JAMA Psychiatry | Brief Report

Transition to Schizophrenia Spectrum Disorder Following Emergency Department Visits Due to Substance Use With and Without Psychosis

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IMPORTANCE Episodes of substance-induced psychosis are associated with increased risk of developing a schizophrenia spectrum disorder. However, there are limited data on the transition risk for substance use without psychosis.

OBJECTIVES To quantify the risk of transition to schizophrenia spectrum disorder following an incident emergency department (ED) visit for (1) substance-induced psychosis and (2) substance use without psychosis and to explore factors associated with transition.

DESIGN, SETTINGS, AND PARTICIPANTS A population-based retrospective cohort study (January 2008 to March 2022) of all individuals, aged 14 to 65 years, in Ontario, Canada, with no history of a psychotic disorder. Individuals with incident ED visits for substance use with and without psychosis were compared with members of the general population.

MAIN OUTCOMES AND MEASURES Transition to schizophrenia spectrum disorder using a chart-validated algorithm. Associations between ED visits for substance use and subsequent transition were estimated using cause-specific hazard models.

RESULTS The study included 9 844 497 individuals, aged 14 to 65 years (mean [SD] age, 40.2 [14.7] years; 50.2% female) without a history of psychosis. There were 407 737 individuals with an incident ED visit for substance use, of which 13 784 (3.4%) ED visits were for substance-induced psychosis. Individuals with substance-induced psychosis were at a 163-fold (age- and sex-adjusted hazard ratio [aHR], 163.2; 95% CI, 156.1-170.5) increased risk of transitioning, relative to the general population (3-year risk, 18.5% vs 0.1%). Individuals with an ED visit for substance use without psychosis had a lower relative risk of transitioning (aHR, 9.8; 95% CI, 9.5-10.2; 3-year risk, 1.4%), but incurred more than 3 times the absolute number of transitions (9969 vs 3029). Cannabis use had the highest transition risk among visits with psychosis (aHR, 241.6; 95% CI, 225.5-258.9) and the third-highest risk among visits without psychosis (aHR, 14.3; 95% CI, 13.5-15.2). Younger age and male sex were associated with a higher risk of transition, and the risk of male sex was greater in younger compared with older individuals, particularly for cannabis use.

CONCLUSIONS AND RELEVANCE The findings of this cohort study suggest that ED visits for substance use were associated with an increased risk of developing a schizophrenia spectrum disorder. Although substance-induced psychoses had a greater relative transition risk, substance use without psychosis was far more prevalent and resulted in a greater absolute number of transitions. Several factors were associated with higher transition risk, with implications for counseling and early intervention.

Supplemental content

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JAMA Psychiatry. doi:10.1001/jamapsychiatry.2023.3582
Published online September 27, 2023.

Substance-induced psychoses are brief episodes of delusions or hallucinations triggered by intoxication or withdrawal, and they are a common cause of first-episode psychosis.[1] Studies have found that between 25% and 50% of people with first-episode substance-induced psychosis subsequently transition to a chronic psychotic disorder.[1,2] Less is known about the risk of transition for people with substance use presentations without psychosis (eg, for acute intoxication), despite them being far more common.[3,4] In addition, detailed risk factors for transitioning for individuals with substance use, either with or without psychosis, are lacking. Substance use–related emergency department (ED) visits are increasing in high-income countries.[5-7] There is also concern that cannabis legalization may increase cannabis-related ED visits.[6,8] Consequently, clinicians need information on the prognosis of substance-related ED visits, with implications for counseling and referral.

Our aim was to estimate the risk of transitioning to schizophrenia spectrum disorder following an ED visit for substance use in an individual without a history of psychosis. We had 2 objectives. First, we wanted to estimate the relative risk of transition and absolute number of transitions following incident ED visits for substance-induced psychosis and substance use without psychosis. Second, we wanted to compare differences in transition by substance type, age, and sex.

