Appendix A.

First-episode studies without specialized substance use disorder treatment

Author	Design, Follow-up Period, and Country	Participants	Groups	Measures and Method (if available)	Substance use outcomes	Mental health outcomes	Functional outcomes	Study Dropout (if available)
Archie et al. (91)	Prospective cohort study. Follow-up: 12 months. Canada.	N=200 new in- and outpatients, ages 16-50. 78% of clients were male, 61% were white, and mean age was 24. Diagnoses were schizophrenia (48%), schizophreniform (17%), schizoaffective (10%), delusional disorder (4%), brief psychotic disorder (3%), or psychotic disorder NOS (19%). 60% of clients had lifetime cannabis use; 38% current drug abuse, 26% current hazardous alcohol use, 18% current heavy drinking.	Comparison 1: Patients with drug abuse vs. Patients who did not meet criteria for drug abuse Comparison 2: Patients with concurrent drug abuse and hazardous alcohol use vs. Patients who did not meet this criteria Comparison 3: Patients with hazardous alcohol use vs. Patients without alcohol misuse	Diagnoses: Structured Clinical Interview for DSM (SCID)-IV (2). Substance use: Alcohol Use Disorders Identification Test (AUDIT) (3). Drug Abuse Screening Test (DAST) (4). Assessments conducted by non-clinical, research staff.	At 12-month follow-up, significant reductions occurred in drug abuse (32% to 17%), hazardous alcohol use (21% to 10%), and concurrent drug abuse and hazardous alcohol use (11% to 2%), but not in heavy drinking (16% to 13%).	No significant differences in prevalence of involuntary hospitalizations between drug abusers and non-drug abusers, hazardous alcohol users and non-hazardous users, and concurrent abusers and non-concurrent abusers at 12 months.	No significant differences in prevalence of arrests between drug abusers and non-drug abusers, hazardous alcohol users and non-hazardous users, and concurrent abusers and non-concurrent abusers at 12 months.	N=49 missing at follow-up. No significant baseline differences between missing and non-missing.
Baeza et al. (5)	Case control study. Follow-up: 6 months after first admission Spain.	N=110 youth with first-episode psychosis, ages 9-17, who were new admissions to psychiatry departments. 67% of clients were male with mean age 16 years. Clients used	Cannabis users vs. Non-cannabis users	Diagnoses: Kiddie Schedule for Affective Disorders and Schizophrenia (6). Substance	Cannabis use decreased significantly at six months (from n=32 to n=15), but alcohol and other drug use did not. Cannabis	Although cannabis users had significantly higher positive symptoms at the initial assessment, they had lower positive,	No functional outcomes	N=9 missing at follow-up.

		cannabis (29%), alcohol (22%), cocaine (8%), and smaller proportions of other drugs.		use: urine toxicology Self-report measure not reported. Assessments conducted by clinical staff.	users had higher positive symptoms at initial assessment, but at six months they had lower positive, negative, general, and total symptom scores, especially those who stopped using.	negative, general, and total negative symptom scores at 6 months, especially among those who stopped using cannabis, compared to the non-cannabis users		
Grech et al. (7)	Prospective cohort study. Follow-up: 4 years. United Kingdom.	N=119 patients <60 years old with recent onset psychosis. 66% were male, 33% were African/African-Carribean, and mean age was 25 years. Diagnoses were schizophrenia (42%), affective psychoses (26%), schizoaffective (9%), delusional disorder (9%), atypical psychosis (7%), and schizophreniform (6%). 38% reported cannabis use at admission.	(1) History of cannabis use at index but not follow up, (2) No history of cannabis use at index and use at follow up, (3) History of cannabis use at index and use at follow up (4) No use at either index or follow up	Diagnoses: Present State Examination (8) and Operational Criteria Checklist (9). Substance use: Self-report semi-structured interview unknown. Follow-up assessments conducted by research staff blind to admission data.	Of 25 clients with cannabis use at baseline, 9 (36%) reported abstinence at follow-up.	There was a significant increase in course of illness for clients with history of cannabis use at index and use at follow up. There was a significant increase in positive psychotic symptoms for clients with history of cannabis use at index and use at follow up. There were no significant differences in negative psychotic symptoms between no	No functional outcomes	Complete data on 98 of 119 clients. No significant baseline differences between missing and non-missing data.

