

Webtable 1: Summary of studies included for psychotic outcomes

Cohort label & author	Setting & sample size	Baseline screening	Cannabis measure & age	Exposure n (%)	Follow-up & attrition [‡]	Outcome, number & %	Confounders adjusted for	Main results	Dose response effects
CHDS ^{33,34}	Birth cohort, Christchurch, New Zealand (n = 1055)	SCL-90 for past month symptoms Ages 16, 18, & 21	Use since prior measure, ages 16, 18, 21, 25 Frequency of use past 1 year: None, <1/month >1/month, >1/week, daily	Age 18: 427 (42%) Age 21: 473 (47%) Age 25: 444 (44%)	Up to 7 years Attrition 17%	Ages 18, 21 & 25 Past month symptoms from Symptom Checklist 90 (SCL-90)	Past psychotic symptoms & cannabis use, past psychiatric disorders, other substance dependence, peer affiliations, childhood adversity, life events, IQ, personality traits, social, demographic and family variables Also used fixed effects model for non-observed fixed confounders	Ever use: [*] Crude OR = 1.9 (1.6 to 2.2) Adjusted OR = 1.3 (1.0 to 1.6) Frequency of use (adjusted): <1/month OR = 1.1 (1.1 to 1.2) >1/month OR = 1.3 (1.1 to 1.4) >1/week OR = 1.4 (1.1 to 1.7) Daily OR = 1.6 (1.2 to 2.0) Test for trend p < 0.001	Evidence from linear term for frequency of use
Dunedin ^{31, 32}	Birth cohort, Dunedin, New Zealand (n = 759)	DISC-C used for psychotic symptoms at age 11	Used cannabis >3 times Ages 15 & 18	Age 15 29 (3.8%) Age 18 236 (31%)	8-11 years Attrition 4%	DIS at age 26 used for past year: Psychotic symptoms ≈ 25% Schizophreniform disorder 25 (3.3%)	Stratified analyses adjusted for sex, socio-economic status, other drug use, psychotic symptoms at age 11 Whole sample analysis adjusted for confounders above and also IQ	Whole sample: [*] <i>Schizophreniform disorder</i> Crude OR = 3.1 (1.5 to 6.6) Adjusted OR = 2.9 (1.2 to 7.0) Cannabis use by age 15 [†] : <i>Schizophrenia symptoms</i> Adjusted β = 6.6 (0.9), p<0.001 <i>Schizophreniform disorder</i> Adjusted OR = 3.1 (0.7 to 13.3) Cannabis use age 15-18 [†] : <i>Schizophrenia symptoms</i> Adjusted β = 1.0 (0.4), p<0.01 <i>Schizophreniform disorder</i> Adjusted OR = 1.4 (0.5 to 3.7) Cannabis use by age 18 Stratified by COMT genotype [§] Adjusted results for <i>schizophreniform disorder</i> Val/val OR = 10.9 (2.2 to 54.1) Val/met OR = 2.5 (0.8 to 8.2) Met/met OR = 1.1 (0.2 to 5.4)	Not studied

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ECA ²⁴	Case-control nested within adult population based cohort study, USA (n = 2295)	DIS interview for psychotic symptoms	DIS interview for: Lifetime ever use & daily use 'Never used' included use of cannabis <5 times Age 18-49	Ever use: 381 (21%) Daily use: 87 (4.8%)	1 year Attrition 20%	DIS interview for any self-reported psychotic experience 507 (11.4%)	Age, gender, school attendance, educational level, marital status, employment status, baseline mental health problems (excluded if psychotic symptoms), other drug and alcohol use	Ever use: Crude OR = 1.3 (1.0 to 1.7) Adjusted (excluding other drugs) OR = 1.3 (1.0 to 1.7) Daily use: Crude OR = 2.4 (1.6 to 3.6) Adjusted (including other drugs) OR = 2.0 (1.3 to 3.1)	Not studied Stronger effect for daily use than ever use, though CI overlap
EDSP ²⁵	Adult population based cohort, Munich, Germany (n = 2437)	SCL-90-R used for paranoid and psychoticism subscales Scores summed, and identified as 'predisposed to psychosis' if score >90 th percentile	Ever use >5 times Frequency at heaviest: None, <1/month, 3-4/month, 1-2/week, 3-4/week, daily Ages 14-24	Ever use 320 (13.1%)	3-4 years Attrition 16%	M-CIDI used for: Broad psychosis (≥1 symptom) 424 (17.4%) Narrow psychosis (≥2 symptoms) 174 (7.1%)	Age, sex, socio-economic status, urbanicity, childhood trauma, other drug use, smoking, alcohol use, predisposition to psychosis	Broad psychosis (Ever use) Crude OR = 1.8 (1.4 to 2.4) Adjusted OR = 1.7 (1.1 to 2.5) Narrow psychosis (ever use) Adjusted OR = 2.2 (1.5 to 3.3) Broad psychosis (Frequency) Crude OR = 1.2 (1.2 to 1.4) Adjusted OR (but not for other substance use) = 1.2 (1.1 to 1.3)	Evidence from 6-level frequency of use variable examined as linear term (broad psychosis only reported)
NEMESIS ²⁶	Adult population based cohort, Netherlands (n = 4045)	CIDI for psychotic symptoms 47% of subjects with symptoms on CIDI re-interviewed with SCID	Lifetime ever use & Cumulative frequency from baseline to follow-up, summed as lowest, middle & highest levels Age 18-64	Ever use: 312 (7.6%)	3 years Attrition 30%	BPRS for: Any psychotic symptoms (BPRS>1) 38 (0.94%) Pathology level symptoms (BPRS>4) 10 (0.25%) 'Need for care' from CIDI, SCID, & BPRS 7 (0.17%)	Age, sex, ethnicity, marital status, education, urbanicity, discrimination, and other drug use Subjects with any lifetime ever psychotic symptoms at baseline excluded	Ever use: <i>Any symptoms</i> Crude OR = 3.3 (1.5 to 7.2) Adjusted OR = 2.1 (0.8 to 5.7) <i>Pathology level symptoms</i> Crude OR = 28.5 (7.3 to 110.9) Adjusted OR = 16.9 (3.3 to 86.1) <i>Need for care</i> Crude OR = 16.2 (3.6 to 72.5) Adjusted OR = 10.5 (1.8 to 63.2) Cumulative frequency <i>Any symptoms</i> Adjusted OR = 1.7 (1.0 to 2.7) <i>Pathology level symptoms</i> Adjusted OR = 3.7 (2.0 to 7.0) <i>Need for care</i> Adjusted OR = 3.5 (1.6 to 7.4)	Evidence from 3-level frequency of use variable examined as linear term