Key Points

Question What is the risk of developing schizophrenia spectrum disorder following an emergency department (ED) visit caused by substance use with and without psychosis?

Findings In this cohort study of 9.8 million people, individuals with an ED visit for substance-induced psychosis or substance use without psychosis were at increased risk of developing schizophrenia spectrum disorder within 3 years relative to the general population.

Meaning These findings suggest that people who present to the ED for substance use, with or without psychosis, are at increased risk of developing schizophrenia spectrum disorder.

Methods

Study Design, Population, and Data Sources

We conducted a cohort study of all Ontario, Canada, residents, aged 14 to 65 years, between January 2008 and March 2022, who were eligible for the province's health coverage, which provides universal access to all hospital and medically necessary physician-based services. Data on all ED visits, hospitalizations, and outpatient physician visits and sociodemographic characteristics were obtained using 6 individual-level linked databases. Individual-level data on race and ethnicity are not available within the ICES (formerly known as the Institute for Clinical Evaluative Sciences) databases and were not used in this study. We excluded individuals who had 1 or more hospitalizations, ED visits, or outpatient visits for psychosis (substance induced, affective, or nonaffective) in the preceding 2 years. We identified all individuals with substance use ED visits with and without psychosis and examined substance subtypes (cannabis, cocaine, amphetamines, polysubstance use, alcohol, and other) (see eMethods 1 in Supplement 1 for details). This project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which authorizes ICES to collect personal health information without consent for health system management, evaluation, monitoring, or planning.

Outcome

Transition to schizophrenia spectrum disorder was defined, using a medical record–validated algorithm, as a diagnosis of schizophrenia or schizoaffective disorder (*International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* [*ICD-10*] code F20x or F25x and *DSM-IV* code 295x) from a general or psychiatric hospital bed, or from 2 or more outpatient visits or ED visits, occurring within 12 months of each other (eMethods 2 in Supplement 1).[9]

Statistical Analysis

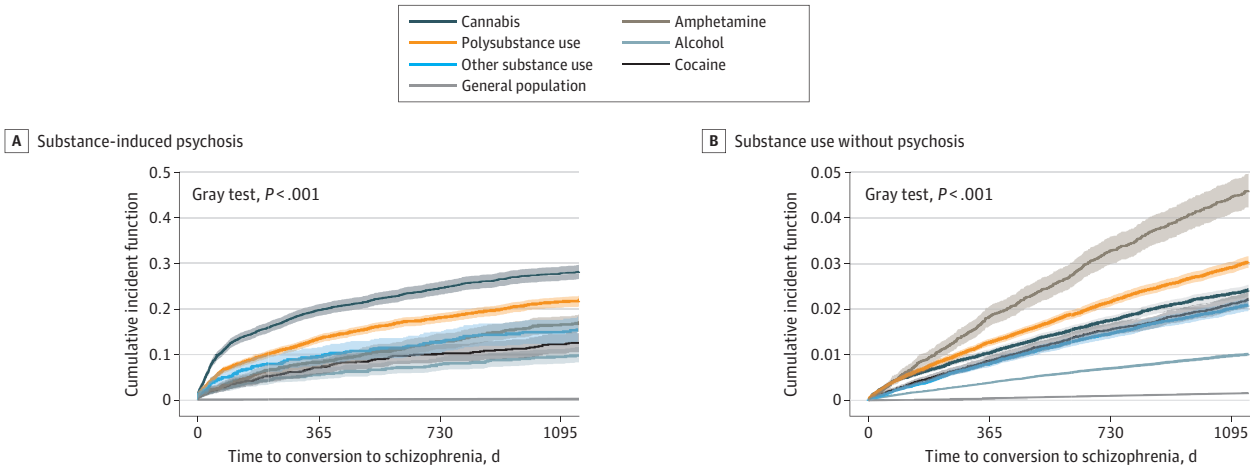
We evaluated the risk of transition to a diagnosis of schizophrenia spectrum disorder for individuals with an ED visit for substance use and for the general population. Members of the general population were assigned an index date matching the index date distribution of the substance-induced psychosis group (eMethods 3 in Supplement 1). We calculated cumulative incidence functions and cause-specific Cox proportional hazards for the transition to schizophrenia spectrum disorder, relative to the general population of Ontario, both overall and by substance type, accounting for the competing risk of all-cause mortality. We ran 2 models: (1) adjusted for age and sex only and (2) further adjusted for clinically relevant prespecified variables: neighborhood income quintiles, rural residence, prior acute mental health care (for mood, anxiety, self-harm, or other), prior outpatient mental health care (family medicine or psychiatry), and type of substance at incident visit. We estimated cause-specific Cox models to identify factors associated with transition, including age-sex interactions (see eMethods 3 in Supplement 1 for model details).

