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# Psychosis and substance use: what clinicians need to know

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# Talk Outline

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- Substance-related psychosis
- How much first episode psychosis is related to substance use?
- Does substance-related psychosis progress to schizophrenia?
- Why is comorbid psychosis and substance use so common?
- What are outcomes like for individuals with substance-related psychosis?
- Assessing comorbid substance use in psychosis
- Assessing psychosis risk in substance use
- Managing comorbid substance use and psychosis

## Substance-related psychosis

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# Substance-induced psychosis

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- Signs & symptoms of psychosis in the context of substance use
- Symptoms develop during (or within a month of) substance intoxication or withdrawal
- Substance used is aetiologically related to the disturbance
- Symptoms are not better accounted for by a psychotic disorder that is not substance induced

# Substance-induced psychosis vs primary psychosis

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- Substance-induced psychosis in the absence of an underlying primary psychosis presents in way very similar to primary psychosis that is triggered/exacerbated by substance abuse (*Bramness et al, 2012; Glasner-Edwards & Mooney, 2014; McKetin et al, 2016*)
- Methamphetamine-induced psychosis may be associated with more visual and somatic or tactile hallucinations and less severe negative affect (*Wang et al, 2016*)

# Substance-related psychosis

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- Difficulty distinguishing clinically between these aetiologies, particularly if there is ongoing substance use
- Comorbid substance use very common in people with mental health issues
- Increasingly, studies of long-term outcomes suggest not easily separable
- Consider those with psychotic Sx vulnerable to psychosis development

# Methamphetamine-related psychosis: an opportunity for assertive intervention and prevention

*Methamphetamine-related psychosis is a growing public health concern. All individuals with transient amphetamine-related psychotic symptoms should be considered to be at risk for future development of an enduring psychotic illness, and prioritized for early intervention of integrated care across substance use and mental health services.*

Contemporary views of psychosis challenge the simple categorical distinction between brief drug-induced psychoses and more enduring disorders such as schizophrenia. Psychoses are seen increasingly as heterogeneous disorders with a spectrum of illness profiles and course trajectories [11]. Substantial evidence exists that diagnoses of drug-induced psychosis have poor predictive validity. A high

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# Substance-related psychoses are not all equivalent

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- Care should be assertive early intervention, as for other brief psychotic disorders
- Need for monitoring and ongoing support
- Decisions regarding care should consider
  - the different risks associated with each substance
  - *for example* considering a heightened risk for transition from cannabis-induced psychosis versus alcohol-induced psychosis
  - comorbid use of other substances
  - individual risk factors for psychosis (family history, minority status, early life trauma)

# Service use differences

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- Less likely to seek help
- Less adherent to treatment
- Engage poorly in care
- Often present in crisis to ED
- In ED, may receive care for acute behavioural agitation
- In MHS, for psychosis but not for drug use
- In D&A, for drug use but not psychosis

# How much first episode psychosis is related to substance use?

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# Hospital admissions for First Episode Psychosis