						cannabis use group and any of the groups. There were no significant differences in illness course and positive psychotic symptoms between no cannabis and other groups, including clients wtih history of cannabis use at index but not follow-up and clients with no history of cannabis use at index and use at follow-up.		
Harrison et al. (10)	Prospective cohort study. Follow-up: 14 months. United Kingdom.	N=85 clients 16-50 years, with first-episode schizophrenia. 74% had a history of substance use. 48% of sample was male; mean age 26 years.	Comparison 1: (a) Persistent non-users (b) Persistent users Comparison 2: (a) No history of substance use (b) Baseline only users	Diagnoses: DSM-IV, assessed by two senior clinicians Substance use: Substance Use Rating Scale (11, 12).	Over 14 months, current use of cannabis decreased from 32% to 18.5% and problem drinking decreased from 30% to 15%.	Persistent users had significantly higher scores for positive syndrome, overall severity of illness and depressive features. No significant differences for negative and disorganization syndromes but positive syndrome scores changed over	There were no main effects of group for any of the cognitive function measures.	N=67 missing follow-up data. No significant baseline differences between missing and non-missing.

						time across groups.		
Kovasznay et al. (13)	Longitudinal observation study. Follow-up: 6 months. United States.	N=176 clients with schizophrenia (N=87) or affective psychosis (N=89). Median age was 28; 51% were male and 22% were nonwhite. Most common substance of abuse was alcohol.	Lifetime substance use disorder vs. no lifetime substance use disorder	Diagnoses: SCID-III (14). Follow-up diagnoses obtained by two psychiatrists and consensus panel.	Clients with affective psychosis and a history of substance use disorders were more likely to be drinking alcohol at least weekly.	In the schizophrenia group, individuals with lifetime substance use disorder had psychiatric functioning via the BPRS. There were no differences in positive or negative symptoms or current hallucinations or delusions.	In the schizophrenia group, individuals with lifetime substance use disorder had lower past month functioning.	N=31 missing follow-up data. No significant baseline differences between missing and non-missing.
Lambert et al. (15) and Hinton et al. (16).	Prospective cohort study. Follow-up: 18 months. Australia.	N=643 new admissions, ages 15-29, with first-episode psychosis diagnoses of schizophreniform (42%), schizophrenia (23%), schizoaffective (7%), bipolar I with psychotic symptoms (20%), and other psychoses. Most were male (66%);	Decreased or remitted substance use disorder vs. persistent substance use disorder vs. no substance use disorder.	Diagnoses: DSM-IV assessment with reliability assessment of 115 randomly selected clients using SCID-IV (17). Baseline and follow-up assessments	At 18 months, 155 (37.9%) were abstinent, 91 (22.2%) had decreased use, and 163 (39.9%) had persistent substance use disorders.	Clients with decreased or remitted substance use disorder were more likely to be in remission of positive symptoms than clients with persistent substance use disorder. Clients with decreased or	No functional outcomes	N=291 had missing 18-month follow-up data. Differences between missing and non-missing unknown.

