, J. A., DAHLBERG, L. L. & ZWI, A. B. 2002. The world report on violence and health. *The Lancet*, 360, 1083-1088.
- KUMARI, S., MALIK, M., FLORIVAL, C., MANALAI, P. & SONJE, S. 2017. An assessment of five (PANSS, SAPS, SANS, NSA-16, CGI-SCH) commonly used symptoms rating scales in schizophrenia and comparison to newer scales (CAINS, BNSS). *Journal of addiction research & therapy*, 8.
- KUYPERS, K., VERKES, R., VAN DEN BRINK, W., VAN AMSTERDAM, J. & RAMAEKERS, J. 2020. Intoxicated aggression: Do alcohol and stimulants cause dose-related aggression? A review. *European Neuropsychopharmacology*, 30, 114-147.
- KWON, M., YANG, S., PARK, K. & KIM, D.-J. 2013. Factors that affect substance users' suicidal behavior: a view from the Addiction Severity Index in Korea. *Annals of General Psychiatry*, 12, 35.
- LABRUM, T., SIMONSSON, P. & SOLOMON, P. L. 2018. Stigma Contributes to the Risk of Violence by Persons with Mental Illness. *Journal of Psychosocial Rehabilitation and Mental Health*, 5, 209-212.
- LAM, J. A. & ROSENHECK, R. 1998. The effect of victimization on clinical outcomes of homeless persons with serious mental illness. *Psychiatr Serv*, 49, 678-83.
- LAM, J. N., MCNIEL, D. E. & BINDER, R. L. 2000. The relationship between patients' gender and violence leading to staff injuries. *Psychiatric Services*, 51, 1167-1170.
- LAMBERT, M., CONUS, P., LUBMAN, D. I., WADE, D., YUEN, H., MORITZ, S., NABER, D., MCGORRY, P. D. & SCHIMMELMANN, B. G. 2005. The impact of substance use disorders on clinical outcome in 643 patients with first-episode psychosis. *Acta Psychiatr Scand*, 112, 141-8.
- LAMSMA, J. & HARTE, J. M. 2015. Violence in psychosis: Conceptualizing its causal relationship with risk factors. *Aggression and Violent Behavior*, 24, 75-82.
- LANGEVELD, J., BJØRKLY, S., AUESTAD, B., BARDER, H., EVENSEN, J., TEN VELDEN HEGELSTAD, W., JOA, I., JOHANNESSEN, J. O., LARSEN, T. K., MELLE, I., OPJORDSMOEN, S., RØSSBERG, J. I.,

- RUND, B. R., SIMONSEN, E., VAGLUM, P., MCGLASHAN, T. & FRIIS, S. 2014. Treatment and violent behavior in persons with first episode psychosis during a 10-year prospective follow-up study. *Schizophrenia Research*, 156, 272-276.
- LANGEVELD, J., BJØRKLY, S., EVENSEN, J., JOA, I., JOHANNESSEN, J. O., LARSEN, T. K., MELLE, I., OPJORDSMOEN, S., RØSSBERG, J. I., RUND, B. R., SIMONSEN, E., VAGLUM, P., WENCHE, MCGLASHAN, T. & FRIIS, S. 2018. A 10-year follow-up study of violent victimization in first episode psychosis: Risk and protective factors. *Psychiatry Research*, 259, 545-549.
- LARGE, M. M. & NIELSEN, O. 2011. Violence in first-episode psychosis: A systematic review and meta-analysis. *Schizophrenia Research*, 125, 209-220.
- LÁTALOVÁ, K. 2014. Violence and duration of untreated psychosis in first-episode patients. *International Journal of Clinical Practice*, 68, 330-335.
- LATALOVA, K., KAMARADOVA, D. & PRASKO, J. 2014. Violent victimization of adult patients with severe mental illness: a systematic review. *Neuropsychiatric Disease and Treatment*, 12, 1925.
- LEE, R., PETTY, F. & COCCARO, E. F. 2009. Cerebrospinal fluid GABA concentration: Relationship with impulsivity and history of suicidal behavior, but not aggression, in human subjects. *Journal of Psychiatric Research*, 43, 353-359.
- LEUNER, H. 1961. Psychotherapy with hallucinogens. *Hallucinogenic Drugs*, 67, 67-73.
- LEUNG, A. & CHUE, P. 2000. Sex differences in schizophrenia, a review of the literature. *Acta Psychiatrica Scandinavica*, 101, 3-38.
- LIAKONI, E., GARTWYL, F., RICKLIN, M., EXADAKTYLOS, A. K. & KRAHENBUHL, S. 2018. Psychoactive substances and violent offences: A retrospective analysis of presentations to an urban emergency department in Switzerland. *PLoS One*, 13, e0195234.
- LIDZ, C. W., MULVEY, E. P. & GARDNER, W. 1993. The accuracy of predictions of violence to others. *Jama*, 269, 1007-1011.
- LINCOLN, T. M. & HODGINS, S. 2008. Is Lack of Insight Associated With Physically Aggressive Behavior Among People With Schizophrenia Living in the Community? *The Journal of Nervous and Mental Disease*, 196.
- LINDQVIST, P. & ALLEBECK, P. 1990. Schizophrenia and assaultive behaviour: the role of alcohol and drug abuse. *Acta Psychiatr Scand*, 82, 191-5.
- LIPSKY, S., CAETANO, R., FIELD, C. A. & LARKIN, G. L. 2005. Psychosocial and substance-use risk factors for intimate partner violence. *Drug and Alcohol Dependence*, 78, 39-47.
- LOGAN, G. D., SCHACHAR, R. J. & TANNOCK, R. 1997. Impulsivity and Inhibitory Control. *Psychological Science*, 8, 60-64.
- LONG, J. & MONGAN, D. 2014. Alcohol consumption in ireland 2013.
- LOPEZ-GARCIA, P., ASHBY, S., PATEL, P., PIERCE, K. M., MEYER, M., ROSENTHAL, A., TITONE, M., CARTER, C. & NIENDAM, T. 2019. Clinical and neurodevelopmental correlates of aggression in early psychosis. *Schizophrenia Research*, 212, 171-176.
- LUETTGEN, J., CHRAPKO, W. E. & REDDON, J. R. 1998. Preventing violent re-offending in not criminally responsible patients. An evaluation of a continuity of treatment program. *Int J Law Psychiatry*, 21, 89-98.
- LUKASIEWICZ, M., GERARD, S., BESNARD, A., FALISSARD, B., PERRIN, E., SAPIN, H., TOHEN, M., REED, C. & AZORIN, J.-M. 2013. Young Mania Rating Scale: how to interpret the numbers? Determination of a severity threshold and of the minimal clinically significant difference in the EMBLEM cohort. *International Journal of Methods in Psychiatric Research*, 22, 46-58.
- MALLA, A. K., NORMAN, R. M. G. & WILLIAMSON, P. 1993. Stability of positive and negative symptoms in schizophrenia. *The Canadian Journal of Psychiatry*, 38, 617-621.
- MALONEY, E., DEGENHARDT, L., DARKE, S., MATTICK, R. P. & NELSON, E. 2007. Suicidal behaviour and associated risk factors among opioid-dependent individuals: a case-control study. *Addiction*, 102, 1933-1941.
- MANCINELLI, R., BINETTI, R. & CECCANTI, M. 2007. Woman, alcohol and environment: Emerging risks for health. *Neuroscience & Biobehavioral Reviews*, 31, 246-253.
- MANIGLIO, R. 2009. Severe mental illness and criminal victimization: a systematic review. *Acta Psychiatr Scand*, 119, 180-91.

- MANTHEY, J., SHIELD, K. D., RYLETT, M., HASAN, O. S. M., PROBST, C. & REHM, J. 2019. Global alcohol exposure between 1990 and 2017 and forecasts until 2030: a modelling study. *The Lancet*, 393, 2493-2502.
- MARKIEWICZ, I., PILSZYK, A. & KUDLAK, G. 2020. Psychological factors of aggressive behaviour in patients of forensic psychiatry wards with the diagnosis of schizophrenia. *International Journal of Law and Psychiatry*, 72, 101612.
- MARSHALL, C., DEIGHTON, S., CADENHEAD, K. S., CANNON, T. D., CORNBLATT, B. A., MCGLASHAN, T. H., PERKINS, D. O., SEIDMAN, L. J., TSUANG, M. T., WALKER, E. F., WOODS, S. W., BEARDEN, C. E., MATHALON, D. & ADDINGTON, J. 2016. The Violent Content in Attenuated Psychotic Symptoms. *Psychiatry Research*, 242, 61-66.
- MARSHALL, C., DENNY, E., CADENHEAD, K. S., CANNON, T. D., CORNBLATT, B. A., MCGLASHAN, T. H., PERKINS, D. O., SEIDMAN, L. J., TSUANG, M. T., WOODS, S. W., WALKER, E. & ADDINGTON, J. 2014. The content of attenuated psychotic symptoms in those at clinical high risk for psychosis. *Psychiatry Research*, 219, 506-512.
- MARTINOTTI, G., CINOSI, E., SANTACROCE, R., PAPANTI, D., PASQUINI, A., MANCINI, V., CORBO, M., FIORI, F., SARCHIONE, F., MARCHETTI, D., VERROCCHIO, M. C., DI GIANNANTONIO, M., TORRENS, M., SCHIFANO, F., MORLAN COARASA, M. J. & MERINO DEL VILLAR, C. 2017. Substance-related psychopathology and aggressiveness in a nightlife holiday resort: Results from a pilot study in a psychiatric inpatient unit in Ibiza. *Human Psychopharmacology: Clinical and Experimental*, 32, e2586.
- MCEVOY, J. P., APPERSON, L. J., APPELBAUM, P. S., ORTLIP, P., BRECOSKY, J., HAMMILL, K., GELLER, J. L. & ROTH, L. 1989. Insight in schizophrenia: its relationship to acute psychopathology. *Journal of Nervous and Mental Disease*.
- MCGINTY, E. E., CHOKSY, S. & WINTEMUTE, G. J. 2016. The Relationship Between Controlled Substances and Violence. *Epidemiologic Reviews*, mxv008.
- MCHUGH, M. C. 2005. Understanding gender and intimate partner abuse. *Sex Roles*, 52, 717-724.
- MCMAHON, E. M., KEELEY, H., CANNON, M., ARENSMAN, E., PERRY, I. J., CLARKE, M., CHAMBERS, D. & CORCORAN, P. 2014. The iceberg of suicide and self-harm in Irish adolescents: a population-based study. *Social Psychiatry and Psychiatric Epidemiology*, 49, 1929-1935.
- MCNIEL, D. E. & BINDER, R. L. 1995. Correlates of accuracy in the assessment of psychiatric inpatients' risk of violence. *The American Journal of Psychiatry*.
- MCNIEL, D. E., BINDER, R. L. & GREENFIELD, T. K. 1988. Predictors of violence in civilly committed acute psychiatric patients. *Am J Psychiatry*, 145, 965-70.
- MECHOULAM, R. & PARKER, L. A. 2013. The endocannabinoid system and the brain. *Annual review of psychology*, 64, 21-47.
- MICZEK, K. A., DEBOLD, J. F., HWA, L. S., NEWMAN, E. L. & DE ALMEIDA, R. M. M. 2015. Alcohol and violence: neuropeptidergic modulation of monoamine systems. *Annals of the New York Academy of Sciences*, 1349, 96-118.
- MICZEK, K. A., FISH, E. W., DE BOLD, J. F. & DE ALMEIDA, R. M. 2002. Social and neural determinants of aggressive behavior: pharmacotherapeutic targets at serotonin, dopamine and ?-aminobutyric acid systems. *Psychopharmacology*, 163, 434-458.
- MILLER, M. M. & POTTER-EFRON, R. T. 1990. Aggression and Violence Associated with Substance Abuse. *Journal of Chemical Dependency Treatment*, 3, 1-35.
- MILLER, N. S., GOLD, M. S. & MAHLER, J. C. 1991. Violent Behaviors Associated with Cocaine Use: Possible Pharmacological Mechanisms. *International Journal of the Addictions*, 26, 1077-1088.
- MILTON, J., AMIN, S., SINGH, S. P., HARRISON, G., JONES, P., CROUDACE, T., MEDLEY, I. & BREWIN, J. 2001. Aggressive incidents in first-episode psychosis. *Br J Psychiatry*, 178, 433-40.
- MINAS, I., STUART, G. W., KLIMIDIS, S., JACKSON, H. J., SINGH, B. S. & COPOLOV, D. L. 1992. Positive and negative symptoms in the psychoses: multidimensional scaling of SAPS and SANS items. *Schizophrenia research*, 8, 143-156.
- MIYATA, J. 2019. Toward integrated understanding of salience in psychosis. *Neurobiology of Disease*, 131, 104414.