Results

Our 14-year cohort included 9 844 497 people (mean [SD] age, 40.2 [14.7] years; 50.2% female) without a history of psychosis, of whom 407 737 (4.1%) had an incident ED visit for substance use (eTable 1 in Supplement 1 lists patient characteristics). Of the 407 373 individuals with incident ED visits for substance use, 13 784 (3.4%) had a substance-induced psychosis ED visit. There was wide variation in risk of transition based on substance type and presence of substance-induced psychosis (**Figure 1**).

Within 3 years, 18.5% of people with an ED visit for substance-induced psychosis (range, 8.9% for alcohol to 26.0% for cannabis) and 1.4% of people with substance use without psychosis (range, 0.9% for alcohol to 3.7% for amphetamines) transitioned. Relative to the general population, the

Figure 1. Risk of Transition to Schizophrenia Spectrum Disorder Based on Substance Type and Presence of Substance-Induced Psychosis



No. at risk				
Cannabis	3557	2349	1695	1300
Alcohol	1379	1091	911	769
Cocaine	1053	805	657	500
Amphetamine	1811	1370	975	654
Polysubstance use	5143	3680	2799	2193
Other substance use	841	610	475	390
General population	9771825	8255246	6697487	5467121

No. at risk				
Cannabis	65904	56074	46471	37675
Alcohol	254802	235000	219288	200103
Cocaine	39473	34812	30732	26563
Amphetamine	15570	13037	10850	8574
Polysubstance use	76341	68350	61459	54423
Other substance use	55434	48922	43495	38760
General population	9771825	8255246	6697487	5467121

Cumulative incidence function curves comparing transition to schizophrenia spectrum disorder following first-presentation emergency department visits for substance-induced psychosis (A) and substance use without psychosis (B) compared with the general population over 3 years.

risk of transition was 163.2-fold greater (age- and sex-adjusted hazard ratio [age-sex HR], 163.2; 95% CI, 156.1-170.5) and 9.8-fold greater (age-sex HR, 9.8; 95% CI, 9.8-10.2) for individuals with ED visits for substance use with and without psychosis, respectively. After adjustment for further variables, ED visits for substance-induced psychosis (further-adjusted hazard ratio [further-adjusted HR], 62.0; 95% CI, 58.8-65.4) and substance use without psychosis (further-adjusted HR, 4.8; 95% CI, 4.6-5.0) had an attenuated but still elevated risk of transition. Cannabis was the highest-risk substance-induced psychosis (age-sex HR, 241.6; 95% CI, 225.5-258.9). For substance use without psychosis, amphetamines (age-sex HR, 28.4; 95% CI, 26.1-30.9), polysubstance use (age-sex HR, 18.7; 95% CI, 17.8-19.6), and cannabis (age-sex HR, 14.3; 95% CI, 13.5-15.2) were the highest-risk presentations. Substance use visits without psychosis were far more common than visits with psychosis, and they incurred more than 3 times the absolute number of transitions (9969 vs 3029) (**Table**).