		mean age 22 years. Baseline substance use disorders were cannabis (71%), polysubstance (16%), and other substances (13%).		conducted by clinicians.		remission of SUD had increased probability of psychotic symptom remission and clients with persistent substance use disorder had decreased probability of remission.		
Turkington et al. (18)	Prospective cohort study. Follow-up: 1 year. Ireland.	N=188 individuals with first-episode psychosis, ages 18-64, from general psychiatric services. Mean age was 34 years, with 62% male.	Individuals with substance misuse at both baseline and 1 year follow up vs. Individuals with substance misuse at baseline but not follow up vs individuals with no substance misuse at either baseline or follow up.	Diagnoses: Operational Criteria Checklist for Psychotic Illness (9). Information on assessors unknown.	At baseline, 43% had substance misuse (abuse or dependence), mostly alcohol and/or cannabis. At one-year follow-up, the rate of substance misuse decreased to 22.9%.	Those who persisted with substance misuse had more depressive symptoms at baseline. At follow-up, persistent misusers had more depressive symptoms, more positive symptoms of psychosis, and more relapses.	Persistent users had worse global functioning than those who stopped or never used.	N=91 missing from follow-up data (n=6) or not eligible because of diagnosis (n=85).
Verdoux et al. (19)	Prospective cohort study. Follow up: 2 years. France.	N=65 individuals with psychosis admitted to acute ward of regional psychiatric hospitals. Sample was 62% men, with mean age of 32 years. Diagnoses were schizophrenia (37%) and other psychotic disorders (63%),	Long (>3 months) vs short (<3 months) duration of untreated psychosis	Diagnoses: DSM-IV using Life Chart and hospital records. Substance use: Life chart and hospital records.	At baseline 20 clients (30.8%) had a history of alcohol use disorder, and 15 (23.1%) had a history of drug use disorder. By six months, alcohol and drug use	No psychiatric outcomes by substance use disorder status.	No functional outcomes by substance use disorder status.	N=1 missing at 1-year follow-up; N=6 missing at 18 and 24 months. No significant baseline differences

		with 31% having history of alcohol use disorder and 23% having history of drug use disorders at baseline.		Assessments conducted by clinical psychologist and psychiatrist.	decreased to 5 of 64 (7.8%) and 4 of 64 (6.3%). The lower proportions remained stable for two years.			between missing and non-missing.

Author	Design, Follow-up Period, and Country	Participants	Interventions	Measurement	Substance use outcomes	Mental health outcomes	Functional outcomes	Study Dropout
Addington et al. (20)	Prospective cohort study. Follow-up: 3 years Canada.	N=203 inpatients and outpatients enrolled in Calgary Early Psychosis Program, with no more than three months previous treatment. 70% of clients were male; 77% were single; mean age = 25 years. Most clients had schizophrenia (70%); other diagnoses were schizophreniform, (15%) and other psychoses. 48% of clients had no substance abuse diagnosis; the most common abuse or dependence diagnoses were alcohol (16%), cannabis (15%), or both (11%).	Early intervention program that integrates substance abuse treatment, which is "addressed at each stage of the program, including the work with families."	Diagnoses: SCID-IV (17). Substance use: Case Manager Rating Scale for Substance Use Disorders (21). Assessments were conducted by trained research clinicians.	Between baseline and year 1, substance misuse significantly declined. Little additional improvement between year 1 and 2. Significant decline in the number of clients with an alcohol, cannabis, and other drug use disorders over the 3-year period.	No significant differences in mental health symptoms at each follow up between alcohol users and non-users; significantly more positive symptoms and levels of depression among cannabis users at one year follow up, even after controlling for demographics	No significant differences in quality of life between alcohol users and non-users at any follow up; lower quality of life found in cannabis users than non-cannabis users in year 2 but no significant differences found in year 1 or 3. The mild use and substance misuse groups had higher equal or better cognition at follow up than non-users; compared to mild users or misusers, non-users scored more poorly on cognitive tasks of verbal memory, verbal fluency,	N=44 missing at 2 years. N=16 missing at 3 years. No significant differences in missing and non-missing except those missing at year 2 had higher negative symptoms at year 1, and those missing at year 3 had higher negative symptoms at year 2.

							cognitive flexibility, and visuospatial ability at year 1, and verbal memory, verbal fluency, and visuospatial ability at year 2 follow-up.	
Carr et al. (22)	Prospective cohort study. Follow-up: 18 months. Canada.	N=243 first-episode psychosis outpatients enrolled in the Early Intervention Program for Psychoses (PEPP) who were diagnosed with first-episode of psychosis, between 16-50 years of age, and met criteria for alcohol or drug abuse at baseline. Sample is 78% males and mean age = 25 years. Majority of sample (72%) diagnoses with schizophrenia spectrum; others were psychosis NOS (9%), mood disorders (7%),	PEPP (group-based program) clients who met criteria for alcohol or drug abuse at baseline vs. PEPP clients who did not meet criteria for alcohol or drug abuse at baseline	Diagnoses: SCID-III (14). Substance use: AUDIT (3) and DAST (4). Assessments conducted by masters-level research assistants. Diagnoses confirmed based on clinical review and clinical opinion by consulting psychiatrist.	Decreased alcohol and drug misuse at 3 months, especially for clients with alcohol diagnosis; at 6 and 18 months, alcohol reductions maintained for clients without an alcohol diagnosis but worsened for clients with an alcohol diagnosis; drug reductions maintained by both groups at 6 and 18 months	No mental health outcomes	No functional outcomes	N=48 to 97 clients were missing substance use follow-up data. No significant differences in missing data between those with and without substance use diagnoses.

