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### Webtable 1: Summary of studies included for psychotic outcomes

<table>
<thead>
<tr>
<th>Cohort label &amp; author</th>
<th>Setting &amp; sample size</th>
<th>Baseline screening</th>
<th>Cannabis measure &amp; age</th>
<th>Exposure n (%)</th>
<th>Follow-up &amp; attrition</th>
<th>Outcome, number &amp; %</th>
<th>Confounders adjusted for</th>
<th>Main results</th>
<th>Dose response effects</th>
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</table>
| CHDS33,34             | 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 | Up to 7 years | 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 |
| Dunedin31,32          | Birth cohort, Dunedin, New Zealand (n = 759) | DISC-C used for psychotic symptoms at age 11 | Ages 15 & 18 | Used cannabis >3 times | 8-11 years | 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:* 
Schizophreniform disorder 
Crude OR = 3.1 (1.5 to 6.6) 
Adjusted OR = 2.9 (1.2 to 7.0) | Not studied |
|                       |          |                    | Age 15  
29 (3.8%) |               | Attrition 4% |               |                       |                          | Cannabis use by age 15\textsuperscript{:} 
Schizophrenia symptoms 
Adjusted $\beta$ = 6.6 (0.9), p < 0.001 
Schizophreniform disorder 
Adjusted OR = 3.1 (0.7 to 13.3) | |
|                       |          |                    | Age 18  
236 (31%) |               |               |               |                       |                          | Cannabis use by age 15-18\textsuperscript{:} 
Schizophrenia symptoms 
Adjusted $\beta$ = 1.0 (0.4), p < 0.01 
Schizophreniform disorder 
Adjusted OR = 1.4 (0.5 to 3.7) | |
|                       |          |                    |               |               |               |               |                       |                          | Cannabis use by age 18 
Stratified by COMT genotype\textsuperscript{8} 
Adjusted results for schizophreniform disorder 
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) | |
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<tr>
<td>ECA²⁴</td>
<td>Case-control nested within adult population based cohort study, USA (n = 2295)</td>
<td>DIS interview for psychotic symptoms</td>
<td>DIS interview for: Lifetime ever use &amp; daily use 'Never used' included use of cannabis &lt;5 times Age 18-49</td>
<td>Ever use: 381 (21%) Daily use: 87 (4.8%)</td>
<td>1 year</td>
<td>DIS interview for any self-reported psychotic experience 507 (11.4%)</td>
<td>Age, gender, school attendance, educational level, marital status, employment status, baseline mental health problems (excluded if psychotic symptoms), other drug and alcohol use</td>
<td>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)</td>
<td>Not studied Stronger effect for daily use than ever use, though CI overlap</td>
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<tr>
<td>EDSP²⁵</td>
<td>Adult population based cohort, Munich, Germany (n = 2437)</td>
<td>SCL-90-R used for paranoid and psychoticism subscales</td>
<td>Ever use &gt;5 times Frequency at heaviest: None, &lt;1/month, 3-4/month, 1-2/week, 3-4/week, daily Ages 14-24</td>
<td>Ever use 320 (13.1%)</td>
<td>3-4 years</td>
<td>M-CIDI used for: Broad psychosis (≥1 symptom) 424 (17.4%) Narrow psychosis (≥2 symptoms) 174 (7.1%)</td>
<td>Age, sex, socio-economic status, urbanicity, childhood trauma, other drug use, smoking, alcohol use, predisposition to psychosis</td>
<td>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)</td>
<td>Evidence from 6-level frequency of use variable examined as linear term (broad psychosis only reported)</td>
</tr>
<tr>
<td>NEMESIS²⁶</td>
<td>Adult population based cohort, Netherlands (n = 4045)</td>
<td>CIDI for psychotic symptoms 47% of subjects with symptoms on CIDI re-interviewed with SCID</td>
<td>Lifetime ever use &amp; Cumulative frequency from baseline to follow-up, summed as lowest, middle &amp; highest levels Age 18-64</td>
<td>Ever use: 312 (7.6%)</td>
<td>3 years</td>
<td>BPRS for: Any psychotic symptoms (BPRS&gt;4) 38 (0.94%) Pathology level symptoms (BPRS&gt;4) 10 (0.25%) 'Need for care' from CIDI, SCID, &amp; BPRS 7 (0.17%)</td>
<td>Age, sex, ethnicity, marital status, education, urbanicity, discrimination, and other drug use Subjects with any lifetime ever psychotic symptoms at baseline excluded</td>
<td>Ever use: Any symptoms Crude OR = 3.3 (1.5 to 7.2) Adjusted OR = 2.1 (0.8 to 5.7) Pathology level symptoms Crude OR = 28.5 (7.3 to 110.9) Adjusted OR = 16.9 (3.3 to 86.1) Need for care Crude OR = 16.2 (3.6 to 72.5) Adjusted OR = 10.5 (1.8 to 63.2)</td>
<td>Evidence from 3-level frequency of use variable examined as linear term</td>
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<td>NPMS27</td>
<td>Adult population based sample, UK (n = 2413)</td>
<td>PSO used for past year psychotic symptoms</td>
<td>Used in past year but not dependent</td>
<td>18 months</td>
<td>PSQ for psychotic symptoms since initial interview 134 (4.4%)</td>
<td>Psychotropic drugs and therapy, IQ score, marital status, urbanicity, support group, life events, smoking, alcohol, age, gender, CIS-R score at baseline</td>
<td>Used past year</td>
<td>Crude OR = 1.1 (0.5, 2.5) Adjusted OR = 0.7 (0.3, 1.7)</td>
<td>Suggestion of increasing effect for dependent compared to non-dependent</td>
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<td>Over-sampled for baseline mental disorder</td>
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<td>Dependent past year</td>
<td>32%</td>
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<td>Age 16-74</td>
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<td>Swedish conscripts28–30</td>
<td>Adult population based conscript cohort, Sweden (n = 48,481)</td>
<td>Psychologist / psychiatrist interview for ICD-8 diagnoses</td>
<td>Ever use</td>
<td>27 years</td>
<td>Admissions with ICD8/9 clinical diagnosis of schizophrenia / schizoaffective disorder 362 (0.7%)</td>
<td>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</td>
<td>Ever use:</td>
<td>Crude HR = 2.2 (1.7 to 2.8) Adjusted HR = 1.5 (1.1 to 2.0)</td>
<td>Evidence from 6-level frequency of use variable examined as linear term</td>
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<tr>
<td></td>
<td>Frequency: None, 1 time, 2-4 times, 5-10 times, 11-50 times, &gt;50 times</td>
<td></td>
<td>Ever use 5391</td>
<td>No data on attrition available</td>
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<tr>
<td></td>
<td>(10.8%)</td>
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<td>&gt;50 times: 731 (1.5%)</td>
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<td>Age 18-20</td>
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‡ 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); † Val15 met 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.