

**Webtable 2: Summary of studies included for affective outcomes**

Cohort label & author	Setting & sample size	Baseline screening	Cannabis measure & age	Exposure n (%)	Follow-up & attrition <sup>‡</sup>	Outcome, number & %	Confounders adjusted for	Main results	Dose response effects
AddHealth <sup>47</sup>	School based cohort, USA  (n = 13,110)	Baseline suicidal behaviour included in questionnaires but not excluded or adjusted for in study	Age 14-16  7 categories from never used to use >6 times per month	No data	≈1 year  Maximum attrition 29%. No data on N ineligible for follow-up as Grade12 at baseline	Suicide attempt Total 3.6% Women 5.1% Men 2.0 %	No crude results given  Age, family structure and welfare status	Adjusted OR for use >6/month: Boys Black 5.9 P<0.001 Hispanic 2.9 P<0.05 White 6.8 P<0.001  Girls Black 10.3 P<0.001 Hispanic 4.5 P<0.001 White 3.4 P<0.001	Not reported
AddHealth <sup>48</sup>	School based cohort, USA  (n = 4,834)	Baseline depression using CES-D (excluded if score above threshold score)	Age 14-16  Ever used vs never	12.9%	≈1 year  Attrition 12%	CES-D depression score above threshold	Age, family structure, income, gender, rural residence, ethnicity, and attachment	Crude OR* = 2.1 (1.3 to 3.2) Adjusted OR = 1.6 (0.9 to 2.7)	Not reported
Baltimore <sup>49 †</sup>	School based cohort, originally basis for RCT <sup>†</sup> Baltimore, USA  (n = 1588)	Baltimore "What's Happening?" interview & NIDA youth interviews for depression	Early onset cannabis ever use (ages 8-15 years)  Early onset 8-level frequency of use: None, once, 2 times, 3-4 times, 5-9 times, 10-19 times, 20-39 times, >40 times	Ever use by age 15 = 234 (11%)  Used 1-2 times = 107 (5%)  Used >2 times = 127 (6%)	Up to 14 years  Maximum attrition 12%	Used NIMH interview at mean age 22 for:  Suicidal ideation 197 (9%)  Suicide attempt 148 (7%)	Sex, cohort, race, RCT intervention status, free lunch status, other drug use, childhood depression, parental legal and illicit drug use and parental psychopathology	Suicidal ideation: Cannabis use Crude OR = 1.5 (1.0 to 2.4) Adjusted OR = 1.8 (1.0 to 3.2) Frequency of use Crude OR = 1.5 (0.8 to 2.7) Adjusted OR = 1.7 (0.9 to 3.1)  Suicide attempt: Cannabis use Crude OR = 2.2 (1.4 to 3.4) Adjusted OR = 2.4 (1.3 to 4.3) Frequency of use Crude OR = 1.9 (1.0 to 3.5) Adjusted OR = 2.4 (1.3 to 4.5)	8-level frequency of cannabis use examined
Berkeley <sup>39</sup>	Work based cohort, Berkeley, USA  (n = 88)	None reported	Frequency of drug use collected by video interview at age 14	Not given	4 years (to age 18)  No data on attrition given	CES-D for depressive symptoms  Women 22.5% Men 19.8%	Crude results only	Association between cannabis use at age 14 and dysthymia at age 18:  Men r = 0.27 p<0.05  Women r = -0.08 'ns'	Not reported

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CHDS <sup>35,36</sup>	Birth cohort, Christchurch, New Zealand  (n = 927)	DISC used for DSM III R diagnosis of depression or anxiety in past 1 year  Age 15	Self and parent reported Never used to used >6 times  Age 14-15	Used by age 15 9.8%	1 year  Maximum attrition 26%	DIS/DISC for DSM III R depression or anxiety over past year  Anxiety 7.5% Depression 8.3% Suicidal ideation 8.8%	Family functioning, associating with drug using peers, tobacco use, alcohol use, family history of dependence, gender, offending, IQ, future educational plans, and conduct, anxiety and depressive disorders at age 15	Anxiety Crude OR = 2.7 (1.3 to 4.1) Adjusted OR = 1.2 (0.5 to 2.8)  Depression Crude OR = 2.9 (1.6 to 5.1) Adjusted OR = 1.4 (0.7 to 2.7)  Suicidal ideation Crude OR = 3.6 (2.1 to 6.1) Adjusted OR = 1.4 (0.7 to 2.8)  Similarly, associations in crude analyses all non-significant after adjustment in 2 year follow-up	Studied for 2 year follow-up