All first psychosis in NSW

Hospital admissions

July 2005-July 2015

Aged 16-64

Total: n=41794

17460 (41.8%) females

24334 (58.2%) males



# First Episode Psychosis across the age span

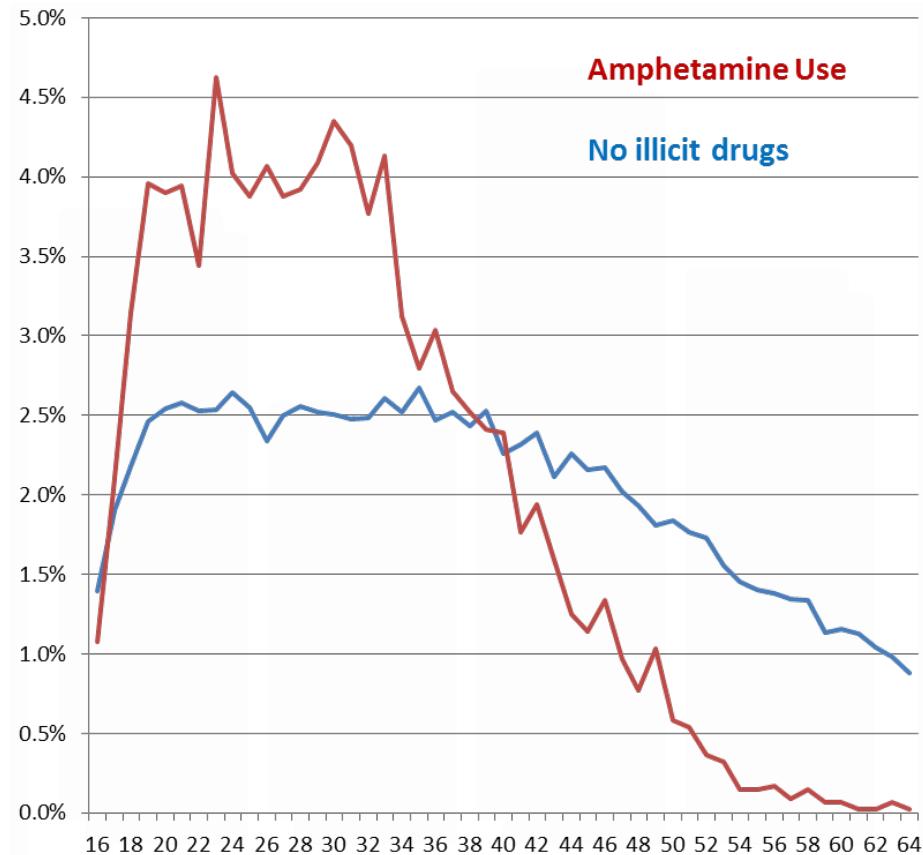
Total FEP: n=41794

Amphetamine-related: n=4645

Psychosis peaks from late adolescence

Amphetamine-related psychosis peaks from late adolescence to early 30's

Psychosis onset can occur at any age and *may* be related to drug use



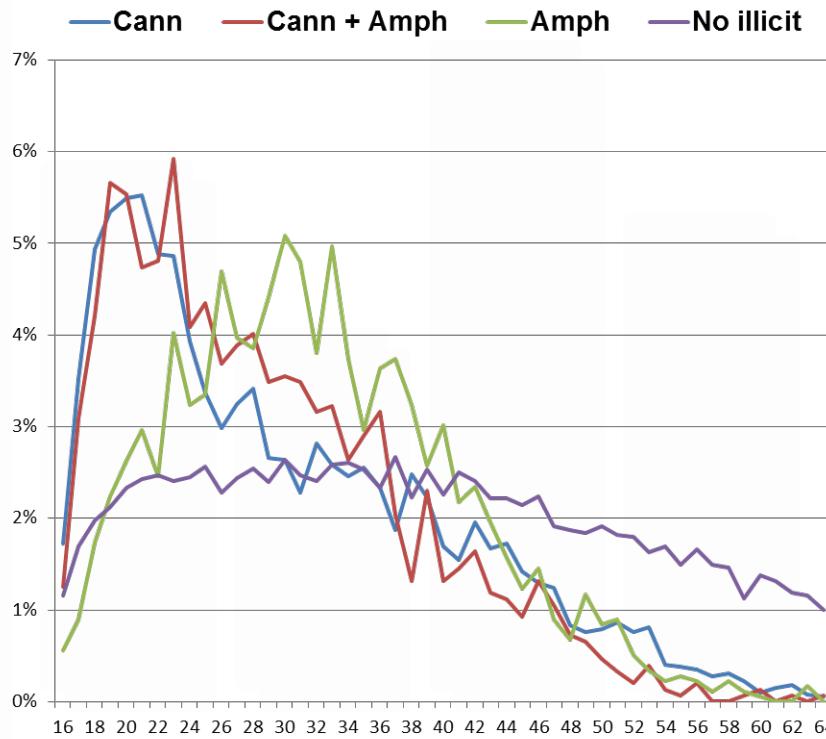
# The role of cannabis

Cannabis use is common in individuals presenting with first psychosis

Cannabis-related psychosis peaks earlier

Cannabis plus amphetamine peaks earlier

Amphetamine alone peaks later but risk persists



# Does substance-related psychosis progress to schizophrenia?

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# Substance/drug related psychosis

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- Brief psychotic syndromes triggered by substance use
- Persisting for days or weeks after intoxication has resolved
- Estimated incidence 1.5-6.5 per 100,000 person years
- Up to 25% of first hospital admissions may include this diagnosis
- Often excluded from studies of early psychosis

