BJPsych
The British Journal of Psychiatry (2008) 193, 357–363. doi: 10.1192/bjp.bp.107.046375

Table DS1 Summary of studies included for outcomes in psychosis (full version)

Cohort label	Setting and sample size at baseline	Baseline diagnoses	Cannabis measure	Exposure *n* (%)	Follow-up	Outcome *n* (%)	Main results	Confounders adjusted for	Other relevant points
Brisbane[9]	Consecutive in-patient admissions, Brisbane, Australia *n*=81	Recent onset (within 3 years) DSM–IV psychotic disorder	TLFB for days of cannabis use 6 weeks prior to admission and during follow-up Urine drug screening used to validate self-reports	Cannabis dependence year prior to admission: 57 (70.4)	6 months	Relapse[a] 27 (39)	Number of days of cannabis use associated with relapse Adjusted HR=1.06 (95% CI 1.02–1.10) (calculated from table) Good agreement between urine screening and self-report for cannabis use (Cohen's kappa=0.90; 60.5% of sample tested)	Baseline psychotic and affective symptoms, other substance use, medication adherence, duration of untreated psychosis, demographic variables, measures of social functioning prior to admission, life stress, and measures of family environment	Similar results if exclude substance-induced psychoses
Calgary[12]	Consecutive admissions of adolescents to Calgary Early Psychosis Program, Canada *n*=69	Incident cases of DSM–IV non-affective psychosis	CMRS for level of cannabis use (scale 0–4)	–	2 years	1. Quality of Life Scale at years 1 and 2 2. Employment or productivity at years 1 and 2	1. QOL Cannabis at baseline and cannabis at 1 year were both associated with ↓ QOL at 2 years ($P<0.05$) but these associations disappeared after adjustment 2. Employment/productivity Cannabis at baseline was associated with ↓ employment, and this persisted after adjustment: OR for 1-year unemployment=2.0 (95% CI 1.1–3.7) OR for 2-year unemployment=2.7 (95% CI 1.3–5.8)	Positive or negative symptoms at years 1 and 2	
CEPP[13]	Consecutive admissions to Calgary Early Psychosis Program Canada *n*=200	Incident cases of DSM–IV schizophrenia, schizophreniform disorder, other schizophrenia-spectrum disorders	CMRS for level of cannabis use	–	1 year	Adherence[b] (adherent, inadequate, non-adherent) Inadequate or non-adherence: 110 (59)	Increasing level of cannabis use at baseline was associated with ↓ 1-year adherence status, $P=0.04$ in crude analysis Non-significant in adjusted model (though this model includes cannabis use at 1-year)	Family involvement, premorbid function, age, 1-year cannabis use. Also probably alcohol use, age of onset, insight , quality of life, though not clear if these in final model	
HGDH[16]	Participants recruited as part of multicentre RCT in North America and Western Europe *n*=262	Incident cases (onset past 5 years) of DSM–IV schizophrenia, schizoaffective disorder or schizophreniform disorder	SCID interview for cannabis use disorder (dependent participants excluded)	74 (28)	12 weeks	1. Response:[c] 81 (32) 2. Mean change in PANSS total	1. Non-response OR in cannabis use disorder compared to non-use=1.08 (95% CI 0.90–1.29) 2. Change in PANSS total Olanzapine group, mean (s.d.) Cannabis use=15.9 (18) Non-cannabis=20.2 (23), $P=0.31$ Haloperidol group, mean (s.d.) Cannabis use=13.4 (18) Non-cannabis=18.6 (19), $P=0.39$	Non-response results adjusted for randomised treatment (haloperidol *v.* olanzapine)	