CHDS <sup>37</sup>	Birth cohort, Christchurch, New Zealand  (n = 1,063)	DISC used for DSM III R diagnosis of depression or anxiety in past 1 year Ages 14-16  CIDI for DSM-IV depression since last assessment Ages 18 & 21	Not used Used <monthly (1-11 times) Used monthly (12-50 times) Used weekly (>50 times)  Age 15 past yr Ages 16, 18, 21 since last seen	None given	6 years  Maximum attrition 16%	DISC, past year DSM-III-R major depression Ages 15 & 16  CIDI for DSM-IV depression, & suicidal ideas & attempts since last assessment Ages 18 & 21	Measures of adverse life-events, deviant peer affiliations, alcohol abuse, age leaving school and home, baseline depression  Also adjusted for non-observed fixed confounders	Depression Crude OR calculated from data = 1.3 (1.2 to 1.4) Adjusted OR calculated from data = 1.2 (1.0 to 1.4)  Suicidal ideation Adjusted OR calculated from data = 1.4 (1.2 to 1.7)	4-level frequency of cannabis use examined as exposure
Chicago <sup>50</sup>	School based cohort, Chicago, USA  (n = 953)	6-item scale of depressive symptoms	Used <40 times Used >40 times Age 15-16	None given	17 years (to age 33)  Maximum attrition 20%	Suicidal ideation (9%)  Suicide attempt (4.1%)	Crude results only	Suicidal thoughts Men OR = 1.2 (0.5 to 2.7) Women OR = 0.6 (0.1 to 2.9)  Suicidal attempts Men OR = 0.3 (0.04 to 2.9) Women OR = 1.8 (0.5 to 6.8)	Not reported
Columbia <sup>45</sup>	Adult population based sample, Columbia  (n = 2,226)	SCL-90 for anxiety or depressive symptoms	Regular use (≥1/month) Age 12-17	Not given	2 years  No data on attrition given	SCL-90 upper quartile compared to lower 3 quartiles	Age, gender, socio-economic status, and baseline anxiety and depression symptoms	Anxiety Adjusted OR = 1.5 (1.1 to 2.0)  Depression Adjusted OR = 1.5 (1.1 to 2.1)  Additionally adjusted for depression at baseline: OR = 1.3 (1.0 to 1.8)	Not reported

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Dunedin <sup>38</sup>	Birth cohort, Dunedin, New Zealand  (n = 484)	Used DISC for DSM-III disorders at age 15	Never used Used 1-2 times Used >2 times At ages 13 & 15  Past year use: None, <1/month, >1/month, >1/week At ages 18 & 21	Ever used 1% age 13  Ever used 143 (15%) age 15	3 years  Maximum attrition 10%	DIS/DISC for DSM-III depression or anxiety disorder over past year combined as "internalising disorder" at age 15, 18 & 21	Gender, tobacco and alcohol use, parental attachment, family background measures, behaviour problems in childhood, mental disorder at baseline	Cannabis use age 15 and Internalising disorder age 18 Adjusted OR = 1.2 (ns)  No significant relationship between frequency of cannabis use at age 18 and Internalising disorder at age 21 after adjustment	4-level scale of cannabis frequency examined
Dunedin <sup>31</sup>	Birth cohort, Dunedin, New Zealand  (n = 759)	Not reported. Data from other publications indicates subjects were screened for depression at these ages, but not excluded or adjusted for here	Used <3 times versus ≥3 times  Ages 15 & 18	Age 15 29 (3.3)  Age 18 236 (31.1)	7-11 years (to age 26)  Attrition 4%	DIS interview:  DSM IV depressive disorder 118 (15.5%)  DSM IV depressive symptoms	Socio-economic status, gender, psychotic symptoms, and other drug use  No adjustment for previous depressive symptoms	Depression symptoms (adjusted) Cannabis use age <15 β = -1.8 (SE 2.26), p=0.43 Cannabis use age 15-18 β = 1.6 (SE 0.88), p=0.08  Depressive disorder (adjusted) Cannabis use age <15 OR=0.9 (0.3 to 3.2) Cannabis use age 15-18 OR=1.6 (1.0 to 2.5)	Not reported