- MLADA, K., FORMANEK, T., VEVERA, J., LATALOVA, K., WINKLER, P. & VOLAVKA, J. 2021. Serious physical assault and subsequent risk for rehospitalization in individuals with severe mental illness: a nationwide, register-based retrospective cohort study. *Annals of General Psychiatry*, 20.
- MODESTIN, J. & AMMANN, R. 1996. Mental disorder and criminality: male schizophrenia. *Schizophr Bull*, 22, 69-82.
- MOELLER, H.-J. 2009. Standardised rating scales in Psychiatry: Methodological basis, their possibilities and limitations and descriptions of important rating scales. *The world journal of biological psychiatry*, 10, 6-26.
- MOJTABAI, R. 2006. Psychotic-like experiences and interpersonal violence in the general population. *Social Psychiatry and Psychiatric Epidemiology*, 41, 183-190.
- MONAHAN, J. 1981. *Predicting violent behavior: An assessment of clinical techniques*, Sage Publications Beverly Hills, CA.
- MONAHAN, J. 1992. Mental disorder and violent behavior. Perceptions and evidence. *Am Psychol*, 47, 511-21.
- MONAHAN, J., BONNIE, R. J., APPELBAUM, P. S., HYDE, P. S., STEADMAN, H. J. & SWARTZ, M. S. 2001. Mandated community treatment: beyond outpatient commitment. *Psychiatr Serv*, 52, 1198-205.
- MONAHAN, J. & STEADMAN, H. J. 1996. Violence and mental disorder: Developments in risk assessment.
- MONAHAN, J., VESSELINOV, R., ROBBINS, P. C. & APPELBAUM, P. S. 2017. Violence to Others, Violent Self-Victimization, and Violent Victimization by Others Among Persons With a Mental Illness. *Psychiatric Services*, 68, 516-519.
- MONGAN, D. 2016. Overview of alcohol consumption, alcohol-related harm and alcohol policy in Ireland. *Drugnet Ireland*, 1-3.
- MOORE, T. J., GLENMULLEN, J. & FURBERG, C. D. 2010. Prescription Drugs Associated with Reports of Violence Towards Others. *PLoS ONE*, 5, e15337.
- MOORE, T. M. & STUART, G. L. 2005. A review of the literature on marijuana and interpersonal violence. *Aggression and Violent Behavior*, 10, 171-192.
- MORE, N. D. 2010. Spiritualizing Violence: Sport, Philosophy and Culture in Nietzsche's View of the Ancient Greeks. *International Journal of Sport and Society*, 1.
- MORGAN, M. Y. 2015. Acute alcohol toxicity and withdrawal in the emergency room and medical admissions unit. *Clinical Medicine*, 15, 486-489.
- MULLEN, P. E., BURGESS, P., WALLACE, C., PALMER, S. & RUSCHENA, D. 2000. Community care and criminal offending in schizophrenia. *Lancet*, 355, 614-7.
- MURRAY, R. M., PAPARELLI, A., MORRISON, P. D., MARCONI, A. & DI FORTI, M. 2013. What can we learn about schizophrenia from studying the human model, drug-induced psychosis? *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, 162, 661-670.
- NATIONAL SURVEY ON DRUG USE AND HEALTH 2010. Center for Behavioral Health Statistics and Quality. National Survey on Drug Use and Health, 2010. ICPSR32722-v1.
- NATIONS, U. 2019. World Drug Report; United Nations Vienna, Austria The United Nations Office on Drugs and Crime (UNODC).
- NEDERLOF, A. F., MURIS, P. & HOVENS, J. E. 2013. The epidemiology of violent behavior in patients with a psychotic disorder: A systematic review of studies since 1980. *Aggression and Violent Behavior*, 18, 183-189.
- NEWHILL, C. E., MULVEY, E. P. & LIDZ, C. W. 1995. Characteristics of violence in the community by female patients seen in a psychiatric emergency service. *Psychiatric Services*.
- NIELSSEN, O. & LARGE, M. 2010. Rates of Homicide During the First Episode of Psychosis and After Treatment: A Systematic Review and Meta-analysis. *Schizophrenia Bulletin*, 36, 702-712.
- NIJMAN, H. L. I., MURIS, P., MERCKELBACH, H. L. G. J., PALMSTIERNA, T., WISTEDT, B., VOS, A. M., VAN RIXTEL, A. & ALLERTZ, W. 1999. The staff observation aggression scale-revised (SOAS-R). *Aggressive Behavior: Official Journal of the International Society for Research on Aggression*, 25, 197-209.

- NIKATHIL, S., OLAUSSEN, A., GOCENTAS, R. A., SYMONS, E. & MITRA, B. 2017. Review article: Workplace violence in the emergency department: A systematic review and meta analysis. *Emergency Medicine Australasia*, 29, 265-275.
- NOLAN, K. A., CZOBOR, P., ROY, B. B., PLATT, M. M., SHOPE, C. B., CITROME, L. L. & VOLAVKA, J. 2003. Characteristics of Assaultive Behavior Among Psychiatric Inpatients. *Psychiatric Services*, 54, 1012-1016.
- NORSTRÖM, T. & PAPE, H. 2010. Alcohol, suppressed anger and violence. *Addiction*, 105, 1580-1586.
- NTOUNAS, P., KATSOULI, A., EFSTATHIOU, V., PAPPAS, D., CHATZIMANOLIS, P., TOULOUMIS, C., PAPAGEORGIOU, C. & DOUZENIS, A. 2018. Comparative study of aggression – Dangerousness on patients with paranoid schizophrenia: Focus on demographic data, PANSS, drug use and aggressiveness. *International Journal of Law and Psychiatry*, 60, 1-11.
- O'DWYER, C., MONGAN, D., MILLAR, S. R., RACKARD, M., GALVIN, B., LONG, J. & BARRY, J. 2019. Drinking patterns and the distribution of alcohol-related harms in Ireland: evidence for the prevention paradox. *BMC Public Health*, 19.
- OECD ONLINE DATABASE, A. C. 2022. OECD (2022), Alcohol consumption (indicator). Organisations for Economic Co-operation and Development.
- OGLOFF, J. R. P. & DAFFERN, M. 2006. The dynamic appraisal of situational aggression: an instrument to assess risk for imminent aggression in psychiatric inpatients. *Behavioral Sciences & the Law*, 24, 799-813.
- ORGANISATION, W. H. 2018. Global Status Report on Alcohol and Health 2018. Geneva, Switzerland World Health Organisation
- ORGANIZATION, W. H. 2019. WHO Global Report on Trends in Prevalence of Tobacco Use 2000 - 2025. Geneva, Switzerland World Health Organisation
- OSGOOD, D. W., JOHNSTON, L. D., O'MALLEY, P. M. & BACHMAN, J. G. 1988. The Generality of Deviance in Late Adolescence and Early Adulthood. *American Sociological Review*, 53, 81.
- OSTROWSKY, M. K. 2011. Does marijuana use lead to aggression and violent behavior? *J Drug Educ*, 41, 369-89.
- OUELLET-PLAMONDON, C., ABDEL-BAKI, A., SALVAT, E. & POTVIN, S. 2017. Specific impact of stimulant, alcohol and cannabis use disorders on first-episode psychosis: 2-year functional and symptomatic outcomes. *Psychol Med*, 47, 2461-2471.
- OYEFESO, A., GHODSE, H., CLANCY, C. & CORKEFY, J. M. 1999. Suicide among drug addicts in the UK. *British Journal of Psychiatry*, 175, 277-282.
- PAGLIA, A. & ROOM, R. 1998. Alcohol and aggression: General population views about causation and responsibility. *Journal of Substance Abuse*, 10, 199-216.
- PAPANTI, D., SCHIFANO, F., BOTTEON, G., BERTOSSI, F., MANNIX, J., VIDONI, D., IMPAGNATIELLO, M., PASCOLO-FABRICI, E. & BONAVIGO, T. 2013. "Spicephrenia": a systematic overview of "Spice"-related psychopathological issues and a case report. *Human Psychopharmacology: Clinical and Experimental*, 28, 379-389.
- PARROTT, A. C. 2002. Recreational Ecstasy/MDMA, the serotonin syndrome, and serotonergic neurotoxicity. *Pharmacology Biochemistry and Behavior*, 71, 837-844.
- PAYNE, J., MALLA, A., NORMAN, R., WINDELL, D. & BROWN, N. 2006. Status of First-Episode Psychosis Patients Presenting for Routine Care in a Defined Catchment Area. *The Canadian Journal of Psychiatry*, 51, 42-47.
- PEDERSEN, W. & SKARDHAMAR, T. 2010. Cannabis and crime: findings from a longitudinal study. *Addiction*, 105, 109-18.
- PESCOSOLIDO, B. A., MANAGO, B. & MONAHAN, J. 2019. Evolving Public Views On The Likelihood Of Violence From People With Mental Illness: Stigma And Its Consequences. *Health Aff (Millwood)*, 38, 1735-1743.
- PESCOSOLIDO, B. A., MARTIN, J. K., LONG, J. S., MEDINA, T. R., PHELAN, J. C. & LINK, B. G. 2010. "A Disease Like Any Other"? A Decade of Change in Public Reactions to Schizophrenia, Depression, and Alcohol Dependence. *American Journal of Psychiatry*, 167, 1321-1330.
- POPOVICI, I., HOMER, J. F., FANG, H. & FRENCH, M. T. 2012. Alcohol use and crime: findings from a longitudinal sample of U.S. adolescents and young adults. *Alcohol Clin Exp Res*, 36, 532-43.