# Substance/drug induced psychosis

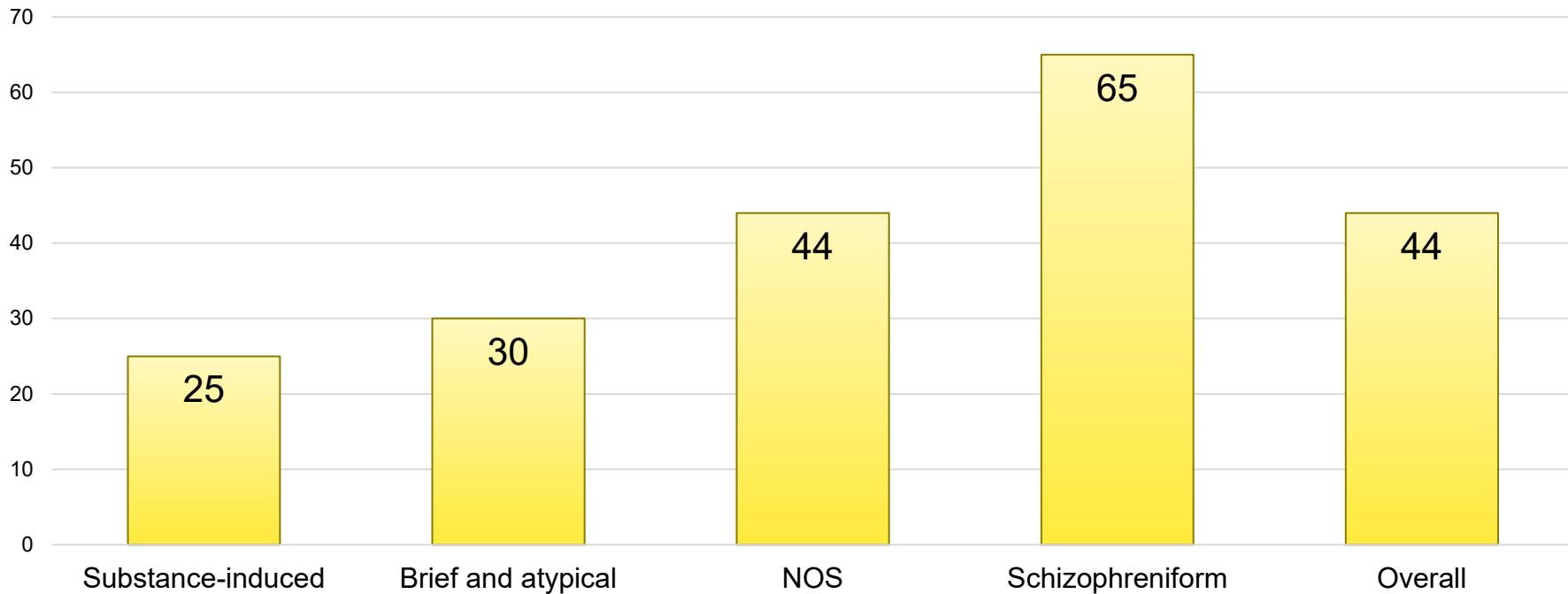
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- A significant proportion of people later transition to schizophrenia
- Estimates vary widely:
  - as high as **66%** (Addington et al 2006)
  - as low as **17%** (Starzer et al 2017)
- Examined this question in recent meta-analysis to synthesize the results of longitudinal observational studies of transition from substance-induced psychosis to schizophrenia