		and substance-induced psychosis (8%). Drugs of choice were primarily cannabis (61%), cannabis and alcohol (20%), and alcohol (9%).						
Edwards et al. (23)	Single-blind randomized control trial. Follow-up: 3, 6 months post-intervention Australia.	N=47 outpatient youth newly admitted to integrated mental health service for cannabis-use with first-episode psychosis. Most were diagnosed with schizophrenia or schizophreniform disorders (71.7%), followed delusional or other psychosis (17.4%) and affective psychosis (10.9%). Almost half had a diagnosis of cannabis abuse or dependence (48.9%), and about three-quarters reported using cannabis in the past 4 weeks. There were no	Cannabis and Psychosis (CAP) Therapy for 3 months involving 10 weekly cognitive-behavioral harm minimization sessions delivered individually vs. Psychoeducation (PE)	Diagnoses: SCID-IV (17). Substance use: Cannabis and Substance Use Assessment Schedule (24). Information on assessors unknown.	No significant group differences in cannabis use or readiness to change outcomes	No significant group differences in psychopathology outcomes	No significant group differences in psychosocial functioning	Follow-up participation rates were similar across conditions (end of treatment: CAP, N=22, PE, N=23; and 6 months: CAP, N=23, PE, N=17).

		baseline differences with respect to demographic or clinical variables.						
Gleeson et al. (25)	Single-blind randomized control study. Follow-up: 7 months after starting treatment. Australia.	N=82 first-episode psychosis outpatients, ages 15-25, from the Early Psychosis Prevention and Intervention Center. 63% of clients were male, with average age 20 years. Clients had diagnoses of schizophrenia (33%), psychotic disorder NOS (30%), schizophreniform (11%), and other related disorders. Substance abuse/dependence was primarily cannabis (52%), alcohol (25%), amphetamine (19%), or hallucinogen (15%).	Relapse Prevention Treatment combined with usual treatment (individual and family-based cognitive-behavioral therapy) vs. treatment as usual	Diagnoses: SCID-IV (17). Substance use: WHO Alcohol, Smoking, and the Substance Dependence Scale (26). Assessments conducted by trained research staff.	No significant group differences in substance use measures	Decreased relapse rates (i.e., hospital readmissions); improved Scale for the Assessment of Negative Symptoms score; no significant group differences on other symptom measures or in medication adherence	No significant group differences in quality of life, health satisfaction, and social and occupational functioning	N=1 missing at follow-up. No significant baseline differences between missing and non-missing.
Kavanagh et al. (27)	Randomized control trial. Follow-up: 6	N=25 inpatients, ages 18–35, with early psychosis and	Standard care plus Start Over and Survive (SOS) curriculum, a 3-	Diagnoses: Clinical record review and consensus.	No significant group differences in substance use	No mental health outcomes assessed due	No functional outcomes	Any missing data at follow-up were rated as

	weeks, 6 months,12 months after starting treatment. Australia.	current misuse of non-opioid drugs. Sample was mostly male (60%) and white (84%) with mean age 23 years. 48% had a chart diagnosis of schizophrenia or schizophreniform disorders. 88% used alcohol and 76% used marijuana during the previous 3 months.	hour manualized intervention for substance misuse in early psychosis vs. Standard care only (medication, inpatient and aftercare services with case management or general practice consultations)	Substance use disorders confirmed by Composite International Diagnostic Interview (28). Operational Criteria Checklist (9). Assessments conducted by trained research staff blind to treatment condition.	at 6 and 12 months for a subset of those who were engaged in treatment and received motivational enhancement.	to attrition and missing data		“unimproved” on substance use.

Note: NOS=not otherwise specified

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