- PRESTON, N. J., ORR, K. G., DATE, R., NOLAN, L. & CASTLE, D. J. 2002. Gender differences in premorbid adjustment of patients with first episode psychosis. *Schizophrenia research*, 55, 285-290.
- PUTKONEN, H., KOMULAINEN, E., VIRKKUNEN, M. & LONNQVIST, J. 2001. Female homicide offenders have greatly increased mortality from unnatural deaths. *Forensic Sci Int*, 119, 221-4.
- RABANY, L., WEISER, M., WERBELOFF, N. & LEVKOVITZ, Y. 2011. Assessment of negative symptoms and depression in schizophrenia: Revision of the SANS and how it relates to the PANSS and CDSS. *Schizophrenia Research*, 126, 226-230.
- RAJA, M. & AZZONI, A. 2005. Hostility and violence of acute psychiatric inpatients. *Clin Pract Epidemiol Ment Health*, 1, 11.
- REAGU, S., JONES, R., KUMARI, V. & TAYLOR, P. J. 2013. Angry affect and violence in the context of a psychotic illness: A systematic review and meta-analysis of the literature. *Schizophrenia Research*, 146, 46-52.
- REGIER, D. A. 1990. Comorbidity of Mental Disorders With Alcohol and Other Drug Abuse. *JAMA*, 264, 2511.
- REISS JR, A. J. & ROTH, J. A. 1994. *Understanding and preventing violence, Vol. 4: Consequences and control*, National Academy Press.
- RESNICK, H. S., ACIERNO, R. & KILPATRICK, D. G. 1997. Health impact of interpersonal violence 2: Medical and mental health outcomes. *Behavioral medicine*, 23, 65-78.
- RIPPON, T. J. 2000. Aggression and violence in health care professions. *Journal of advanced nursing*, 31, 452-460.
- ROBERTS, L., FORD, L., PATEL, N., VALE, J. A. & BRADBERRY, S. M. 2017. 11 analytically confirmed cases of mephedrone use among polydrug users. *Clinical Toxicology*, 55, 181-186.
- ROGERS, R., GILLIS, J. R., TURNER, R. E. & FRISE-SMITH, T. 1990. The clinical presentation of command hallucinations in a forensic population. *The American journal of psychiatry*.
- ROSENBERG, S. D., LU, W., MUESER, K. T., JANKOWSKI, M. K. & COURNOIS, F. 2007. Correlates of adverse childhood events among adults with schizophrenia spectrum disorders. *Psychiatr Serv*, 58, 245-53.
- ROUVE, N., BAGHERI, H., TELMON, N., PATHAK, A., FRANCHITTO, N., SCHMITT, L., ROUGÉ, D., LAPEYRE-MESTRE, M. & MONTASTRUC, J.-L. 2011. Prescribed drugs and violence: a case/noncase study in the French Pharmacovigilance Database. *European Journal of Clinical Pharmacology*, 67, 1189-1198.
- ROY, M.-A., MAZIADÉ, M., LABBÉ, A. & MÉRETTE, C. 2001. Male gender is associated with deficit schizophrenia: a meta-analysis. *Schizophrenia research*, 47, 141-147.
- RUBIO, G., MARÍN-LOZANO, J., FERRE, F., MARTÍNEZ-GRAS, I., RODRIGUEZ-JIMENEZ, R., SANZ, J., JIMENEZ-ARRIERO, M. A., CARRASCO, J. L., LORA, D., JURADO, R., LÓPEZ-TRABADA, J. R. & PALOMO, T. 2012. Psychopathologic differences between cannabis-induced psychoses and recent-onset primary psychoses with abuse of cannabis. *Comprehensive Psychiatry*, 53, 1063-1070.
- RUEVE, M. E. & WELTON, R. S. 2008. Violence and mental illness. *Psychiatry (Edgmont)*, 5, 34-48.
- SADDICHHA, S., SUR, S., SINHA, B. N. P. & KHESS, C. R. J. 2010. How Is Substance Use Linked to Psychosis? A Study of the Course and Patterns of Substance Dependence in Psychosis. *Substance Abuse*, 31, 58-67.
- SALAGER-MEYER, F. 2008. Scientific publishing in developing countries: Challenges for the future. *Journal of English for Academic Purposes*, 7, 121-132.
- SARA, G. E., BURGESS, P. M., MALHI, G. S., WHITEFORD, H. A. & HALL, W. C. 2014. Cannabis and stimulant disorders and readmission 2 years after first-episode psychosis. *Br J Psychiatry*, 204, 448-53.
- SAXON, L., BORG, S. & HILTUNEN, A. J. 2010. Reduction of aggression during benzodiazepine withdrawal: Effects of flumazenil. *Pharmacology Biochemistry and Behavior*, 96, 148-151.
- SBORDONE, R. J., WINGARD, J. A., GORELICK, D. A. & ELLIOTT, M. L. 1979. Severe aggression in rats induced by mescaline but not other hallucinogens. *Psychopharmacology*, 66, 275-280.

- SCHANDA, H., STOMPE, T. & ORTWEIN-SWOBODA, G. 2010. [Increasing criminality in patients with schizophrenia: fiction, logical consequence or avoidable side effect of the mental health reforms?]. *Neuropsychiatr*, 24, 170-81.
- SCHIFANO, F. 2017. Symptoms of Drug Abuse in the Workplace. *Addiction at Work: Tackling Drug Use and Misuse in the Workplace*.
- SCHIFANO, F., ALBANESE, A., FERGUS, S., STAIR, J. L., DELUCA, P., CORAZZA, O., DAVEY, Z., CORKERY, J., SIEMANN, H., SCHERBAUM, N., FARRE, M., TORRENS, M., DEMETROVICS, Z. & GHODSE, A. H. 2011. Mephedrone (4-methylmethcathinone; 'meow meow'): chemical, pharmacological and clinical issues. *Psychopharmacology (Berl)*, 214, 593-602.
- SCHIFANO, F., CHIAPPINI, S., CORKERY, J. M. & GUIRGUIS, A. 2019. Assessing the 2004–2018 Fentanyl Misusing Issues Reported to an International Range of Adverse Reporting Systems. *Frontiers in Pharmacology*, 10.
- SCHIFANO, F., PAPANTI, G. D., ORSOLINI, L. & CORKERY, J. M. 2016. Novel psychoactive substances: the pharmacology of stimulants and hallucinogens. *Expert Review of Clinical Pharmacology*, 9, 943-954.
- SCHIFANO, F., ZANGANI, C., CHIAPPINI, S., GUIRGUIS, A., BONACCORSO, S. & CORKERY, J. M. 2020. Substance-Use Disorders and Violence. Springer International Publishing.
- SCHIMMELMANN, B. G., CONUS, P., COTTON, S. M., KUPFERSCHMID, S., KAROW, A., SCHULTZE-LUTTER, F., MCGORRY, P. D. & LAMBERT, M. 2011. Cannabis use disorder and age at onset of psychosis--a study in first-episode patients. *Schizophr Res*, 129, 52-6.
- SCHOELER, T., PETROS, N., DI FORTI, M., PINGAULT, J. B., KLAMERUS, E., FOGLIA, E., SMALL, A., MURRAY, R. & BHATTACHARYYA, S. 2016. Association Between Continued Cannabis Use and Risk of Relapse in First-Episode Psychosis: A Quasi-Experimental Investigation Within an Observational Study. *JAMA Psychiatry*, 73, 1173-1179.
- SCOTT, H., JOHNSON, S., MENEZES, P., BINDMAN, J., THORNICROFT, G., MARSHALL, J., BEBBINGTON, P. & KUIPERS, E. 1998. Substance misuse and risk of aggression and offending among the severely mentally ill. *British Journal of Psychiatry*, 172, 345-350.
- SEEDAT, S., SCOTT, K. M., ANGERMEYER, M. C., BERGLUND, P., BROMET, E. J., BRUGHA, T. S., DEMYTTENAERE, K., DE GIROLAMO, G., HARO, J. M., JIN, R., KARAM, E. G., KOVESS-MASFETY, V., LEVINSON, D., MEDINA MORA, M. E., ONO, Y., ORMEL, J., PENNELL, B.-E., POSADA-VILLA, J., SAMPSON, N. A., WILLIAMS, D. & KESSLER, R. C. 2009. Cross-National Associations Between Gender and Mental Disorders in the World Health Organization World Mental Health Surveys. *Archives of General Psychiatry*, 66, 785.
- SEVY, S., ROBINSON, D. G., HOLLOWAY, S., ALVIR, J. M., WOERNER, M. G., BILDER, R., GOLDMAN, R., LIEBERMAN, J. & KANE, J. 2001. Correlates of substance misuse in patients with first-episode schizophrenia and schizoaffective disorder. *Acta Psychiatr Scand*, 104, 367-74.
- SHAFI, A., GALLAGHER, P., STEWART, N., MARTINOTTI, G. & CORAZZA, O. 2017. The risk of violence associated with novel psychoactive substance misuse in patients presenting to acute mental health services. *Human Psychopharmacology: Clinical & Experimental*, 32, n/a-N.PAG.
- SHORE, D., ANDERSON, D. J. & CUTLER, N. R. 1978. Prediction of self-mutilation in hospitalized schizophrenics. *The American journal of psychiatry*.
- SIEVER, L. J. 2008. Neurobiology of aggression and violence. *American journal of psychiatry*, 165, 429-442.
- SIMONSEN, E., FRIIS, S., HAAHR, U., JOHANNESSEN, J. O., LARSEN, T. K., MELLE, I., OPJORDSMOEN, S., RUND, B. R., VAGLUM, P. & MCGLASHAN, T. 2007. Clinical epidemiologic first-episode psychosis: 1-year outcome and predictors. *Acta Psychiatrica Scandinavica*, 116, 54-61.
- SLADE, P. D. & COOPER, R. 1979. Some conceptual difficulties with the term 'schizophrenia' An alternative model. *British Journal of Social and Clinical Psychology*, 18, 309-317.
- SMITH, P. H., HOMISH, G. G., LEONARD, K. E. & COLLINS, R. L. 2013. Marijuana withdrawal and aggression among a representative sample of U.S. marijuana users. *Drug and Alcohol Dependence*, 132, 63-68.
- SMITH, P. H., HOMISH, G. G., LEONARD, K. E. & CORNELIUS, J. R. 2012. Intimate partner violence and specific substance use disorders: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychology of Addictive Behaviors*, 26, 236.

- SOLOWIJ, N. 1998. *Cannabis and cognitive functioning*, Cambridge University Press.
- SORGI, P., RATEY, J. J., KNOEDLER, D. W., MARKERT, R. J. & REICHMAN, M. 1991. Rating aggression in the clinical setting: A retrospective adaptation of the Overt Aggression Scale: Preliminary results. *The Journal of neuropsychiatry and clinical neurosciences*.
- SOYKA, M. 1994. Substance abuse and dependency as a risk factor for delinquency and violent behaviour in schizophrenic patients--how strong is the evidence? *J Clin Forensic Med*, 1, 3-7.
- SOYKA, M., GRAZ, C., BOTTLENDER, R., DIRSCHEDL, P. & SCHOECH, H. 2007. Clinical correlates of later violence and criminal offences in schizophrenia. *Schizophr Res*, 94, 89-98.
- SPIDEL, A., LECOMTE, T., GREAVES, C., SAHLSTROM, K. & YUILLE, J. C. 2010. Early psychosis and aggression: Predictors and prevalence of violent behaviour amongst individuals with early onset psychosis. *International Journal of Law and Psychiatry*, 33, 171-176.
- SPITZER, R. L. 1992. The Structured Clinical Interview for DSM-III-R (SCID). *Archives of General Psychiatry*, 49, 624.
- SPRINGER, K. W., MAGER STELLMAN, J. & JORDAN-YOUNG, R. M. 2012. Beyond a catalogue of differences: A theoretical frame and good practice guidelines for researching sex/gender in human health. *Social Science & Medicine*, 74, 1817-1824.
- STANFORD, M., HOUSTON, R., MATHIAS, C., VILLEMARETTE-PITTMAN, N., HELFRITZ, L. & CONKLIN, S. 2003. Characterizing Aggressive Behavior. *Assessment*, 10, 183-90.
- STEADMAN, H. J., MULVEY, E. P., MONAHAN, J., ROBBINS, P. C., APPELBAUM, P. S., GRISSO, T., ROTH, L. H. & SILVER, E. 1998. Violence by People Discharged From Acute Psychiatric Inpatient Facilities and by Others in the Same Neighborhoods. *Archives of General Psychiatry*, 55, 393.
- STEELE, J. L. & PERALTA, R. L. 2020. Are Polydrug Users More Physically and Verbally Aggressive? An Assessment of Aggression Among Mono- Versus Polydrug Users in a University Sample. *Journal of Interpersonal Violence*, 35, 4444-4467.
- STEINERT, T., WIEBE, C. & GEBHARDT, R. P. 1999. Aggressive behavior against self and others among first-admission patients with schizophrenia. *Psychiatr Serv*, 50, 85-90.
- STEVENSON, A. 2010. *Oxford dictionary of English*, Oxford University Press, USA.
- STONE, J. M., FISHER, H. L., MAJOR, B., CHISHOLM, B., WOOLLEY, J., LAWRENCE, J., RAHAMAN, N., JOYCE, J., HINTON, M., JOHNSON, S., YOUNG, A. H. & MIDATA, C. 2014. Cannabis use and first-episode psychosis: relationship with manic and psychotic symptoms, and with age at presentation. *Psychol Med*, 44, 499-506.
- STUART, H. 2003. Violence and mental illness: an overview. *World Psychiatry*, 2, 121.
- SUBSTANCE, A. & MENTAL HEALTH SERVICES, A. 2013. Drug Abuse Warning Network, 2011: national estimates of drug-related emergency department visits. Substance Abuse and Mental Health Services Administration Rockville, MD.
- SWANSON, J., SWARTZ, M., ESTROFF, S., BORUM, R., WAGNER, R. & HIDAY, V. 1998. Psychiatric impairment, social contact, and violent behavior: evidence from a study of outpatient-committed persons with severe mental disorder. *Social Psychiatry and Psychiatric Epidemiology*, 33, S86-S94.
- SWANSON, J. W., BORUM, R., SWARTZ, M. S. & MONAHAN, J. 1996. Psychotic symptoms and disorders and the risk of violent behaviour in the community. *Criminal Behaviour and Mental Health*, 6, 309-329.
- SWANSON, J. W., HOLZER, C. E., 3RD, GANJU, V. K. & JONO, R. T. 1990. Violence and psychiatric disorder in the community: evidence from the Epidemiologic Catchment Area surveys. *Hosp Community Psychiatry*, 41, 761-70.
- SWANSON, J. W., SWARTZ, M. S., VAN DORN, R. A., ELBOGEN, E. B., WAGNER, H. R., ROSENHECK, R. A., STROUP, T. S., MCEVOY, J. P. & LIEBERMAN, J. A. 2006a. A National Study of Violent Behavior in Persons With Schizophrenia. *Archives of General Psychiatry*, 63, 490.
- SWANSON, J. W., VAN DORN, R. A., MONAHAN, J. & SWARTZ, M. S. 2006b. Violence and Leveraged Community Treatment for Persons With Mental Disorders. *American Journal of Psychiatry*, 163, 1404-1411.
- SWARTZ, M. S., WAGNER, H. R., SWANSON, J. W., STROUP, T. S., MCEVOY, J. P., CANIVE, J. M., MILLER, D. D., REIMHERR, F., MCGEE, M., KHAN, A., VAN DORN, R., ROSENHECK, R. A. &