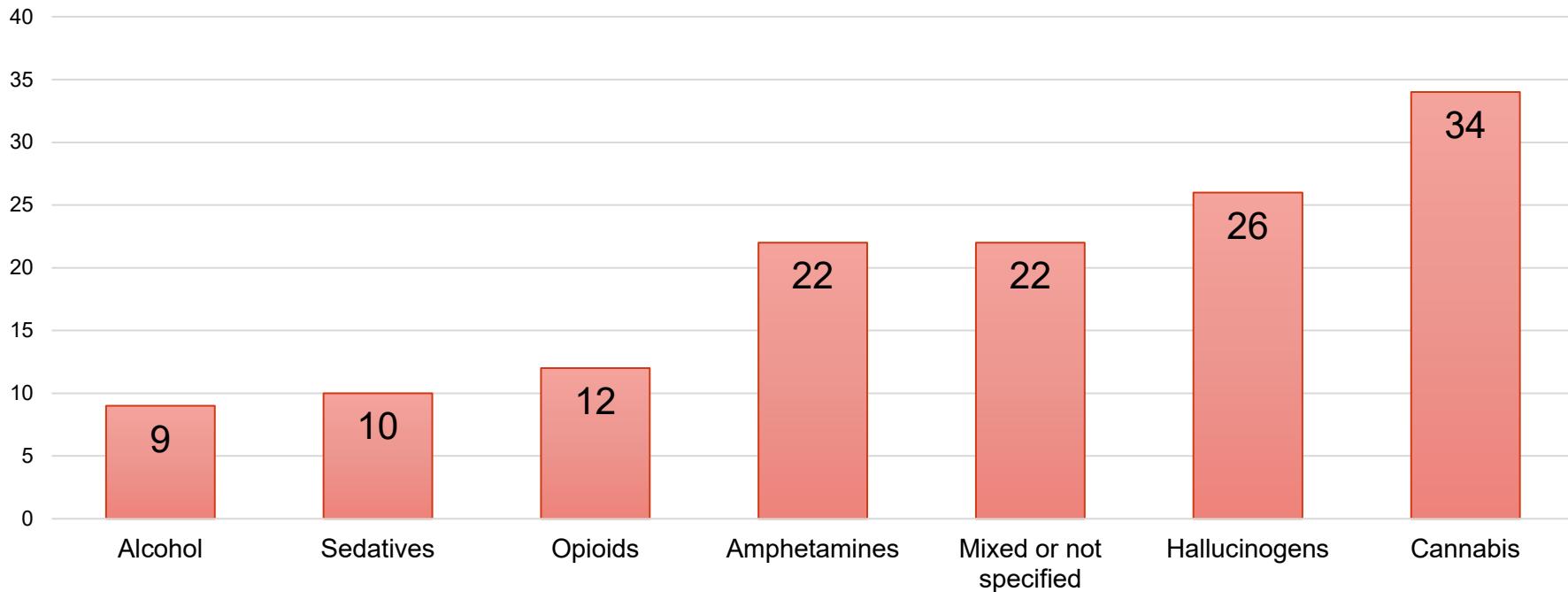
## Transition of Substance-Induced, Brief, and Atypical Psychoses to Schizophrenia: A Systematic Review and Meta-analysis

Benjamin Murrie<sup>1</sup>, Julia Lappin<sup>2,3</sup>, Matthew Large<sup>2</sup>, and Grant Sara<sup>\*,4,5</sup>

## Transition Rate to Schizophrenia by initial type of Psychosis(%)



## Transition Rate to Schizophrenia (% by Substance Type)



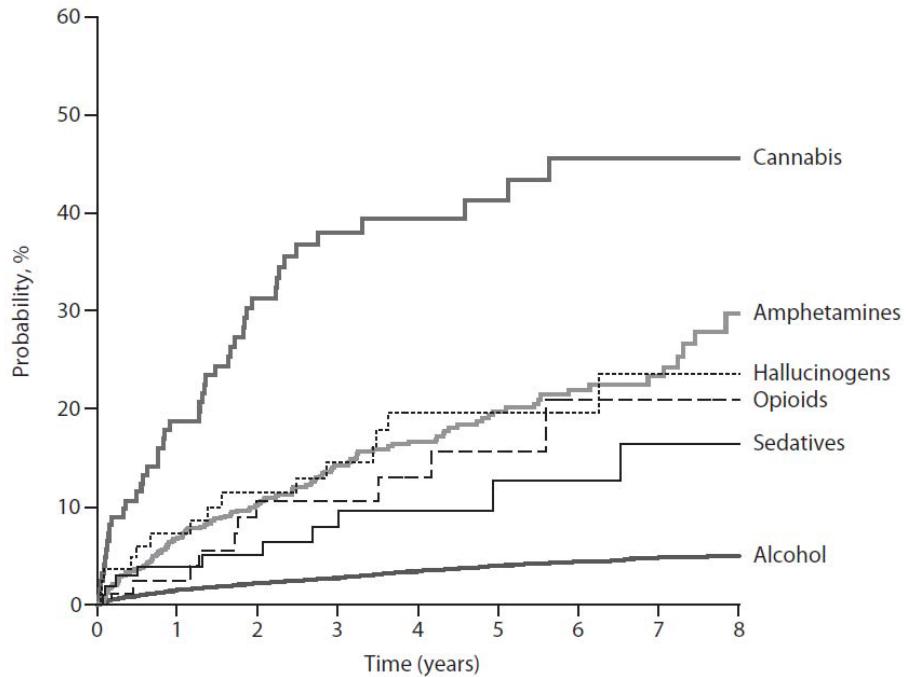
# Results – Subgroup Analysis of Substance-Induced Psychosis