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Table DS1 *(continued)*

Cohort label	Setting and sample size at baseline	Baseline diagnoses	Cannabis measure	Exposure *n* (%)	Follow-up	Outcome *n* (%)	Main results	Confounders adjusted for	Other relevant points
Homburg[20]	Cohort from patients admitted to hospital between 1986–1992, with matched control cohort, Homburg, Germany *n*=78	Prevalent or incident ICD–10 schizophrenia Excluded if diagnosis of drug-induced psychosis	Cannabis misuse defined as regular use for many months and interfered with social function or was prominent in therapy. Controls had schizophrenia but no history of alcohol or drug use	39 (50)	About 6 years	1. GAS score 2. Rehospitalisation (admissions per year) 3. BPRS sub-scales: anxiety/depression, anergia, activation, hostile, thought disturbance 4. AMDP sub-scales: paranoid, depressive, psycho-organic, maniform, vegetative, apathetic, hostility 5. Single status 6. Living alone 7. Employment	1. GAS score, mean (s.d.): Cannabis misuse=55.7 (14.8) Non-misuse 62.5 (15.4), NS 2. Rehospitalisation, mean (s.d.): Cannabis misuse=0.98 (0.8); Non-misuse=0.35 (0.3), $P<0.001$ 3. BPRS sub-scales: Thought disturbance ↑ in cannabis misuse, $P<0.05$ Other sub-scales all NS 4. AMDP sub-scales: Hostility ↑ in cannabis misuse, $P<0.05$ Other sub-scales all NS 5. Single status: Cannabis misuse=89% Non-misuse=69%, NS 6. Living alone: Cannabis misuse=59% Non-misuse=65%, NS 7. Employment: NS Cannabis misuse=19% Non-misuse=46%, NS	Age, gender, and year of admission Some adjustment for alcohol and other drug use by restriction of cases (excluded if mainly misused drugs other than cannabis)	
Madrid-A[18]	Consecutive in-patient admissions, Spain *n*=63	Prevalent or incident DSM–IV schizophrenia or schizoaffective disorder	Cannabis misuse 7 days prior to admission (misuse not defined)	14 (22)	5 months	Score ⩾2 on OAS physical aggression sub-scale: 16 (25)	Cannabis use was not correlated with violent behaviour during hospitalisation No details of analysis given	None	
Madrid-B[19]	Out-patient sample, Madrid, Spain *n*=82	Prevalent or incident ICD–10 schizophrenia	Addiction Severity Index Scale	Cannabis dependence 20 (24)	6 months	1. PANSS scores 2. Relapse (not defined) 8 (9.8) 3. Non-adherence[d] 25 (30.5) 4. Admission to hospital 6 (7.3)	1. PANSS scores Cannabis dependence associated with ↓ negative symptoms, but no association with positive symptoms 2. Relapse Cannabis associated with ↑ OR[e]=3.6 (95% CI 0.6–21.4), P=0.08 3. Non-adherence Cannabis associated with ↑ OR[e]=3.1 (95% CI 1.0–10.2), P=0.03 4. Admission Cannabis associated with ↑ OR[e]=7.5 (95% CI 0.9–87.0); P=0.01	PANSS negative results adjusted for (some of) alcohol and other drug dependence, and socio-demographic variables	

Table DS1 *(continued)*

Cohort label	Setting and sample size at baseline	Baseline diagnoses	Cannabis measure	Exposure *n* (%)	Follow-up	Outcome *n* (%)	Main results	Confounders adjusted for	Other relevant points
Manchester[15]	Consecutive in-patient admissions, Manchester, UK *n*=112	Incident cases of psychosis	Cannabis use or non-use at baseline from self-report and informer-report	23 (36)	10–12 years	1. Deficit schizophrenia[f] 2. Neurocognitive function (9 tests) 3. SANS/SAPS 4. Service contact	1. Deficit schizophrenia ↓ in cannabis use, *P*=0.032 2. Neurocognitive function Cannabis use associated with ↑ score (better function) on 5 of 9 tests (design memory, verbal fluency, object assembly, block design, picture completion) 3. SANS/SAPS, NS 4. Service contact, NS	Age at onset, for neurocognitive analyses only No baseline differences in negative symptoms, premorbid adjustment, or social function	Cannabis users had significantly more positive symptoms, and less neurological soft signs at baseline
Melbourne[11,g]	In-patient and out-patient sample from Mental Health Services in Melbourne, Australia *n*=126	Incident cases of psychosis (<6 months treatment)	Cannabis misuse using the CUAD scale Measures at assessments prior to episode of relapse used for analyses	During follow-up: 43 (42)	15 months	Relapse:[a] 34 (35)	Cannabis misuse group: Relapse *n*=23/40 (58%) No substance use group: Relapse *n*=8/47 (17%) Crude OR[g]=5.8 (95% CI 2.2–15.0), *P*<0.001 Adjusted OR[g]=5.1 (95% CI 1.8–14.1), *P*=0.002	Alcohol and other substance misuse, BPRS score at baseline	
Navarra[17]	In-patient and out-patient sample from Community Mental Health Centres in Navarro, Spain *n*=75	Prevalent or incident DSM–III schizophrenia	Cannabis use ⩾2 times/week for >1 year, coded as: non-use/use at baseline only/use at baseline and follow-up Results presented here are for any baseline use of cannabis	Use at baseline only: 24 (39) Use at baseline and follow-up: 14 (23)	1 year	1. Relapse (undefined) 2. Readmission 3. Adherence (with medication and appointments)	1. Relapse Non-use=16.7% Baseline use=47.4% OR[e]=4.5 (95% CI 1.2–21.1), *P*=0.01 2. Readmission Non-use=16.7% Baseline use=23.7% OR[e]=1.6 (95% CI 0.4–7.8), *P*=0.51 3. Adherence Non-use=66.7% Baseline use=60.5% OR[e]=0.8 (95% CI 0.2–2.5), *P*=0.63	Results for relapse were then adjusted for adherence and stress though no results for any baseline cannabis use or base-line only are presented Results presented from adjusted model difficult to interpret. Authors state that 'continuing cannabis consumption was strongest predictor of relapse'	
Sydney-A[21]	Sample recruited from Community Mental Health Centres in North Sydney, Australia *n*=101	Clinical diagnoses of schizophrenia, schizophreniform disorder or schizo-affective disorder	Number of days of use in previous month (0–28)	Cannabis use in 6-months prior to start part of inclusion criteria 69% used in month before start	10 months	1. BPRS score 2. CDSS score	1. BPRS score Cannabis associated with ↑ in BPRS score (per day of use): Crude β=0.13 (95% CI 0.00–0.26)[e]. Adjusted β=0.08 (95% CI 0.02–0.15)[e] 2. CDSS score Cannabis associated with ↑ in CDSS score (per day of use): Crude β=0.04 (95% CI −0.70–0.78)[e]. Adjusted β=NS	1. BPRS score Prior BPRS scores, current CDSS score, gender 2. CDSS score Prior BPRS scores, prior CDSS scores, current amphetamine use, age	Alcohol and other drug use did not have a significant effect on outcome and were thus omitted from final model