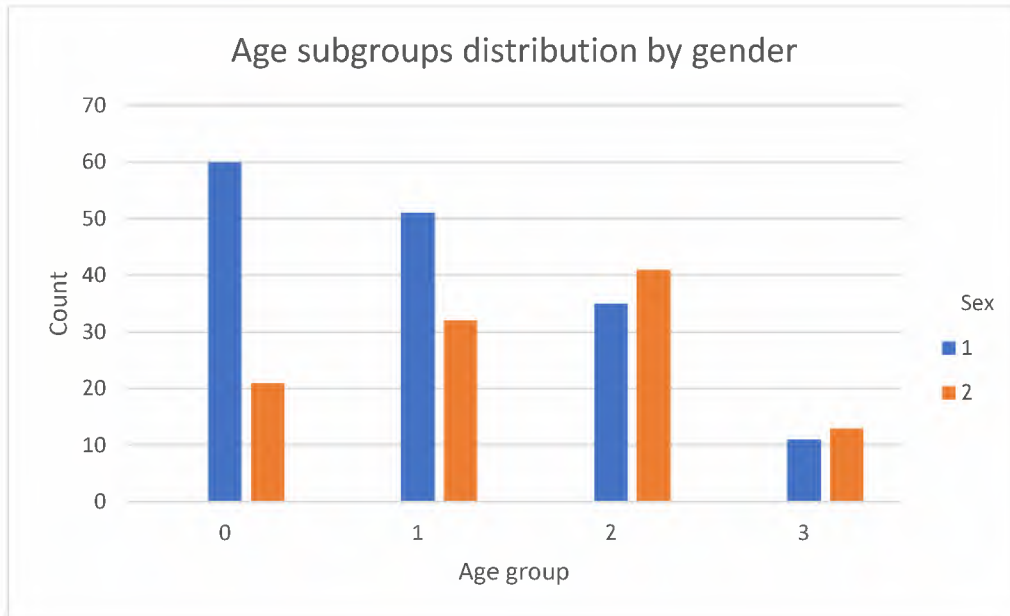
- LIEBERMAN, J. A. 2006. Substance Use in Persons With Schizophrenia: Baseline Prevalence and Correlates From the NIMH CATIE Study. *The Journal of Nervous and Mental Disease*, 194.
- TAE, C. H., KANG, K. J., MIN, B.-H., AHN, J. H., KIM, S., LEE, J. H., RHEE, P.-L. & KIM, J. J. 2014. Paradoxical reaction to midazolam in patients undergoing endoscopy under sedation: Incidence, risk factors and the effect of flumazenil. *Digestive and Liver Disease*, 46, 710-715.
- TAKACS, R., UNGVARI, G. S. & GAZDAG, G. 2015. Reasons for acute psychiatric admission of patients with dementia. *Neuropsychopharmacol Hung*, 17, 141-5.
- TANDON, R. 2014. Schizophrenia and Other Psychotic Disorders in Diagnostic and Statistical Manual of Mental Disorders (DSM)-5: Clinical Implications of Revisions from DSM-IV. *Indian journal of psychological medicine*, 36, 223-225.
- TAYLOR, P. J. 1985. Motives for Offending among Violent and Psychotic Men. *British Journal of Psychiatry*, 147, 491-498.
- TAYLOR, P. J. 2008. Psychosis and Violence: Stories, Fears, and Reality. *The Canadian Journal of Psychiatry*, 53, 647-659.
- TAYLOR, P. J. & GUNN, J. 1984. Violence and psychosis. I. Risk of violence among psychotic men. *Br Med J (Clin Res Ed)*, 288, 1945-9.
- TAYLOR, P. J. & GUNN, J. 1999. Homicides by people with mental illness: myth and reality. *British Journal of Psychiatry*, 174, 9-14.
- TAYLOR, P. J., LEESE, M., WILLIAMS, D., BUTWELL, M., DALY, R. & LARKIN, E. 1998. Mental disorder and violence: a special (high security) hospital study. *The British Journal of Psychiatry*, 172, 218-226.
- TAYLOR, S. P. & HULSIZER, M. R. 1998. 6 - Psychoactive Drugs and Human Aggression  
Correspondence concerning this chapter should be addressed to Stuart P. Taylor, Department of Psychology, Kent State University, Kent, OH 44242, or to Michael R. Hulsizer, who is now at the Department of Behavioral and Social Sciences, Webster University, St. Louis, MO 63119. In: GEEN, R. G. & DONNERSTEIN, E. (eds.) *Human Aggression*. San Diego: Academic Press.
- TENNEIJ, N. H., DIDDEN, R., STOLKER, J. J. & KOOT, H. M. 2009. Markers for aggression in inpatient treatment facilities for adults with mild to borderline intellectual disability. *Research in Developmental Disabilities*, 30, 1248-1257.
- TEPLIN, L. A. 1990. The prevalence of severe mental disorder among male urban jail detainees: comparison with the Epidemiologic Catchment Area Program. *Am J Public Health*, 80, 663-9.
- TETEN, A. L., SCHUMACHER, J. A., BAILEY, S. D. & KENT, T. A. 2009. Male-to-female sexual aggression among Iraq, Afghanistan, and Vietnam veterans: Co-occurring substance abuse and intimate partner aggression. *Journal of Traumatic Stress*, 22, 307-311.
- TOBORE, T. O. 2019. On the Neurobiological Role of Oxidative Stress in Alcohol-Induced Impulsive, Aggressive and Suicidal Behavior. *Substance Use & Misuse*, 54, 2290-2303.
- TOMLINSON, M. F., BROWN, M. & HOAKEN, P. N. S. 2016. Recreational drug use and human aggressive behavior: A comprehensive review since 2003. *Aggression and Violent Behavior*, 27, 9-29.
- TORREY, E. F. 2011. The Association of Stigma With Violence. *American Journal of Psychiatry*, 168, 325-325.
- TOSATO, S., LASALVIA, A., BONETTO, C., MAZZONCINI, R., CRISTOFALO, D., DE SANTI, K., BERTANI, M., BISSOLI, S., LAZZAROTTO, L., MARRELLA, G., LAMONACA, D., RIOLO, R., GARDELLIN, F., URBANI, A., TANSELLA, M., RUGGERI, M. & GROUP, P.-V. 2013. The impact of cannabis use on age of onset and clinical characteristics in first-episode psychotic patients. Data from the Psychosis Incident Cohort Outcome Study (PICOS). *J Psychiatr Res*, 47, 438-44.
- ULLRICH, S., KEERS, R. & COID, J. W. 2014. Delusions, Anger, and Serious Violence: New Findings From the MacArthur Violence Risk Assessment Study. *Schizophrenia Bulletin*, 40, 1174-1181.
- VAN DONGEN, J. D. M., BUCK, N. M. L., BARENDREGT, M., VAN BEVEREN, N. M., DE BEURS, E. & VAN MARLE, H. J. C. 2015. Anti-social personality characteristics and psychotic symptoms: Two pathways associated with offending in schizophrenia. *Criminal Behaviour and Mental Health*, 25, 181-191.