Figure 2 shows the risk of transition within 3 years based on age, sex, and substance use. For all substance use ED visits, younger age and male sex were associated with a higher risk of transition. There were significant age-sex interactions in which the transition risk of male sex relative to female sex was greater in younger individuals, particularly for cannabis use. For example, the risk of transition within 3 years for cannabis-induced psychosis in males relative to females was significantly greater (for the interaction, $P = .03$) for people aged 14 to 18 years (41.3% vs 16.8%; further-adjusted HR, 2.3; 95% CI, 1.5-3.7) compared with people aged 45 to 65 years (17.2% vs 17.0%; further-adjusted HR, 0.9; 95% CI, 0.5-1.6). eTable 2 in Supplement 1 provides complete adjusted risk factors from multivariable models and age-sex interaction *P* values.

Discussion

In this population-based study of 9.8 million people, we found that among individuals with an ED visit for substance use, 18.5% with substance-induced psychosis and 1.4% with substance use without psychosis transitioned to schizophrenia spectrum disorder within 3 years, rates 163.2 and 9.8 times higher, respectively, than the general population (0.1%). Consistent with prior research, substance-induced psychoses, particularly for cannabis use, were at a high risk of transition.[1,2,10] Adding to the literature, we found that substance use without psychosis presentations were also at elevated risk of transition; and given their higher prevalence, they were associated with 3 times the absolute number of transitions. Consequently, primary prevention efforts aimed at reducing substance use and substance use disorders could substantially reduce the population-level burden of chronic psychoses.[11,12]

Our findings also highlight the need for targeted secondary prevention providing early intervention and reducing substance use in the highest-risk groups, which may delay or prevent transition to schizophrenia spectrum disorders.[13-15] Our approach to visually displaying the risk of transition (Figure 2) may help guide conversations between health care practitioners and patients and facilitate clinical decisions. The elevated risk associated with cannabis, particularly for young men, has

Table. Risk of Transition to Schizophrenia Spectrum Disorder Following a First-Presentation Emergency Department Visit for Substance Use With or Without Psychosis