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- Transition rates vary by substance
- **More than one third** with cannabis-induced psychosis develop schizophrenia
- Consistent with literature that cannabis use **doubles the risk** of developing schizophrenia in vulnerable people
- Rates of transition are higher among younger people
- **Familial risk and genetic predisposition** play a key role in the development of cannabis-induced psychosis and later transition to schizophrenia
- No association between transition rate and
  - Sex
  - Duration of follow-up
  - Proportion followed up or
  - Year of publication

# Progression to schizophrenia

Figure 1. Cumulative Probability of Receiving a Schizophrenia Spectrum Disorder Diagnosis (N=18,478)



Niemi-Pynttari et al. Substance-induced psychoses converting into schizophrenia: a register-based study of 18,478 Finnish inpatient cases. J Clinical Psychiatry 2013

# Why is comorbid psychosis and substance use so common?

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# Reasons for high rates of comorbidity

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Possible explanations include:

- shared genetic or environmental factors (such as childhood trauma or neglect, social deprivation) that increase risk for both mental illness and substance use
- a causal link between substance use and the development of new onset psychotic disorders
- self-medication with substances to lessen symptoms of severe mental illness

# Biological models

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- Substances consistently identified in studies of comorbid substance use and psychosis:
  - Cannabis
  - Psychostimulants (methamphetamine/amphetamine)
  - Alcohol
  - Hallucinogens (phencyclidine, LSD)
- Biological models suggest that the effects of these substances on a variety of brain neurotransmitters may *both precipitate and maintain* psychotic symptoms with adverse impact on outcomes

# Cannabis-related psychosis

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- Heavy use of cannabis increases the risk of later psychosis
- Administration of THC to volunteers induces transient psychosis and increases release of dopamine in striatum
- There are plausible biological explanations for the psychotogenic effects of cannabis
- The proportion of THC in “street” cannabis is rising
- Early use of high-potency cannabis increases risk for psychosis particularly in those with other risk factors (family history; genetic risk; childhood adversity; migration; minority status)

(Murray et al, 2017)



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# Methamphetamine-related Psychosis

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- High prevalence of psychosis in methamphetamine users (*Farrell, 2002*)
- Dose-related psychotic symptoms in chronic users (*McKetin, 2013*)
- Significantly increased risk of schizophrenia development in methamphetamine users (*Callaghan, 2012*)



ORIGINAL ARTICLE

# Psychosis with Methylphenidate or Amphetamine in Patients with ADHD

Lauren V. Moran, M.D., Dost Ongur, M.D., Ph.D.,  
John Hsu, M.D., M.S.C.E., Victor M. Castro, M.S., Roy H. Perlis, M.D.,  
and Sebastian Schneeweiss, M.D., Sc.D.

## ABSTRACT

### BACKGROUND

The prescription use of the stimulants methylphenidate and amphetamine for the treatment of attention deficit–hyperactivity disorder (ADHD) has been increasing.

## RESULTS

We assessed 337,919 adolescents and young adults who received a prescription for a stimulant for ADHD. The study population consisted of 221,846 patients with 143,286 person-years of follow up; 110,923 patients taking methylphenidate were matched with 110,923 patients taking amphetamines. There were 343 episodes of psychosis (with an episode defined as a new diagnosis code for psychosis and a prescription for an antipsychotic medication) in the matched populations (2.4 per 1000 person-years): 106 episodes (0.10%) in the methylphenidate group and 237 episodes (0.21%) in the amphetamine group (hazard ratio with amphetamine use, 1.65; 95% confidence interval, 1.31 to 2.09).

## CONCLUSIONS

Among adolescents and young adults with ADHD who were receiving prescription stimulants, new-onset psychosis occurred in approximately 1 in 660 patients. Amphetamine use was associated with a greater risk of psychosis than methylphenidate. (Funded by the National Institute of Mental Health and others.)