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NPMS ²⁷	Adult population based sample, UK (n = 2413) Over-sampled for baseline mental disorder	PSQ used for past year psychotic symptoms	Used in past year but not dependent Dependent past year Age 16-74	Used 109 (4.5%) Dependent 57 (2.4%)	18 months Attrition 32%	PSQ for psychotic symptoms since initial interview 134 (4.4%)	Psychotropic drugs and therapy, IQ score, marital status, urbanicity, support group, life events, smoking, alcohol, age, gender, CIS-R score at baseline	Used past year Crude OR = 1.1 (0.5, 2.5) Adjusted OR = 0.7 (0.3, 1.7) Dependent Crude OR = 3.4 (1.5, 7.7) Adjusted OR = 1.5 (0.6, 3.9)	Not studied Suggestion of increasing effect for dependent compared to non-dependent
Swedish conscripts ²⁸⁻³⁰	Adult population based conscript cohort, Sweden (n = 48,481)	Psychologist / psychiatrist interview for ICD-8 diagnoses	Ever use Frequency: None, 1 time, 2-4 times, 5-10 times, 11-50 times, >50 times Age 18-20	Ever use 5391 (10.8%) >50 times: 731 (1.5%)	27 years No data on attrition available	Admissions with ICD8/9 clinical diagnosis of schizophrenia / schizoaffective disorder 362 (0.7%)	Other drug use, IQ, social personality traits, other diagnoses at conscription (excluded if psychotic at baseline), place of birth, childhood behaviour, family history, alcohol use, family income, paternal occupation, tobacco use, paternal age	Ever use: Crude HR = 2.2 (1.7 to 2.8) Adjusted HR = 1.5 (1.1 to 2.0) Frequency of use: Crude HR = 1.4 (1.3 to 1.5) Adjusted HR = 1.2 (1.1 to 1.3) Stratified by age of first use: First use age ≤15 Adjusted HR for cumulative frequency = 1.2 (0.9 to 1.4) First use age >15 Adjusted HR for cumulative frequency = 1.2 (1.1 to 1.4)	Evidence from 6-level frequency of use variable examined as linear term

‡ Attrition based on proportion of subjects lost to study from baseline cannabis assessment to outcome assessment at follow-up; [†] Additional data kindly provided by study authors; [†] Results adjusting for other drug use not presented as uncertain validity (large increase in confidence intervals for schizophreniform disorder, indicating possible collinearity or problems related to small numbers); [§]val¹⁵⁸met

β = linear regression coefficient. BPRS = Brief psychiatric rating scale. CIDI = Composite international diagnostic interview. CIS-R = clinical interview schedule-revised. DIS = Diagnostic interview schedule. DISC-C Diagnostic interview schedule for children. DSM = Diagnostic and statistical manual of mental disorders. HR = hazard ratio, 95% confidence intervals in parentheses. ICD = International classification of diseases. M-CIDI = Munich version of CIDI. OR = odds ratio, 95% confidence intervals in parentheses. PSQ = Psychosis screening questionnaire. SCID = Structured clinical interview for DSM-III-R. SCL-90 = Symptom checklist 90. SEM = Structural equation modelling