	All substances	Cannabis	Polysubstance	Amphetamines	Other[a]	Cocaine	Alcohol	General population
Substance-induced psychosis								
Population at risk, No.	13 784	3557	5143	1811	841	1053	1379	771 825
Transition, No. (%)[b]	3029 (22.0)	1062 (29.9)	1227 (23.9)	299 (16.5)	138 (16.4)	140 (13.3)	163 (11.8)	20 248 (0.2)
Transition in 1 y, No. (%)	1792 (13.0)	714 (20.1)	695 (13.5)	149 (8.2)	81 (9.6)	75 (7.1)	78 (5.7)	3891 (0.0)
Transition in 3 y, No. (%)	2552 (18.5)	925 (26.0)	1016 (19.8)	256 (14.1)	115 (13.7)	117 (11.1)	123 (8.9)	11 014 (0.1)
Transition in 5 y, No. (%)	2831 (20.5)	1005 (28.3)	1139 (22.1)	283 (15.6)	132 (15.7)	134 (12.7)	138 (10.0)	15 407 (0.2)
Age at transition, mean (SD), y	29.7 (10.4)	26.3 (8.9)	30.4 (10.5)	33.1 (9.2)	30.4 (9.9)	32.0 (9.0)	37.4 (13.1)	39.9 (14.7)
Crude transition per 100 000 person-years[c]	5579.0	9112.6	5952.9	4987.6	3588.6	3028.7	1944.9	26.0
Age- and sex-standardized transition per 100 000 person-years[c]	4357.9	6863.7	4993.7	4215.5	3280.5	2601.0	1954.6	26.5
Age- and sex-adjusted HR (95% CI)[c]	163.2 (156.1-170.5)	241.6 (225.5-258.9)	176.5 (165.3-188.4)	131.3 (116.0-148.7)	120.6 (100.3-145.0)	94.1 (78.4-113.0)	78.0 (65.3-93.2)	1 [Reference]
Further-adjusted HR (95% CI)[c,d]	62.0 (58.8-65.4)	84.9 (78.7-91.6)	48.8 (45.1-52.7)	22.3 (19.2-25.9)	22.0 (18.0-26.8)	16.6 (13.5-20.3)	16.3 (13.5-19.8)	1 [Reference]
Substance use without psychosis[e]								
Population at risk, No.	400 144	65 904	76 341	15 570	55 434	39 473	254 802	9 771 825
Transition, No. (%)[b]	9969 (2.5)	2041 (3.1)	3630 (4.8)	838 (5.4)	1910 (3.4)	1400 (3.5)	4864 (1.9)	20 248 (0.2)
Transition in 1 y, No. (%)	2583 (0.6)	646 (1.0)	935 (1.2)	268 (1.7)	425 (0.8)	327 (0.8)	947 (0.4)	3891 (0.0)
Transition in 3 y, No. (%)	5555 (1.4)	1277 (1.9)	2015 (2.6)	575 (3.7)	984 (1.8)	731 (1.9)	2283 (0.9)	11 014 (0.1)
Transition in 5 y, No. (%)	7433 (1.9)	1652 (2.5)	2692 (3.5)	710 (4.6)	1368 (2.5)	1009 (2.6)	3252 (1.3)	15 407 (0.2)
Age at transition, mean (SD), y	34.2 (12.8)	28.1 (10.0)	34.2 (12.0)	31.9 (9.8)	36.1 (12.1)	35.5 (10.9)	35.0 (13.3)	39.9 (14.7)
Crude transition per 100 000 person-years[c]	222.7	430.2	436.0	886.6	291.7	335.8	131.1	26.0
Age- and sex-standardized transition per 100 000 person-years[c]	206.2	354.7	385.2	825.4	273.0	360.2	128.0	26.5
Age- and sex-adjusted HR (95% CI)[c]	9.8 (9.5-10.2)	14.3 (13.5-15.2)	18.7 (17.8-19.6)	28.4 (26.1-30.9)	13.2 (12.4-14.1)	13.3 (12.3-14.3)	6.1 (5.8-6.4)	1 [Reference]
Further-adjusted HR (95% CI)[c,d]	4.8 (4.6-5.0)	5.2 (4.9-5.6)	5.9 (5.5-6.2)	6.1 (5.6-6.8)	3.5 (3.2-3.7)	3.7 (3.4-4.0)	3.3 (3.2-3.5)	1 [Reference]

Abbreviation: HR, hazard ratio.

[a] Opioids, sedatives, hallucinogens, and volatile substances.

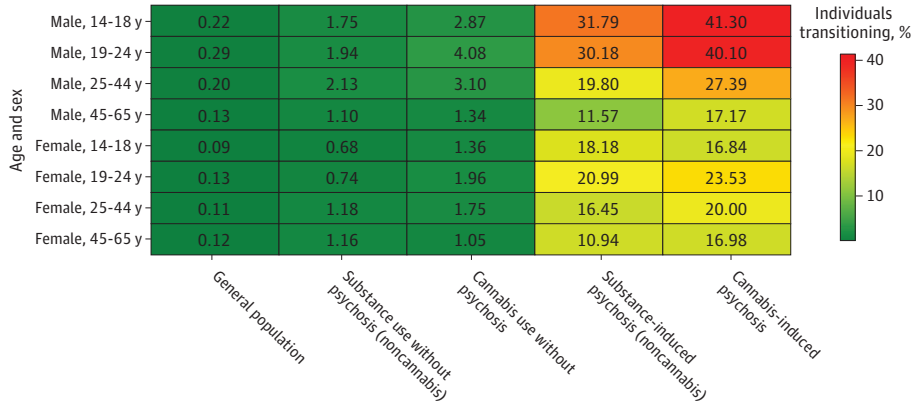
[b] Transitions over maximum follow-up period available.

[c] Transition rates and hazard ratios at 3 years of follow-up.