ECA <sup>41</sup>	Adult population based sample, Baltimore, USA  (n = 13,306)	Used DIS for OCD, and those with prior or current OCD excluded	Used DIS for any use in past year	972 (7.3%) using cannabis only	1 year  Attrition 20%	DIS for DSM-III diagnosis of OCD  105 (0.8%)	Race, ethnicity, education level, marital status, job prestige, gender, other drug use, other psychiatric disorders at baseline (subjects with baseline OCD excluded)  Place of residence and age matched for (in conditional analysis) or included in model (for unconditional)	Matched analysis: 'Crude' OR = 1.8 (0.8 to 3.8) Adjusted OR = 2.9 (1.1 to 7.6)  Unconditional analysis: Adjusted OR = 1.3, p = 0.40	Not reported
ECA <sup>40</sup>	Adult population based sample, Baltimore, USA  (n = 849)	Used DIS and anyone with lifetime ever DSM-III-R symptoms of depression of >2 weeks were excluded from the study.	Used DIS for DSM-III-R diagnosis of cannabis abuse disorder  Ages 18-65	n = 15 (1.8%)	14-16 years  Attrition 45%	Used DIS for DSM-III-R depressive symptoms lasting >2 weeks  267 (14%)	Gender, age, marital status, race, education, household income, life events, chronic illnesses, other psychiatric symptoms, substance use disorders  Subjects with baseline depression symptoms excluded	Depression Crude OR = 4.5 (1.5 to 13.3) Adjusted OR = 4.0 (1.2 to 13.0)  Suicidal ideation Adjusted OR = 4.6 (1.4 to 15.1)	Not reported

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LA Schools <sup>51</sup>	School based cohort, Los Angeles county, USA  (n = 487)	Adolescent psychosocial scales used for emotional distress, self derogation, self acceptance, depression and other related measures	5-7 levels frequency of use measures combined across time points  Ages 13, 17, 21	Not reported	12 years (to age 25)  Maximum attrition 70%	27 variables to assess mental health including suicidal ideation, CES-D for depression, HSC for anxiety	Other drug use, social support and social conformity, emotional distress at baseline including depression  No crude results given	Partial correlation coefficients: Cannabis frequency of use: CESD score = 0.17, p <0.01 Suicide attempt = -0.10, p <0.05  Increased cannabis use during adolescence also associated with suicide attempt (-0.15, p <0.01)	Used linear term for cannabis frequency
LA Schools <sup>52</sup>	School based cohort, Los Angeles county, USA  (n = 470)	Adolescent psychosocial scales used for emotional distress, self derogation, self acceptance, depression and other related measures	Cannabis dependence (DSM-IV) & cannabis problems at mean age 25	Not reported	4 years (to age 29)  Attrition 24%	Latent construct of dysphoria, including CES-D depression, suicidal ideation and anxiety	Unable to differentiate for cannabis only data	Cannabis problems in early adulthood increased later suicidal ideation (p <0.05)  Non-significant results for depression or anxiety	4-level scale of cannabis problems
LAT <sup>53</sup>	School based cohort, New York, USA  (n = 1205)	CES-D for depressive symptoms measured at four 6-month intervals (ages 15-17), but subjects not excluded or measures adjusted for in results given	Frequency at 4 points (ages 15-17) giving 5 trajectories: Abstainers, Experimental, Decreasers, Increases, and High Chronics	Abstainers 82.8% Experimental 8.5% Chronics 1.7%	6 years (to age 23)  Maximum attrition 32%	CES-D for depressive symptoms Also CIDI for DSM-IV lifetime depression (20.3% of abstainers) or anxiety (20.9%)	None	Results only reported for depressive symptoms: depressive symptoms in young adulthood was not significantly different across trajectory groups of cannabis use in adolescence	Not studied
NoRMHS <sup>44</sup>	Adult population based sample, Australia Over-sampled for baseline mental disorder  (n = 968)	CIDI for past 1-year ICD-10 diagnoses Depression or anxiety at baseline not excluded or adjusted for in results given	CIDI for past 1-year ICD-10 diagnosis of harmful use or dependence  Age range 18 to over 85	Harmful use or dependent 3.3%	2 years  Attrition 31%	CIDI for past 1-year ICD-10 diagnoses of depression or anxiety	None	Unadjusted results calculated from table  Depression Crude OR = 1.4 (0.3 to 6.0) Anxiety Crude OR = 0.8 (0.2 to 3.3)	Not studied