# Reasons for high rates of comorbidity

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Possible explanations include:

- shared genetic or environmental factors (such as childhood trauma or neglect, social deprivation) that increase risk for both mental illness and substance use
- a causal link between substance use and the development of new onset psychotic disorders
- **self-medication with substances to lessen symptoms of severe mental illness**

# Reasons for high rates of comorbidity (2)

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A further important consideration in the maintenance of these persistently high rates is that people with severe mental illness are known to have

- Inadequate access to cessation services (incl. smoking cessation)
- Poor social supports
- Impaired cognition
- Poor coping strategies

# **Schizophrenia is associated with increased risk of subsequent substance abuse diagnosis: A nation-wide population-based register study**

Stine Mai Petersen<sup>1,2</sup>, Nanna Gilliam Toftdahl<sup>1,2</sup>, Merete Nordentoft<sup>1,2</sup> & Carsten Hjorthøj<sup>1,2,3</sup> 

**Aims** We aimed to investigate whether or not a diagnosis of schizophrenia increases the risk of a substance abuse diagnosis. **Design** Prospective cohort study using a longitudinal study design. **Setting and participants** Individuals born in Denmark from 1955 to 1999 and registered in the Danish registers between 1 January 1968 and 1 July 2013.

**Measurements** We investigated the associations between schizophrenia and ICD diagnoses of substance abuse, both established through various Danish registers. The Cox regression model was used and adjusted for calendar year, gender, urbanicity, co-abuse, other psychiatric diagnoses, parents' substance abuse and psychiatric history, parents' immigration and parents' socio-economic position. Individuals diagnosed with substance abuse less than a year after diagnosis of schizophrenia were classified as not diagnosed with schizophrenia. **Findings** The cohort consisted of 3 133 968 individuals. During follow-up (103 212 328 person-years at risk), a total of 14 007 individuals developed schizophrenia, with 2885 subsequently diagnosed with substance abuse. A diagnosis of schizophrenia was positively associated with the risk of developing substance abuse [hazard ratio (HR) = 3.69, 95% confidence interval (CI) = 3.56–3.83]. Additionally, adjusting for a co-abuse markedly affected the associations, making schizophrenia primarily associated with an increased risk of abuse of cannabis, alcohol, stimulants and other substances (adjusted HR = 2.48, 95% CI = 2.34–2.64 for cannabis; HR = 1.94, 95% CI = 1.87–2.02 for alcohol; HR = 1.77, 95% CI = 1.61–1.95 for stimulants; HR = 1.36, 95% CI = 1.20–1.54 for other substances). The association was still significant 10–15 years subsequent a diagnosis of schizophrenia (HR = 2.50, 95% CI = 2.26–2.76). **Conclusions** In Denmark a diagnosis of schizophrenia is significantly associated with increased risk of subsequent diagnosis of substance abuse.

## Commentary on Petersen et al. (2019): Development of problematic substance use in the years that follow diagnosis of schizophrenia

*The development of problematic substance use is common in the years that follow a diagnosis of schizophrenia. While the risk for substance use in precipitating psychosis has received much attention, there is a clear need for clinicians to screen and offer intervention for emerging substance use in all individuals with psychosis, even many years following onset.*

increased rates of not only relapse and re-hospitalization, but also violence, suicide and all-cause mortality [6–9]. Barriers to effective treatment include that those with comorbid substance use are less adherent to treatment, engage poorly in care and often present when in crisis [3,10,11]. Nonetheless, for those who do engage, evidence-based approaches exist, including group counsel-