- VAN DORN, R., VOLAVKA, J. & JOHNSON, N. 2012. Mental disorder and violence: is there a relationship beyond substance use? *Social Psychiatry and Psychiatric Epidemiology*, 47, 487-503.
- VARSHNEY, M., MAHAPATRA, A., KRISHNAN, V., GUPTA, R. & DEB, K. S. 2016. Violence and mental illness: what is the true story? *Journal of Epidemiology and Community Health*, 70, 223-225.
- VÁZQUEZ-BARQUERO, J. L., LASTRA, I., NUÑEZ, M. J. C., CASTANEDO, S. H. & DUNN, G. 1996. Patterns of Positive and Negative Symptoms in First Episode Schizophrenia. *British Journal of Psychiatry*, 168, 693-701.
- VERMA, S., POON, L. Y., SUBRAMANIAM, M. & CHONG, S.-A. 2005. Aggression in Asian Patients with First-Episode Psychosis. *International Journal of Social Psychiatry*, 51, 365-371.
- VOLAVKA, J. 2002. Neurobiology and violence - 2nd. ed. . 2nd ed.: American Psychiatric Publishing, Inc. .
- VOLAVKA, J. 2013. Violence in schizophrenia and bipolar disorder. *Psychiatr Danub*, 25, 24-33.
- VOLAVKA, J. & CITROME, L. 2008. Heterogeneity of violence in schizophrenia and implications for long-term treatment. *International Journal of Clinical Practice*, 62, 1237-1245.
- VOLAVKA, J. & CITROME, L. 2011. Pathways to Aggression in Schizophrenia Affect Results of Treatment. *Schizophrenia Bulletin*, 37, 921-929.
- VOLAVKA, J., LASKA, E., BAKER, S., MEISNER, M., CZOBOR, P. & KRIVELEVICH, I. 1997. History of violent behaviour and schizophrenia in different cultures. Analyses based on the WHO study on Determinants of Outcome of Severe Mental Disorders. *Br J Psychiatry*, 171, 9-14.
- VOLKOW, N. D., BALER, R. D., COMPTON, W. M. & WEISS, S. R. B. 2014. Adverse Health Effects of Marijuana Use. *New England Journal of Medicine*, 370, 2219-2227.
- WADE, D., HARRIGAN, S., EDWARDS, J., BURGESS, P. M., WHELAN, G. & MCGORRY, P. D. 2006. Substance misuse in first-episode psychosis: 15-month prospective follow-up study. *Br J Psychiatry*, 189, 229-34.
- WALKER, A., FLATLEY, J., KERSHAW, C. & MOON, D. 2009. Crime in England and Wales 2008/09, Findings from the British Crime Survey and police recorded crime, vol. 1, Home Office, UK.
- WALKER, Z. & SEIFERT, R. 1994. Violent incidents in a psychiatric intensive care unit. *Br J Psychiatry*, 164, 826-8.
- WALLACE, C., MULLEN, P., BURGESS, P., PALMER, S., RUSCHENA, D. & BROWNE, C. 1998. Serious criminal offending and mental disorder. Case linkage study. *Br J Psychiatry*, 172, 477-84.
- WALSH, E., BUCHANAN, A. & FAHY, T. 2002. Violence and schizophrenia: Examining the evidence. *British Journal of Psychiatry*, 180, 490-495.
- WALTON, M. A., EPSTEIN-NGO, Q., CARTER, P. M., ZIMMERMAN, M. A., BLOW, F. C., BUU, A., GOLDSTICK, J. & CUNNINGHAM, R. M. 2017. Marijuana use trajectories among drug-using youth presenting to an urban emergency department: Violence and social influences. *Drug and Alcohol Dependence*, 173, 117-125.
- WÄSTERFORS, D. 2022. *Violence: situation, speciality, politics and storytelling*, Abingdon, Oxon, Routledge.
- WEAVER, T., MADDEN, P., CHARLES, V., STIMSON, G., RENTON, A., TYRER, P., BARNES, T., BENCH, C., MIDDLETON, H., WRIGHT, N., PATERSON, S., SHANAHAN, W., SEIVEWRIGHT, N. & FORD, C. 2003. Comorbidity of substance misuse and mental illness in community mental health and substance misuse services. *British Journal of Psychiatry*, 183, 304-313.
- WEHRING, H. J. & CARPENTER, W. T. 2011. Violence and Schizophrenia. *Schizophrenia Bulletin*, 37, 877-878.
- WHITESIDE, S. P. & LYNAM, D. R. 2001. The Five Factor Model and impulsivity: using a structural model of personality to understand impulsivity. *Personality and Individual Differences*, 30, 669-689.
- WHITING, D., GULATI, G., GEDDES, J. R. & FAZEL, S. 2021. Association of Schizophrenia Spectrum Disorders and Violence Perpetration in Adults and Adolescents from 15 Countries. *JAMA Psychiatry*.
- WHITLOCK, J. 2010. Self-Injurious Behavior in Adolescents. *PLoS Medicine*, 7, e1000240.
- WHO 2004. The world health report 2004 - Changing history
- WHO 2014. Preventing suicide: a global imperative.

- WIECZOREK, W. F., WELTE, J. W. & ABEL, E. L. 1990. Alcohol, drugs and murder: A study of convicted homicide offenders. *Journal of Criminal Justice*, 18, 217-227.
- WILKOWSKI, B. M. & ROBINSON, M. D. 2008. The Cognitive Basis of Trait Anger and Reactive Aggression: An Integrative Analysis. *Personality and Social Psychology Review*, 12, 3-21.
- WILSON, W. H., BAN, T. A. & GUY, W. 1986. Flexible system criteria in chronic schizophrenia. *Comprehensive Psychiatry*, 27, 259-265.
- WINSPER, C., GANAPATHY, R., MARWAHA, S., LARGE, M., BIRCHWOOD, M. & SINGH, S. P. 2013. A systematic review and meta-regression analysis of aggression during the First Episode of Psychosis. *Acta Psychiatrica Scandinavica*, 128, 413-421.
- WISDOM, J. P. & MANUEL, J. I. 2011. Prevalence of Substance Use in People With First-Episode Psychosis. *J Dual Diagn*, 7, 39-49.
- WITT, K., VAN DORN, R. & FAZEL, S. 2013. Risk Factors for Violence in Psychosis: Systematic Review and Meta-Regression Analysis of 110 Studies. *PLoS ONE*, 8, e55942.
- WOLF, A., GRAY, R. & FAZEL, S. 2014. Violence as a public health problem: An ecological study of 169 countries. *Social Science & Medicine*, 104, 220-227.
- WOLKERS, C. P. B., SERRA, M., BARBOSA JÚNIOR, A. & URBINATI, E. C. 2017. Acute fluoxetine treatment increases aggressiveness in juvenile matrinxã (*Brycon amazonicus*). *Fish Physiology and Biochemistry*, 43, 755-759.
- WORLD HEALTH, O. 1973. *Report of the international pilot study of schizophrenia*, World Health Organization.
- WORLD HEALTH ORGANISATION, A. 1996. *Prevention of violence: public health priority*. Geneva: World Health Organization.
- YAMAUCHI, K., ONO, Y., BABA, K. & IKEGAMI, N. 2001. The actual process of rating the global assessment of functioning scale. *Comprehensive Psychiatry*, 42, 403-409.
- YEN, C.-F., YEH, M.-L., CHEN, C.-S. & CHUNG, H.-H. 2002. Predictive value of insight for suicide, violence, hospitalization, and social adjustment for outpatients with schizophrenia: A prospective study. *Comprehensive Psychiatry*, 43, 443-447.
- YESAVAGE, J. A. 1983. Bipolar Illness: Correlates of Dangerous Inpatient Behaviour. *British Journal of Psychiatry*, 143, 554-557.
- YOUNG, R. C., BIGGS, J. T., ZIEGLER, V. E. & MEYER, D. A. 1978. A Rating Scale for Mania: Reliability, Validity and Sensitivity. *British Journal of Psychiatry*, 133, 429-435.
- YU, R., TOPIWALA, A., JACOBY, R. & FAZEL, S. 2019. Aggressive Behaviors in Alzheimer Disease and Mild Cognitive Impairment: Systematic Review and Meta-Analysis. *The American Journal of Geriatric Psychiatry*, 27, 290-300.
- YUDOFKY, S. C., SILVER, J. M., JACKSON, W., ENDICOTT, J. & WILLIAMS, D. 1986. The Overt Aggression Scale for the objective rating of verbal and physical aggression. *Am J Psychiatry*, 143, 35-9.
- ZHOU, J.-S., ZHONG, B.-L., XIANG, Y.-T., CHEN, Q., CAO, X.-L., CORRELL, C. U., UNGVARI, G. S., CHIU, H. F. K., LAI, K. Y. C. & WANG, X.-P. 2016. Prevalence of aggression in hospitalized patients with schizophrenia in China: A meta-analysis. *Asia-Pacific Psychiatry*, 8, 60-69.
- ZISOOK, S., BYRD, D., KUCK, J. & JESTE, D. V. 1995. Command hallucinations in outpatients with schizophrenia. *The Journal of clinical psychiatry*.

## 8. Appendix

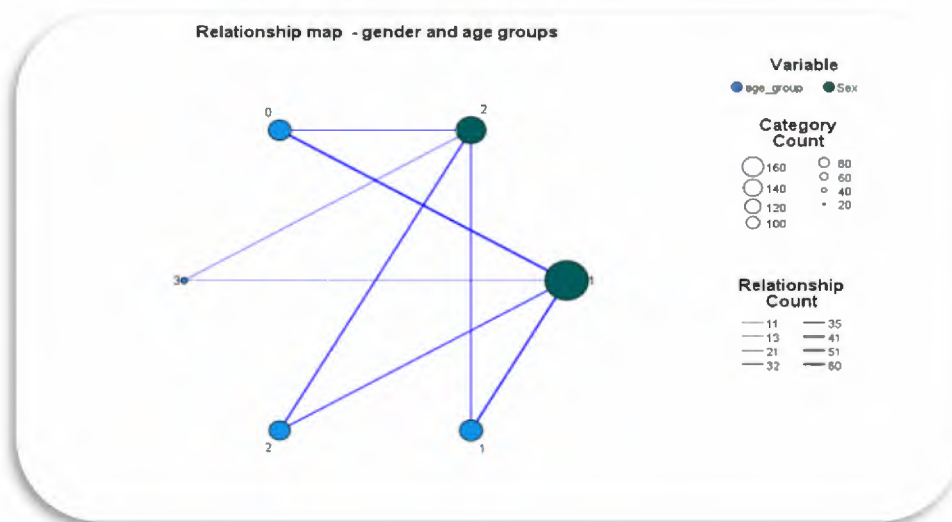
Graphic No: 1



### Legend

Age group 0 - 18 - 24 years, age group 1 - 25 - 34 years, age group, age group 2 - 35 - 49 years, age group 3 - over 50 Gender: Male -1, Female - 2

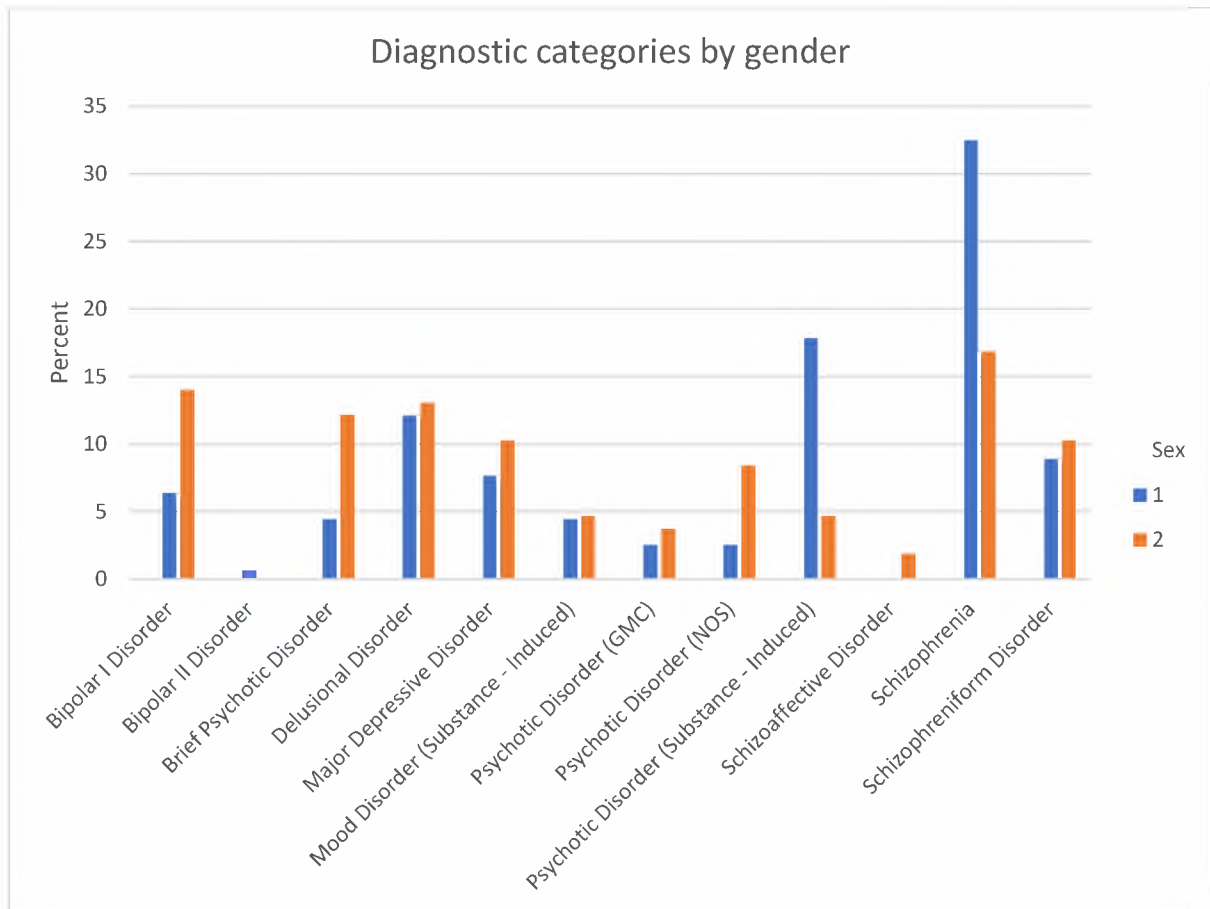
Graphic No: 2



### Legend

Age group 0 - 18 - 24 years, age group 1 - 25 - 34 years, age group, age group 2 - 35 - 49 years, age group 3 - over 50, Gender: Male -1, Female - 2