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Cohort label	Setting and sample size at baseline	Baseline diagnoses	Cannabis measure	Exposure *n* (%)	Follow-up	Outcome *n* (%)	Main results	Confounders adjusted for	Other relevant points
Sydney-B[22]	Non-random sample who provided urine drug screen an admission, Sydney, Australia *n*=45	Prevalent or incident cases of DSM–III psychoses	Urine drug screen within 48 h of admission: (THC positive/THC negative)	THC positive: 23 (51)	Average 17 days	Length of admission in days	THC positive: Mean 13.2 days THC negative: Mean 21.0 days, *P*=0.07	None in analyses However, no other illicit substances detected in urine on screening	
South London Hospitals[14]	Subsample of consecutive admissions to 2 hospitals in South London, UK *n*=119	Recent onset (in past 5 years) cases of DSM–III–R psychoses	Cannabis use (frequent/regular) prior to baseline or in 3 months prior to follow-up, grouped as: use at baseline only/use at follow-up only (excluded from review)/use at both times/no use any time Results presented here include results for any baseline use of cannabis	Use at baseline only: 9 (9) Use at baseline and follow-up: 16 (16)	4 years	1. Positive symptoms[h] (moderate/severe *v.* mild/none) 30 (31) 2. Negative symptoms[h] (present *v.* absent) 50 (51) 3. Course of illness[h] (continuous *v.* non-continuous) 39 (40)	1. Positive symptoms Cannabis use at baseline=48% Non-use at baseline=25% OR[e]=2.8 (95% CI 1.0–8.0), *P*=0.03 Cannabis at baseline only *v.* no use at baseline or follow-up: Crude OR=1.68 (95% CI 0.2–9.1) Adjusted OR=1.61 (95% CI 0.35–7.58) 2. Negative symptoms Cannabis use at baseline=54% Non-use at baseline=51% OR[e]=1.1 (95% CI 0.4–3.2), *P*=0.81 Cannabis at baseline only *v.* no use at baseline or follow-up: Crude OR=0.77 (95% CI 0.1–4.0) Adjusted OR=0.63 (95% CI 0.29–2.86) 3. Continuous course of illness Cannabis use at baseline=56% Non-use at baseline=34% OR[g]=2.4 (95% CI 0.9–6.9), *P*=0.055 Cannabis at baseline only *v.* no use at baseline or follow-up: Crude OR=1.64 (95% CI 0.3–8.5) Adjusted OR=1.68 (95% CI 0.37 7.51)	Age at admission, gender, ethnicity	Results for baseline only likely to be under-estimate of true effect of cannabis as excludes potential effect of continued use

AMDP, Arbeitsgemeinschaft fur Methodik und Dokumentation in der Psychiatrie 1995; β, regression co-efficient; BPRS, Brief Psychiatric Rating Scale; CDSS, Calgary Depression Scale for Schizophrenia; CGI, Clinical Global Impression; CMRS, Case Manager Rating Scale for Substance Use Disorder; CUAD, Chemical Use, Abuse and Dependence; DSM–IV, Diagnostic and Statistical Manual for Mental Disorders (4th edn); GAS, Global Assessment Scale; HR, hazard ratio; ICD–10, International Classification of Diseases (10th edn); NS, not significant; OAS, Overt Aggression Scale; OR, odds ratio; PANSS, Positive and Negative Syndrome Scale; QOL, quality of life; RCT, randomised controlled trial; SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms; SCID, Structured Clinical Interview for DSM–III–R; TLFB, timeline followback procedure; THC, tetrahydrocannibinol.

a. Relapse defined as BPRS symptom exacerbation or psychotic relapse from algorithm detailed in paper.
b. Adherence based on persistence with programme and frequency of adherence with medication.
c. Response (defined as absence of rating >3 on PANSS sub-scales, >30% reduction in total PANSS score, and CGI score <4) *v.* non-response to randomised treatment.
d. Non-adherence based on non-attendance and how many times not taking medication.
e. OR and/or confidence intervals calculated from data in paper.
f. Deficit schizophrenia defined as enduring negative symptoms and failure to return to premorbid level of function.
g. Additional information provided by authors, restricting measures of cannabis use to assessments prior to relapse.
h. Positive symptoms rated using modified 'life-chart' instrument from the Multi-Centre Study on the Course and Outcome of Schizophrenia; negative symptoms rated using lager Negative Symptom Scale; continuous course of illness defined as <6 months of remission.