# What are outcomes like for individuals with substance-related psychosis?

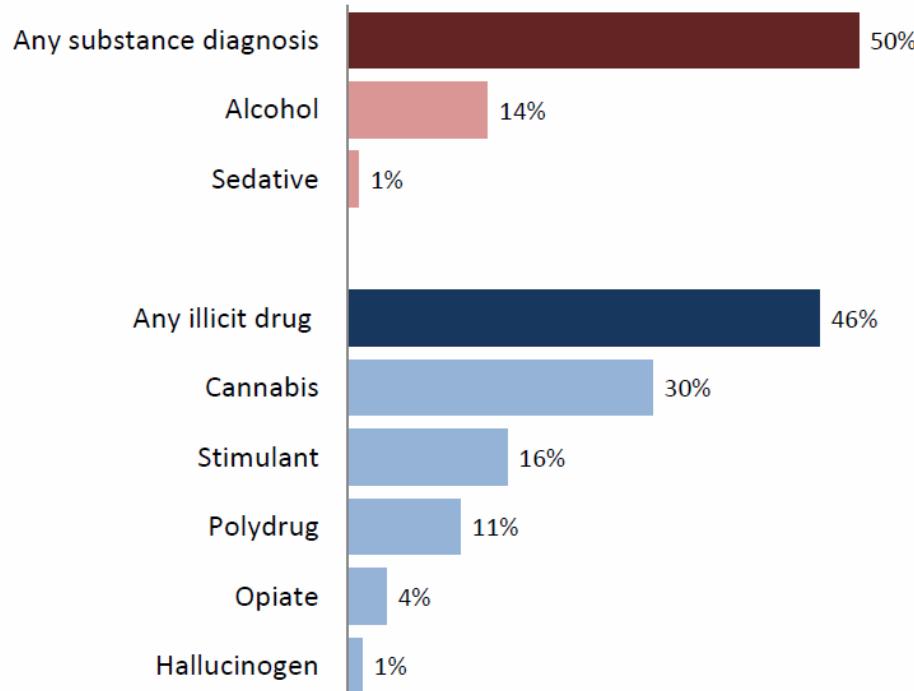
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# First psychosis



System  
Information  
& Analytics  
Branch



*Substance diagnoses at first admission with psychosis.*

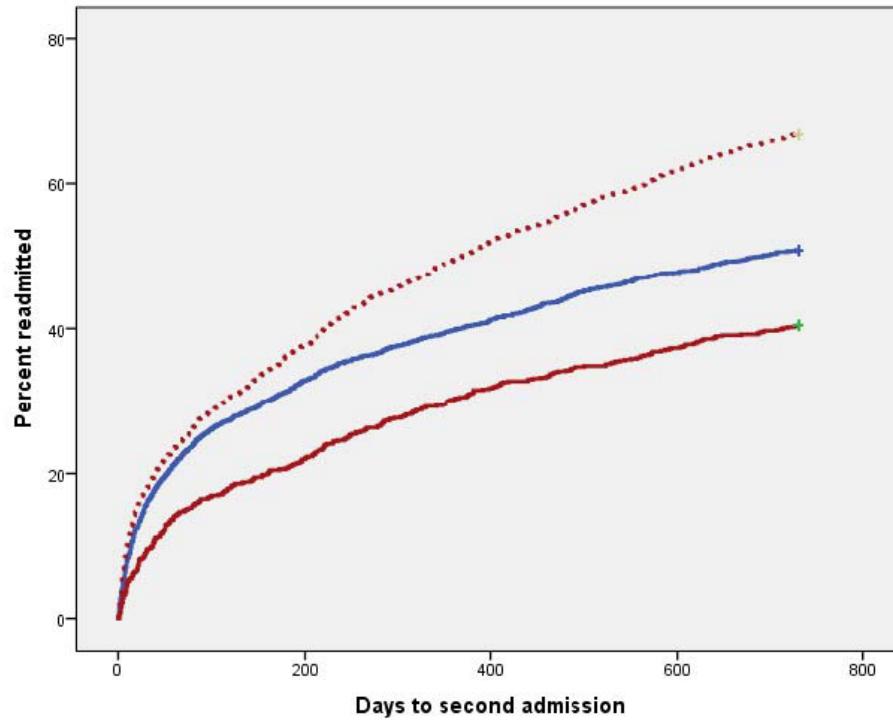
*9,919 NSW residents aged 15-29. Min 5 year clearance period*

Cannabis  
2107 (21%)

Cannabis + Stimulant  
857 (9%)

Stimulant  
685 (7%)

# Outcomes better for those who cease drug use after FEP



Drug misuse ongoing:  
67% readmitted

No drug misuse:  
51% readmitted

Drug misuse ceased:  
40% readmitted

# Greater harms associated with comorbidity

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- Higher rates of relapse and rehospitalisation
- Higher rates violence
- Higher rates suicide
- Higher rates all-cause mortality
- Additional mental health and physical health issues

# Assessing comorbid substance use in psychosis

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# Assessing use of common substances

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- Alcohol
- Tobacco
- Cannabis
- Methamphetamine/psychostimulants
- Hallucinogens/NPS
- Opioids
- Painkillers

# Drug use characteristics

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- Drug of use
- Pattern of use (alone/occasional/daily)
- Escalating use
- Effect on relationships/function
- Polysubstance use
- Mental health symptoms – do they make a link with pattern of use?