Graphic No: 3



Legend: Gender: Male -1, Female - 2

Table No: 1

Psychopathological correlations with gender

	Mean rank		Mann Whitney U	p
	males	females		
DUP	103.09	88.24	1740.500	0.074
GAF	128.16	131.45	7827.500	0.725
SANS	137.83	112.77	6227.000	0.008*
SAPS	123.82	136.74	7133.500	0.171
CDSS	130.88	122.54	7266.000	0.365
YMRS	55.75	55.42	1515.000	0.655
INSIGHT	96.98	95.73	4309.000	0.879

DUP [Duration of Untreated Psychosis] based on Beiser scale, GAF (Global Assessment of Functioning), SAPS (Scale for the Assessment of Positive Symptoms), SANS (Scale for the Assessment of Negative Symptoms), CDSS (Calgary Depression Scale for Schizophrenia), Young Mania Rating Scale (YMRS), Insight - Birchwood Questionnaire, \* = statistically significant

Table No: 2

Psychopathological correlations with age group under and over 35 years

	Mean rank		Mann Whitney U	p
	18-34	Over 35		
DUP	88.43	112.21	3351.500	0.004*
GAF	129.04	130.28	7701.500	0.897
SANS	134.25	117.65	6638.500	0.079
SAPS	137.17	115.30	6413.000	0.022
CDSS	123.22	134.55	6907.000	0.223
YMRS	56.51	57.79	1471.000	0.835
INSIGHT	100.55	89.28	3745.000	0.176

Table No: 3

Clinical correlations with lifetime illicit substance use

	Mean rank		Mann Whitney U	p
	Non-users	Users		
DUP	100.98	93.37	4279.500	0.343
GAF	120.37	126.63	7953.000	0.684
SANS	122.83	131.07	7478.500	0.366
SAPS	118.59	137.05	6948.500	0.045
CDSS	132.14	120.94	7232.000	0.213
YMRS	53.22	59.78	1384.500	0.268
INSIGHT			4126.500	0.310

Table No: 4

Psychopathological correlations with comorbid alcohol use disorder

	Mean rank		Mann Whitney U	p
	Non-users	Users		
DUP	94.65	99.09	3078.000	0.609
GAF	123.87	135.26	6378.000	0.245
SANS	122.84	132.87	6251.000	0.305
SAPS	127.73	125.41	6793.000	0.814
CDSS	120.38	137.01	5774.000	0.087
YMRS	54.94	60.39	1055.500	0.406
INSIGHT	89.26	105.95	3318.000	0.046

DUP [Duration of Untreated Psychosis] based on Beiser scale, GAF (Global Assessment of Functioning), SAPS (Scale for the Assessment of Positive Symptoms), SANS (Scale for the Assessment of Negative Symptoms), CDSS (Calgary Depression Scale for Schizophrenia), Young Mania Rating Scale (YMRS),

Table No: 5

Psychopathological correlations with past month's alcohol use

	Mean rank		Mann Whitney U	p
	Non-users	Users		
DUP	97.56	92.05	2703.000	0.587
GAF	129.76	121.28	4997.000	0.452
SANS	123.18	139.29	4535.000	0.152
SAPS	125.66	134.83	4802.500	0.424
CDSS	125.39	128.47	4901.500	0.784
YMRS	56.11	58.28	884.500	0.097
INSIGHT	91.48	107.33	2569.000	0.780

Table No: 6

Psychopathological correlations with using the substance after contact with services

	Mean rank		Mann Whitney U	p
	Non-users	Users		
DUP	99.76	99.15	3921.000	0.784
GAF	130.36	125.75	6631.000	0.647
SANS	124.19	135.12	6228.000	0.271
SAPS	126.48	133.29	6476.000	0.500
CDSS	128.11	126.10	6706.500	0.838
YMRS	57.99	54.48	1215.500	0.595
INSIGHT	94.62	99.17	3673.000	0.600

DUP [Duration of Untreated Psychosis] based on Beiser scale, GAF (Global Assessment of Functioning), SAPS (Scale for the Assessment of Positive Symptoms), SANS (Scale for the Assessment of Negative Symptoms), CDSS (Calgary Depression Scale for Schizophrenia), Young Mania Rating Scale (YMRS), Insight - Birchwood Questionnaire

Table No: 7

Psychopathological correlations with past month's cannabis use

	Mean rank		Mann Whitney U	p
	Non-users	Users		
DUP	102.02	85.6	3280.500	0.059
GAF	127.52	130.96	6500.000	0.735
SANS	127.99	124.55	6391.000	0.732
SAPS	122.47	141.78	5637.000	0.058
CDSS	129.33	119.7	6083.000	0.33
YMRS	53.33	64.09	1053.000	0.097
INSIGHT	96.54	103.37	3179.000	0.225

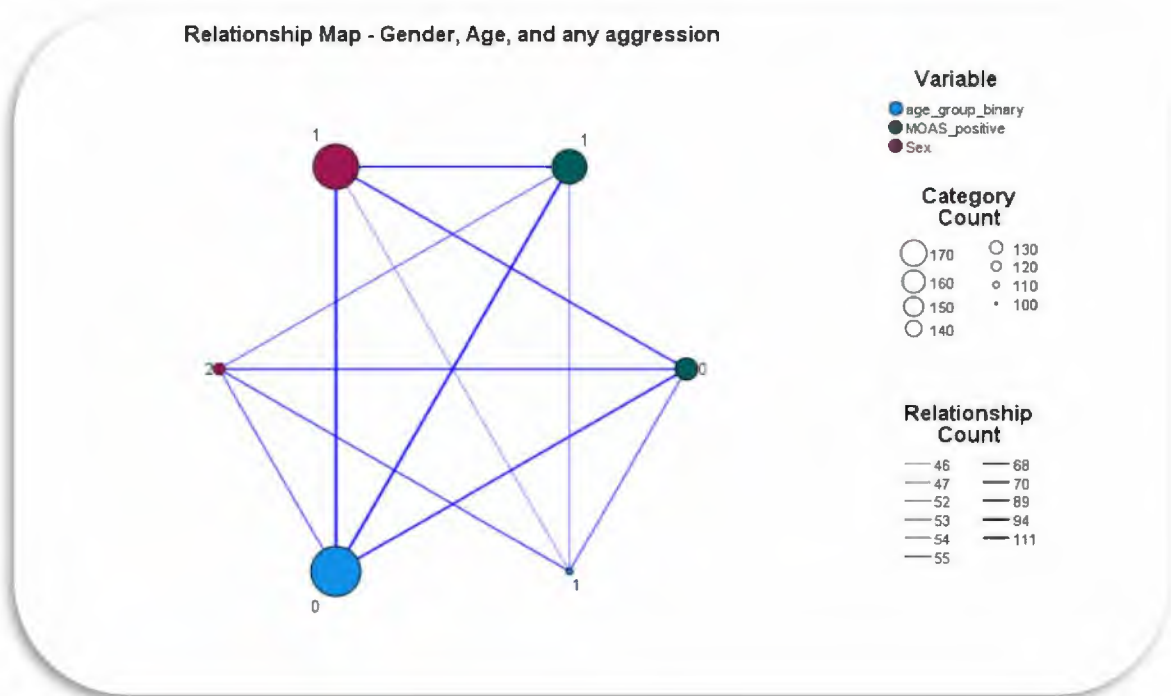
Table No: 8

Psychopathological correlations with the past month's stimulant use

	Mean rank		Mann Whitney U	p
	Non-users	Users		
DUP	96.75	91.44	778.000	0.779
GAF	126.73	149.79	1382.000	0.251
SANS	127.17	115.18	1507.500	0.546
SAPS	127.51	127.27	1789.000	0.99
CDSS	124.95	142.5	1522.500	0.354
YMRS	56.49	56.71	366.000	0.985
INSIGHT	93.85	113.68	773.500	0.242

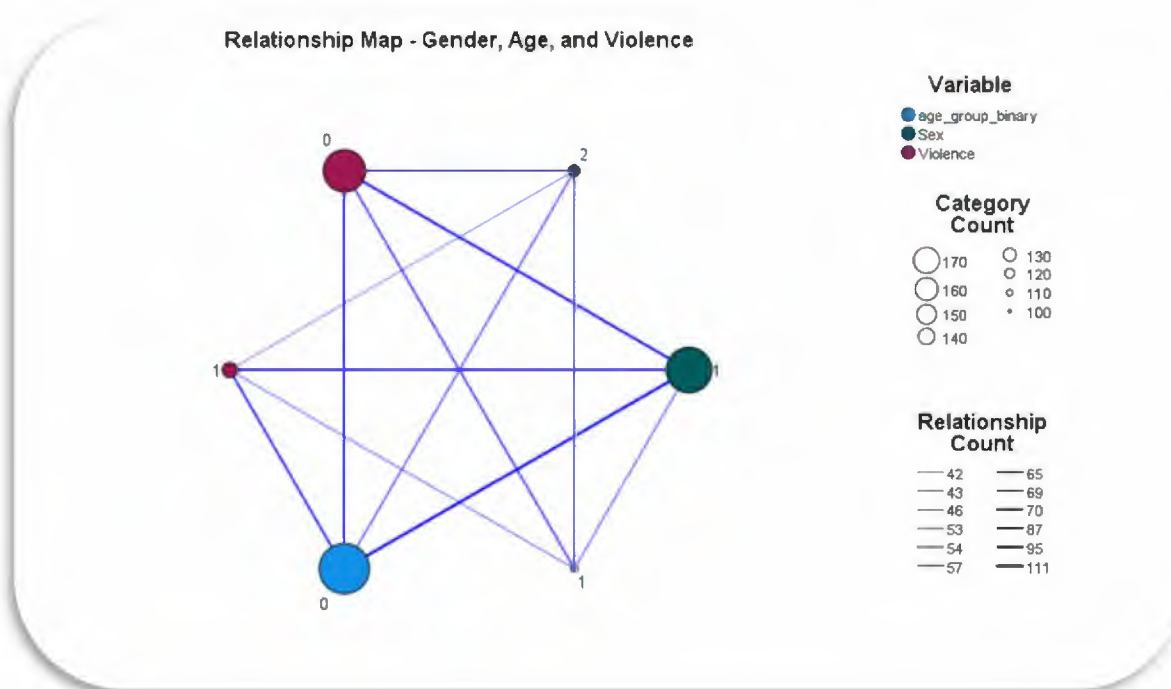
DUP [Duration of Untreated Psychosis] based on Beiser scale, GAF (Global Assessment of Functioning), SAPS (Scale for the Assessment of Positive Symptoms), SANS (Scale for the Assessment of Negative Symptoms), CDSS (Calgary Depression Scale for Schizophrenia), Young Mania Rating Scale (YMRS), Insight - Birchwood Questionnaire

Graphic No: 4



Legend: Age group 0 - under 35 year, Age group 1 - over 35; MOAS positive: 0 - no aggression, 1 - aggression; Sex: 1 - male, 2 - female

Graphic No: 5



Legend: Age group 0 - under 35 year, Age group 1 - over 35; Violence: 0 - not violent, 1 -Violent; Sex: 1 - male, 2 - female