[d] Adjusted for age, sex, neighborhood income quintile, rurality, past 2 years outpatient mental health service use (family medicine yes/no and psychiatry yes/no), past 2 years immediate care substance use (cannabis yes/no, polysubstance use yes/no, amphetamine use yes/no, other substance use yes/no, cocaine yes/no, and alcohol yes/no), and past 2 years immediate care mental health use (anxiety yes/no, depression yes/no, self-harm yes/no, and other mental health condition yes/no).

[e] Individuals with more than 1 first-presentation emergency department (ED) visit for substance use without psychosis (eg, during the study, had a first-presentation ED visit for cannabis and a first-presentation ED visit for alcohol) had 1 ED visit randomly selected. Individuals with substance use without psychosis could also be in the general population based on the timing of ED visit and type of substance.

Figure 2. Risk of Transition to Schizophrenia Spectrum Disorder Within 3 Years Based on Age, Sex, and Substance Use



Visual representation of crude percentage of individuals transitioning to a diagnosis of schizophrenia spectrum disorder within 3 years of different types of first-presentation emergency department visits for substance use and the general population.

implications for public messaging and policy interventions in regions pursuing cannabis legalization.[8]

Limitations

Our analysis has limitations. First, we did not have detailed data on substance-related outpatient visits or patterns of substance use, which may provide additional prognostic information. Further research examining the risk of transition following different types of encounters for substance use is indicated. Second, our study design cannot infer causality, and the observed association between substance use and risk of schizophrenia is likely bidirectional.[4]

Conclusions

The findings of this cohort study suggest that individuals with ED visits for substance use are at elevated risk of developing a schizophrenia spectrum disorder. The ED visits for substance use without psychosis were lower risk but more common and contributed to a higher absolute burden. Several prognostic factors, including cannabis use, younger age, and male sex, were associated with greater risk of transition, with clinical and policy implications.

ARTICLE INFORMATION

Accepted for Publication: July 28, 2023.

Published Online: September 27, 2023. doi:10.1001/jamapsychiatry.2023.3582

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Author Contributions: Dr Myran and Mr Pugliese had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Myran, Harrison, Solmi, Anderson, Fiedorowicz, Perlman, Webber, Finkelstein, Tanuseputro.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Myran, Harrison, Solmi, Perlman.
Critical review of the manuscript for important intellectual content: Myran, Harrison, Pugliese, Solmi, Anderson, Fiedorowicz, Webber, Finkelstein, Tanuseputro.
Statistical analysis: Myran, Harrison, Pugliese, Webber.
Obtained funding: Myran, Tanuseputro.
Administrative, technical, or material support: Harrison, Fiedorowicz.
Supervision: Myran, Solmi, Tanuseputro.

Conflict of Interest Disclosures: Dr Myran reported receiving grants from the Canadian Institutes of Health Research during the conduct of the study. Dr Solmi reported receiving honoraria for participation on advisory boards or presentations from AbbVie, Angelini, Lundbeck, and Otsuka outside the submitted work. No other disclosures were reported.

Funding/Support: Dr Myran was supported with a Research Fellow Salary Award from the Canadian Institutes of Health Research and the University of Ottawa Department of Family Medicine. Dr Tanuseputro was supported by a Physician Services Incorporated Graham Farquharson Knowledge Translation Fellowship. This study was supported by the University of Ottawa site of ICES (formerly known as the Institute for Clinical Evaluative Sciences), which is funded by an annual grant from the Ontario Ministry of Health and Ministry of Long-Term Care. This study also received funding by grant 452360 from the Canadian Institutes of Health Research.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The analyses, conclusions, opinions, and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

Data Sharing Statement: See Supplement 2.

Additional Information: Parts of this material are based on data and/or information compiled and provided by the Canadian Institute for Health Information.