# Assessing Use and Misuse

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- Escalating use
- Use preferred over previously enjoyed activities
- Effect on relationships
- Effect on occupational/scholastic function
- Related social harms (criminal offences, debt)

# Harms associated with use

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- Suicide
- Driving
- Overdose
- Injecting
- Sexual disinhibition or sex work
- Drug-dealing
- Criminal charges
- Physical health harms: multiple and beyond scope of today!

# Common issues to look out for

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- High rates of other mental health issues:
  - Depression
  - Anxiety (including PTSD)
  - Suicidal behaviours
- Polysubstance use (Comorbid alcohol or substance use)
- Increasing use of prescribed meds, eg analgesics, benzos
- Smoking

# Assessing psychosis risk in substance use

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# Assessing psychotic symptoms: nature

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- Hallucinations: typically auditory, also visual, somatic
- Persecutory ideas, suspiciousness, guardedness
- Grandiose ideas (eg special abilities)
- May be associated with euphoric, labile or irritable mood
- Change in behaviour based on these beliefs
- Delusions of reference
- Delusions of control

# Assessing psychotic symptoms: acute effect?

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- Psychotic symptoms occur in many users as **acute** effects of cannabis, psychostimulants, hallucinogens
- Often regarded as benign and self-limiting
- Cannabis: transient Sx may be experienced in context of intoxication
- Psychostimulants: psychotic Sx common effect of use
- Hallucinogens: bad trip

# Assessing psychotic symptoms: chronic effect?

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- Duration of symptoms beyond period of acute effects of use/intoxication
- Emergence of symptoms in periods between use
- Persistence of symptoms increasing
- Chronic substance users may exhibit *kindling*-like effect of psychotic Sx re-emergence on re-use following abstinence

# Common issues to look out for

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- Ask about experience of hallucinations (auditory, visual, somatic) in periods (days/weeks) between drug use
- Ask about persecutory/grandiose/odd ideas or behaviour changes in periods (days/weeks) between drug use
- Is there always a clear relationship between symptoms and substance use pattern?
- If there is regular (daily) use, this is difficult!
- Ask individual and seek collateral (friends and family)

# Managing comorbid substance use and psychosis

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# Approach to management

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- Individual-centred
- Holistic
- Willingness to engage in ongoing mental health care
- Family/carer involvement
- Local options for integrated/co-ordinated care with D&A services
- Local NGOs for support (housing/employment)

# Immediate

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- Non-judgemental
- Assess risks to self (self-harm; vulnerability; STDs)
- Assess risks to others (driving; machinery operation; minors in home)
- Check supports (family/partner)
- Assess readiness for change
- Make substance use monitoring part of the care plan

# Short term

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- Treatment of conditions concurrently is gold standard
- Discuss options for outside help
  - Refer D&A or liaise MH
  - Refer psychologist (if motivated!)
  - NGOs
  - Family support

# Long term

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- Expect relapse
- Contain anxiety
- Be available through successes and failures
- Deal with physical and mental health harms opportunistically
- CBT
- Residential rehabilitation

# Treatment options

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Evidence-based approaches for substance use:

- group counselling
- contingency management
- residential treatment

# Co-ordinated approach to care

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Compared to parallel or sequential care:

- Fewer ED presentations
- Faster recovery times
- Shorter and fewer hospitalisations
- Reduced relapse into substance abuse
- Less deterioration in mental illness symptoms

# Integrated care for both issues concurrently

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- Reduced drop-outs from care
- Improved outcomes in
  - substance use
  - psychiatric symptoms
  - quality of life

# Conclusions

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- Substance-induced psychosis is a common reason for seeking mental health care
- > 1 in 5 first hospital admissions for psychosis in young Australians
- Often excluded from early psychosis services due to perception that self-resolve
- Not benign or self-limiting: transition rate to schizophrenia approx 30%
- Treat psychosis and substance use concurrently
- Outcomes better if abstain but abstinence does NOT ensure no further psychosis

THE CLINICIAN'S GUIDE TO

# ILICIT DRUGS<sup>AND</sup> HEALTH

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