Table No: 9

MOAS score correlations with gender

	Mean rank		Mann Whitney U	p
	Males	Females		
Verbal aggression pre-contact	134.19	127.48	7820.500	0.359
Verbal aggression post-contact	131.79	131.07	8197.500	0.914
Aggression against property pre-contact	132.77	129.60	8042.500	0.480
Aggression against property post-contact	135.36	125.73	7637.000	0.044
Self-aggression pre-contact	130.16	132.24	8059.500	0.727
Self-aggression post-contact	133.04	129.20	8001.000	0.346
Aggression against others pre-contact	131.18	131.98	8192.000	0.896
Aggression against others post-contact	133.62	128.33	7910.000	0.269

MOAS (Modified Overt Aggression Scale)

Table No: 10

Sociodemographic associations with any aggression

	B	S.E.	Wald	df	Sig.	Exp(B)
Gender	-0.104	0.293	0.127	1	0.722	0.901
Age group under 35 years	-0.392	0.291	1.823	1	0.177	0.676
Single marital status	0.161	0.354	0.206	1	0.650	1.174
Educational level	-0.942	0.292	10.399	1	0.001*	0.390
Unemployed status	0.278	0.287	0.935	1	0.333	1.320
Living alone	0.526	0.269	3.807	1	0.051	1.691
Constant	-0.158	0.551	0.082	1	0.774	0.854

Table No: 11

Sociodemographic associations with violence

	B	S.E.	Wald	df	Sig.	Exp(B)
Gender	-0.130	0.292	0.199	1	0.656	0.878
Age group under 35 years	0.036	0.288	0.016	1	0.900	1.037
Single marital status	0.134	0.351	0.146	1	0.702	1.143
Educational level	-0.757	0.296	6.558	1	0.010*	0.469
Unemployment status	0.348	0.283	1.513	1	0.219	1.417
Living alone	0.413	0.267	2.386	1	0.122	1.511
Constant	-0.632	0.551	1.314	1	0.252	0.532

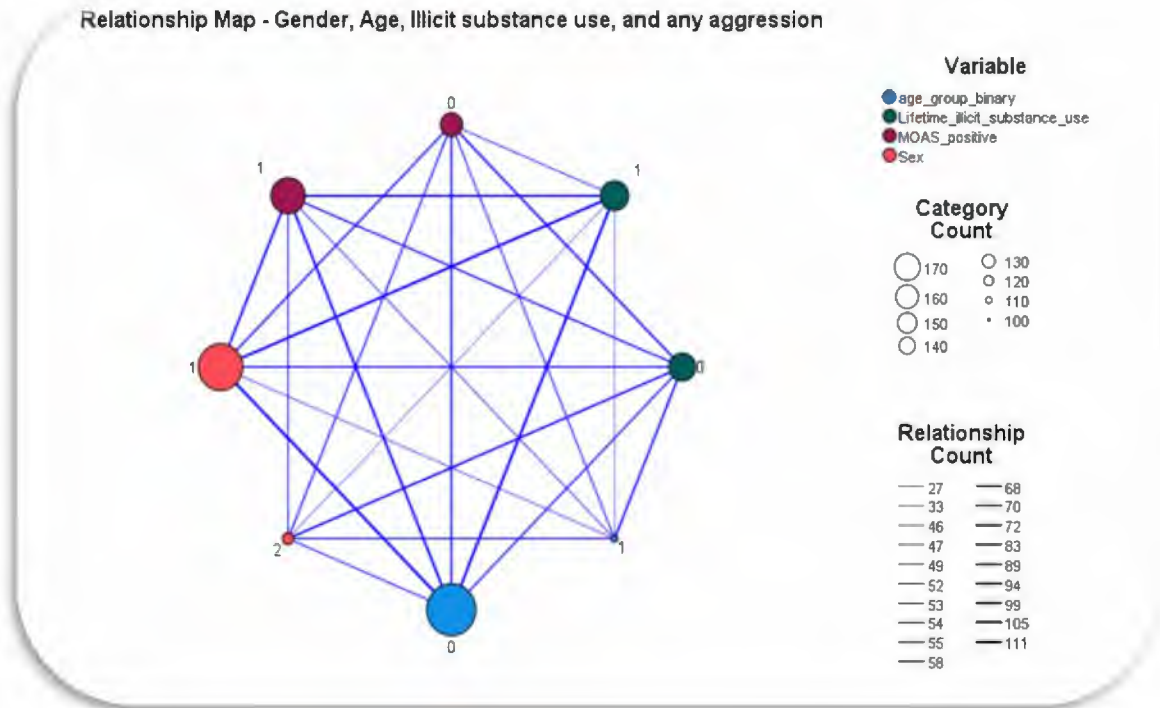
Table No: 12

MOAS score correlations with age groups under 35 and over 35 years

	Mean rank		Mann Whitney U	p
	Under 35	Over 35		
Verbal aggression pre-contact	133.05	128.95	7816.500	0.518
Verbal aggression post-contact	136.87	122.65	7192.500	0.034
Aggression against property pre-contact	133.80	127.71	7693.000	0.180
Aggression against property post-contact	135.51	124.90	7415.500	0.028
Self-aggression pre-contact	130.32	136.08	7842.000	0.352
Self-aggression post-contact	134.27	129.60	7910.000	0.282
Aggression against others pre-contact	133.30	128.53	7774.5	0.443
Aggression against others post-contact	135.48	124.94	7419.500	0.029

MOAS (Modified Overt Aggression Scale)

Graphic No: 6

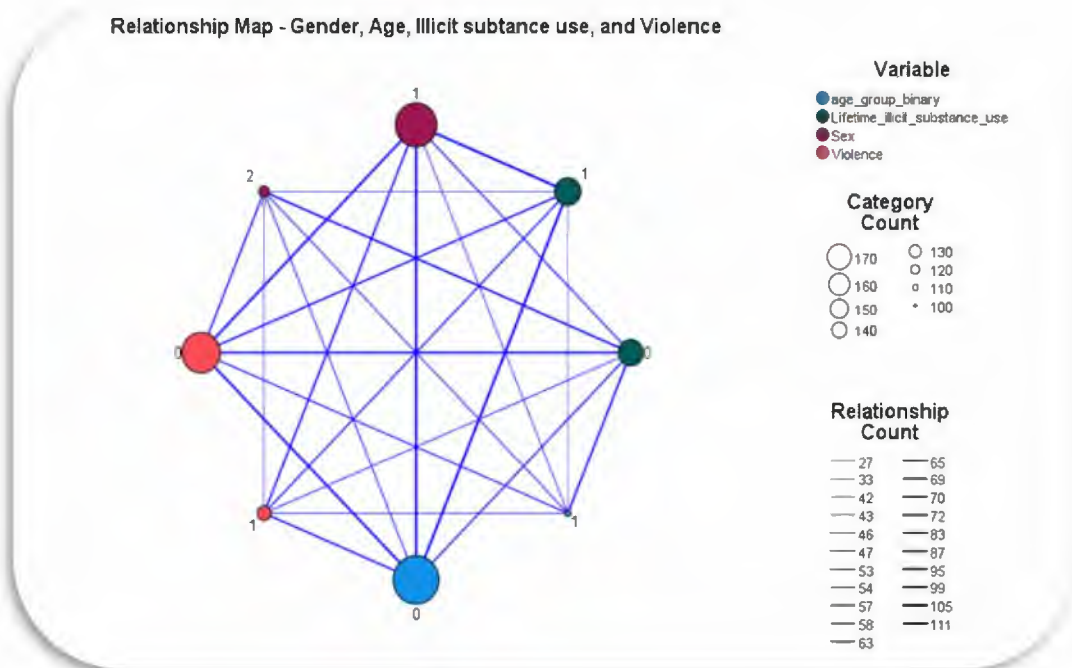


Legend: Age group 0 - under 35 year, Age group 1 - over 35; Lifetime illicit substance use: 0 - never, 1 - user; MOAS positive: 0 - no aggression, 1 - aggression; Sex: 1 - male, 2 - female

Graphic

No:

7



Legend: Age group 0 - under 35 year, Age group 1 - over 35; Lifetime illicit substance use: 0 - never, 1 - user; Violence: 0 - non-violent 1 - violent; Sex: 1 - male, 2 - female

Table No: 13

Correlation of affective disorders and psychopathology.

	Mean rank		Mann Whitney U	P
	No aggression	Any aggression		
DUP	106.90	60.14	1565.500	0.001*
GAF	127.14	137.13	5543.000	0.357
SANS	134.46	106.53	4515.000	0.010*
SAPS	131.45	120.95	5427.000	0.336
CDSS	124.43	137.64	5154.500	0.217
YMRS	46.06	77.76	633.500	0.001*
INSIGHT	92.28	109.51	2796.000	0.064

Table No: 14

Correlation of substance-induced psychosis and psychopathology

	Mean rank		Mann Whitney U	p
	No SUD	SUD		
DUP	100.44	71.95	1229.000	0.031
GAF	128.86	134.02	3471.500	0.712
SANS	127.39	132.22	3433.000	0.727
SAPS	129.23	127.34	3451.500	0.894
CDSS	125.62	140.53	3135.000	0.271
YMRS	57.75	48.28	389.500	0.389
INSIGHT	95.27	107.08	1508.500	0.368

DUP [Duration of Untreated Psychosis] based on Beiser scale, GAF (Global Assessment of Functioning), SAPS (Scale for the Assessment of Positive Symptoms), SANS (Scale for the Assessment of Negative Symptoms), CDSS (Calgary Depression Scale for Schizophrenia), Young Mania Rating Scale (YMRS), Insight - Birchwood Questionnaire, \* = statistically significant

Table No: 15

Correlation of any aggression with psychopathology

	Mean rank		Mann Whitney U	p
	No aggression	Any aggression		
DUP	99.60	95.68	4491.000	0.627
GAF	146.80	114.92	6218.500	<0.001*
SANS	120.89	134.32	7247.000	0.143
SAPS	115.51	141.19	6589.500	0.006*
CDSS	132.39	122.98	7455.000	0.297
YMRS	49.68	64.72	1170.500	0.012
INSIGHT	100.38	92.63	4236.000	0.333

Table No: 16

Association between pre-contact any aggression and psychopathology

	Mean rank		Mann Whitney U	p
	No aggression	Aggression		
DUP	95.47	100.05	4424.500	0.571
GAF	141.02	115.62	6624.000	0.006
SANS	123.08	134.19	7324.000	0.228
SAPS	118.09	143.12	6538.500	0.007
CDSS	129.88	124.33	7557.000	0.543
YMRS	50.93	65.84	1134.500	0.014
INSIGHT	100.03	91.34	4043.500	0.286

Table No: 17

Correlation between any post-contact aggression and psychopathology

	Mean rank		Mann Whitney U	p
	No aggression	Aggression		
DUP	98.72	94.00	3425.000	0.608
GAF	132.51	122.01	6253.500	0.302
SANS	127.29	129.85	6401.000	0.802
SAPS	123.90	142.37	5653.500	0.074
CDSS	134.96	107.89	5067.500	0.007*
YMRS	54.52	63.85	1039.500	0.166
INSIGHT	99.00	89.21	3146.500	0.287

DUP [Duration of Untreated Psychosis] based on Beiser scale, GAF (Global Assessment of Functioning), SAPS (Scale for the Assessment of Positive Symptoms), SANS (Scale for the Assessment of Negative Symptoms), CDSS (Calgary Depression Scale for Schizophrenia), Young Mania Rating Scale (YMRS), Insight - Birchwood Questionnaire, \* = statistically significant

Table No: 18

Associations between violence and psychopathology

	Mean rank		Mann Whitney U	p
	Non-violent	Violent		
DUP	96.04	99.50	4428.000	0.670
GAF	138.65	117.38	6813.500	0.022
SANS	123.91	133.56	7337.500	0.298
SAPS	118.41	143.85	6436.500	0.007
CDSS	128.93	125.44	7586.000	0.704
YMRS	51.40	65.78	1131.500	0.018
INSIGHT	100.19	90.88	3980.500	0.255