REFERENCES

1. Murrie B, Lappin J, Large M, Sara G. Transition of substance-induced, brief, and atypical psychoses to schizophrenia: a systematic review and meta-analysis. *Schizophr Bull*. 2020;46(3):505-516. doi:10.1093/schbul/sbz102

2. Starzer MSK, Nordentoft M, Hjorthøj C. Rates and predictors of conversion to schizophrenia or bipolar disorder following substance-induced psychosis. *Am J Psychiatry*. 2018;175(4):343-350. doi:10.1176/appi.ajp.2017.17020223

3. Nielsen SM, Toftdahl NG, Nordentoft M, Hjorthøj C. Association between alcohol, cannabis, and other illicit substance abuse and risk of developing schizophrenia: a nationwide population based register study. *Psychol Med*. 2017;47(9):1668-1677. doi:10.1017/S0033291717000162

4. Khokhar JY, Dwiel LL, Henricks AM, Doucette WT, Green AI. The link between schizophrenia and substance use disorder: a unifying hypothesis. *Schizophr Res*. 2018;194:78-85. doi:10.1016/j.schres.2017.04.016

5. Degenhardt L, Charlson F, Ferrari A, et al; GBD 2016 Alcohol and Drug Use Collaborators. The global burden of disease attributable to alcohol and drug use in 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Psychiatry*. 2018;5(12):987-1012. doi:10.1016/S2215-0366(18)30337-7

6. Myran DT, Pugliese M, Tanuseputro P, Cantor N, Rhodes E, Taljaard M. The association between recreational cannabis legalization, commercialization and cannabis-attributable emergency department visits in Ontario, Canada: an interrupted time-series analysis. *Addiction*. 2022;117(7):1952-1960. doi:10.1111/add.15834

7. Suen LW, Makam AN, Snyder HR, et al. National prevalence of alcohol and other substance use disorders among emergency department visits and hospitalizations: NHAMCS 2014-2018. *J Gen Intern Med*. 2022;37(10):2420-2428. doi:10.1007/s11606-021-07069-w

8. Murray RM, Hall W. Will legalization and commercialization of cannabis use increase the incidence and prevalence of psychosis? *JAMA Psychiatry*. 2020;77(8):777-778. doi:10.1001/jamapsychiatry.2020.0339

9. Kurdyak P, Lin E, Green D, Vigod S. Validation of a population-based algorithm to detect chronic psychotic illness. *Can J Psychiatry*. 2015;60(8):362-368. doi:10.1177/070674371506000805

10. Niemi-Pynttäri JA, Sund R, Putkonen H, Vorma H, Wahlbeck K, Pirkola SP. Substance-induced psychoses converting into schizophrenia: a register-based study of 18,478 Finnish inpatient cases. *J Clin Psychiatry*. 2013;74(1):e94-e99. doi:10.4088/JCP.12m07822

11. Anglin DM, Galea S, Bachman P. Going upstream to advance psychosis prevention and improve public health. *JAMA Psychiatry*. 2020;77(7):665-666. doi:10.1001/jamapsychiatry.2020.0142

12. Toumbourou JW, Stockwell T, Neighbors C, Marlatt GA, Sturge J, Rehm J. Interventions to reduce harm associated with adolescent substance use. *Lancet*. 2007;369(9570):1391-1401. doi:10.1016/S0140-6736(07)60369-9

13. Stafford MR, Jackson H, Mayo-Wilson E, Morrison AP, Kendall T. Early interventions to prevent psychosis: systematic review and meta-analysis. *BMJ*. 2013;346(7892):f185. doi:10.1136/bmj.f185

14. Fusar-Poli P, Spencer T, De Micheli A, Curzi V, Nandha S, McGuire P. Outreach and support in South-London (OASIS) 2001-2020: twenty years of early detection, prognosis and preventive care for young people at risk of psychosis. *Eur Neuropsychopharmacol*. 2020;39:111-122. doi:10.1016/j.euroneuro.2020.08.002

15. Archie S, Rush BR, Akhtar-Danesh N, et al. Substance use and abuse in first-episode psychosis: prevalence before and after early intervention. *Schizophr Bull*. 2007;33(6):1354-1363. doi:10.1093/schbul/sbm011