Table No: 19

Correlation of pre-contact violence with psychopathology

	Mean rank		Mann Whitney U	p
	Non-violent	Violent		
DUP	96.23	100.34	3849.500	0.636
GAF	139.78	107.03	5348.500	0.001*
SANS	124.07	136.77	6259.500	0.199
SAPS	120.99	147.39	5546.500	0.009*
CDSS	127.05	128.53	6735.500	0.881
YMRS	53.98	64.33	1078.000	0.113
INSIGHT	97.26	94.73	3783.500	0.771

Table No: 20

Correlation of post-contact violence with psychopathology

	Mean rank		Mann Whitney U	p
	Non-violent	Violent		
DUP	99.09	89.47	2335.000	0.374
GAF	132.49	115.73	4242.500	0.164
SANS	125.33	141.56	3903.500	0.188
SAPS	127.00	139.26	4084.000	0.326
CDSS	130.32	112.84	3765.000	0.154
YMRS	57.24	55.53	752.500	0.841
INSIGHT	97.77	89.38	2157.000	0.453

DUP [Duration of Untreated Psychosis] based on Beiser scale, GAF (Global Assessment of Functioning), SAPS (Scale for the Assessment of Positive Symptoms), SANS (Scale for the Assessment of Negative Symptoms), CDSS (Calgary Depression Scale for Schizophrenia), Young Mania Rating Scale (YMRS), Insight - Birchwood Questionnaire, \* = statistically significant

Table No: 21

Correlations between severe violence and psychopathology

	Mean rank		Mann Whitney U	p
	Non-violent	Violent		
DUP	96.32	101.58	1985.500	0.659
GAF	133.38	97.66	2788.000	0.007*
SANS	125.45	137.13	3290.000	0.381
SAPS	122.14	168.34	2261.000	0.001*
CDSS	131.81	91.29	2451.500	0.002*
YMRS	52.08	85.07	299.000	0.001*
INSIGHT	96.14	91.13	1957.500	0.681

DUP [Duration of Untreated Psychosis] based on Beiser scale, GAF (Global Assessment of Functioning), SAPS (Scale for the Assessment of Positive Symptoms), SANS (Scale for the Assessment of Negative Symptoms), CDSS (Calgary Depression Scale for Schizophrenia), Young Mania Rating Scale (YMRS), Insight - Birchwood Questionnaire, \* = statistically significant

Table No: 22

MOAS score correlations with co-morbid alcohol use disorder

	Mean rank		Mann Whitney U	p
	No AUD	AUD		
Verbal aggression pre-contact	124.49	143.54	6228.500	0.013
Verbal aggression post-contact	126.39	139.41	6567.000	0.063
Aggression against property pre-contact	128.06	135.79	6864.500	0.103
Aggression against property post-contact	129.45	132.77	7 111.500	0.510
Self-aggression pre-contact	130.45	130.61	7289.000	0.980
Self-aggression post-contact	129.30	133.10	7085.000	0.377
Aggression against others pre-contact	126.47	139.26	6580.000	0.049
Aggression against others post-contact	126.42	139.35	6572.000	0.010*

MOAS (Modified Overt Aggression Scale), \* = statistically significant

Table No: 23

MOAS score correlations with lifetime substance use

	Mean rank		Mann Whitney U	p
	Non-users	Users		
Verbal aggression pre-contact	124.49	143.54	6228.500	0.013
Verbal aggression post-contact	126.39	139.41	6567.000	0.063
Aggression against property pre-contact	128.06	135.79	6864.500	0.103
Aggression against property post-contact	129.45	132.77	7111.500	0.510
Self-aggression pre-contact	134.61	128.67	7101.000	0.758
Self-aggression post-contact	130.61	128.67	7086.000	0.380
Aggression against others pre-contact	129.31	133.09	6580.000	0.049
Aggression against others post-contact	126.47	139.26	6572.500	0.010*

MOAS (Modified Overt Aggression Scale), \* = statistically significant

Table No: 24

MOAS score correlations with lifetime cannabis use

	Mean rank		Mann Whitney U	p
	Non-user	User		
Verbal aggression pre-contact	127.13	136.91	7849.000	0.175
Verbal aggression post-contact	128.14	135.67	7995.000	0.251
Aggression against property pre-contact	129.18	134.38	8145.500	0.214
Aggression against property post-contact	127.63	136.30	7921.000	0.066
Self-aggression pre-contact	131.78	131.15	8442.000	0.916
Self-aggression post-contact	129.32	134.20	8167.000	0.225
Aggression against others pre-contact	127.64	136.28	7923.500	0.155
Aggression against others post-contact	129.26	134.27	8158.000	0.287

MOAS (Modified Overt Aggression Scale)

Table No: 25

MOAS score correlations with the past month's cannabis use

	Mean rank		Mann Whitney U	p
Verbal aggression pre-contact	130.23	134.66	6775.500	0.576
Verbal aggression post-contact	126.10	144.95	6003.500	0.009*
Aggression against property pre-contact	130.82	133.20	6885.000	0.625
Aggression against property post-contact	127.87	140.54	6334.500	0.015
Self-aggression pre-contact	133.42	126.72	6654.000	0.304
Self-aggression post-contact	130.71	133.48	6864.000	0.513
Aggression against others pre-contact	126.62	143.66	6100.500	0.011
Aggression against others post-contact	130.63	133.67	6849.500	0.557

MOAS (Modified Overt Aggression Scale)

Table No: 26

MOAS score correlations with lifetime stimulant use

	Mean rank		Mann Whitney U	p
	Non-users	Users		
Verbal aggression pre-contact	129.42	136.18	5784.000	0.424
Verbal aggression post-contact	127.84	141.35	5468.500	0.079
Aggression against property pre-contact	130.37	133.06	5974.500	0.606
Aggression against property post-contact	127.57	142.26	5413.000	0.008*
Self-aggression pre-contact	126.66	145.23	5232.000	0.007*
Self-aggression post-contact	129.68	135.34	5835.500	0.231
Aggression against others pre-contact	127.83	141.39	5466.000	0.057
Aggression against others post-contact	129.34	136.46	5767.000	0.198

MOAS (Modified Overt Aggression Scale)

Table No: 27

MOAS score correlations with the past month's stimulant use

	Mean rank		Mann Whitney U	p
	Non-user	User		
Verbal aggression pre-contact	131.03	130.53	1838.000	0.974
Verbal aggression post-contact	129.33	158.37	1434.500	0.038
Aggression against property pre-contact	131.13	128.80	1812.000	0.805
Aggression against property post-contact	130.67	136.40	1764.000	0.569
Self-aggression pre-contact	129.57	154.15	1492.500	0.047
Self-aggression post-contact	130.99	131.20	1842.000	0.980
Aggression against others pre-contact	130.68	136.17	1767.500	0.672
Aggression against others post-contact	130.10	145.18	1623.000	0.112

MOAS (Modified Overt Aggression Scale)

Table No 28.

*Collinearity analysis of alcohol use disorder SAPS in precontact violence*

Model	Unstandardised Coefficients B	Std. Error	Standardised Coefficients Beta	t	Sig.	Tolerance	VIF
1	(Constant)	0.338	0.504		0.672	0.502	
	Alcohol use disorder [AUD]	0.415	0.965	0.049	0.430	0.667	3.413
	SAPS composite value	0.037	0.018	0.146	2.106	0.036	1.261
	Moderator SAPS-AUD	0.047	0.039	0.139	1.204	0.230	3.493

*a. Dependent Variable: precontact violence*

Table No 29.

*Collinearity analysis of polysubstance use and SAPS in precontact violence*

Model	B	Std. Error	Beta	t	Sig.	Tolerance	VIF
1	(Constant)	-0.577	0.724		-0.797	0.426	
	Polysubstance use	1.950	0.893	0.237	2.184	0.030	3.088
	SAPS composite value	0.061	0.030	0.241	2.046	0.042	3.635
	Moderator SAPS-polysubstance use	-0.030	0.035	-0.134	-0.875	0.383	6.151

*a. Dependent Variable: precontact violence*

Table No: 30

Comparative table of the methodology used in first-episode psychosis cohorts examining aggression and violence

Study	Sample size	Service type	Period examined	Temporal relationship with the contact	Source of information	Record of substance use	Location
Current study	264	Community Inpatient Third-level MH Care	1 year	pre- and post-contact	Medical notes Incident forms	yes	EU
Bhugra et al., 2000	36	N/A	2 years	pre-contact	Collateral interview		UK
Crebbin et al., 2008	251	Secondary MH Care	1 year	pre- and post-contact	Medical notes		UK
Dean et al., 2007	495	N/A	2 years	pre-contact	Interview with patient		UK
Foley et al., 2005	157	Community Inpatient Third-level MH Care	2 weeks	pre- and post-contact	Medical notes, incident forms	yes	EU
Harris et al., 2010	85	N/A	3 months	pre-contact	Interview with patient Collateral interview		Australia
Hodgins et al., 2011	301	N/A	>3 years	pre-contact			UK
Humphreys et al., 1992	223	N/A	>3 years	pre-contact			UK
Milton et al., 2001	166	Secondary MH Care	3 years				UK
Munkner et al., 2009	477	N/A	>3 years	pre-contact			EU
Payne et al., 2005	146	Inpatient	< 1 year	pre- and post-contact			Canada
Cont. Study	Sample size	Service type	Period examined	Temporal relationship with the contact	Source of information	Record of substance use	Location
Spidel et al., 2010	118	Case management	1 year	post-contact			Canada
Steinert et al., 1999	138	Inpatient	1 year	pre- and post-contact			EU
Verma et al., 2005	146	N/A	>3 years	pre-contact			Singapore
Volavka et al., 1997	1017	N/A	>3 years	pre-contact			International

Table No: 31

Comparative table of prevalence rates of aggression and violence in first-episode psychosis cohorts

Study	Sample size	Systematic measure of violence	Assessment tool	Aggression	z	p	Violence	z	P
Current study	265	Yes	MOAS	42.4%			13%		
Bhugra et al., 2000	36	Yes	PPHS	NR			22%	1.5	0.1451
Crebbin et al., 2008	251	No		NR			25%	3.5	0.0005*
Dean et al., 2007	495	Yes	PPHS	39%	0.9	0.3828	21%	2.7	0.0065*
Foley et al., 2005	157	Yes	MOAS	29%	2.7	0.006*	9.6%	1	0.2942
Harris et al., 2010	85	Yes	ABQ	56%	2.2	0.0285	27%	3	0.0024*
Hodgins et al., 2011	301	Yes	OI	23.6%	4.8	<0.0001*	13.2%	0.1	0.9439
Humphreys et al., 1992	223	Yes	DBR	NR			20.7%	2.3	0.0225
Milton et al., 2001	166	Yes	MCV	17%	5.5	<0.0001*	9.6%	1.1	0.285
Munkner et al. 2009	477	No	DNCR	30%			7%	2.7	0.0066*
Payne et al., 2005	146	No		31.5%	2.2	0.0298	NR		
Spidel et al., 2010	118	Yes	MOAS	43%	0.1	0.9127	NR		
Steinert et al., 1999	138	Yes	MOAS	34%	1.6	0.107	14%	0.3	0.7794
Verma et al., 2005	146	Yes	MCV	43%	0.1	0.9063	15.9%	0.8	0.4178
Volavka et al., 1997	1017	Yes	PPHS	NR			10.5%	1.2	0.247

Legend: \* = statistically significant, Not recorded (NR), Psychiatric and Personal History Schedule (PPHS), Modified Overt Aggression Scale (MOAS), McArthur Community Violence Instrument (MCVI), Disturbed Behaviour Rating (DBR), Offenders Index (OI), Danish National Crime Register (DNCR)