NPMS <sup>§</sup>	Adult population based sample, UK Over-sampled for baseline mental disorder  (n = 1578)	CIS-R for depression, and excluded if CIS-R ≥12	Never used, Ever used, Used in past year, Dependent past year  Ages 16-74	Ever used 384 (16%)  Dependent 60 (2.5%)	18 months  Attrition 32%	CIS-R score ≥12 (depression & anxiety)  173 (11.0%)	Baseline CIS-R score if <12 (otherwise excluded), other drugs, age, gender, ethnicity, marital status, education qualifications, employment, social class, housing, life events, urbanicity, income, support, smoking, alcohol, medication, hospital treatment or referral	Ever used cannabis Crude OR = 1.4 (0.8 to 2.2) Adjusted OR = 0.8 (0.4 to 1.6)  Dependent Crude OR = 1.2 (0.5 to 3.4) Adjusted OR = 0.9 (0.2 to 3.6)	Not studied  No evidence from dependent compared to ever use groups

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NY Schools <sup>54</sup>	School based cohort, New York, USA  (n = 2579)	6-item scale of depressive symptoms adapted from SCL	Any use in past 30 days  Age 16	413 (16%) of non-depressed at baseline	6 months  Attrition 32%	6 questions on symptoms of depression from revised SCL 538 (20.8%)	Crude results only	No association between cannabis use and depression Crude OR = 1.1 (0.9 to 1.5) (Calculated from table; subjects excluded if baseline depression)	Not reported
NY Schools <sup>55</sup>	School based cohort, New York, USA  (n = 1004)	6-item scale of depressive symptoms adapted from SCL	Ever use by age 16  Months of use age 16 to 1 year prior to outcome measure	Not reported	9 years (to age 25)  Attrition 25%	6-item scale of depressive symptoms and depression sub-scale of HSC Symptoms rated over past 1 year	Race, parental education, level of education, closeness to parents, peer orientation and activity, separation from parents, parental substance use, family history, other drug use, baseline depression score	Ever use: men $\beta = -0.02$ , 'ns' Ever use: women $\beta = 0.01$ , 'ns' Months of use: men $\beta = 0.07$ , 'ns' Months of use: women $\beta = -0.01$ , 'ns'	Not reported
NY State <sup>42</sup>	Adult population based sample, New York State, USA  (n = 698)	Used DISC for DSM-IV depressive disorder and adjusted for previous disorder in analysis	Never, light, >weekly, & >monthly ages 12-21 & 18-27	Age 12-21 9% Age 18-27 13%	6 years  Attrition 6%	DISC for DSM-III-R major depression and anxiety disorders	Age, gender and psychiatric disorder (depression or anxiety) at previous time points No crude results given	Depressive disorders Adjusted OR = 1.1 (1.0 to 1.3)  Anxiety disorders Adjusted OR = 1.2 (1.0 to 1.4)	Odds ratios are for 4-level exposure variable as linear term
NY State <sup>43</sup>	Adult population based sample, New York State, USA  (n = 736)	DISC measures of DSM-IV depressive disorder at average ages 14 & 16	Never, light, moderate (>weekly), heavy (>monthly). Use since last assessment at average ages 14, 16 & 22	Ever use Age 14 29% Age 16 (past 2yrs) 33% Age 22 (past 5yrs) 54%	Average 13 years  Maximum attrition 5%	CIDI for modified DSM-IV criteria for major depression  61 (8.3%)  Average age 27	Age, gender, parental education, family income and prior episodes of depression and substance use disorder	Depression Adjusted OR = 1.2 (1.0 to 1.3)  Trend for risk to increase with earlier cannabis use onset:  Age <14 OR = 1.6 (1.2 to 2.2) Age 14-16 OR = 1.4 (1.1 to 1.9) Age 16-22 OR = 1.2 (0.9 to 1.6)	4-level exposure variable as linear term
Victoria <sup>46</sup>	School based cohort, Victoria, Australia  (n = 1590)	Used CIS-R at 7 time points for depression & anxiety	Frequency of use since prior assessment Not used Used <weekly Used weekly Used daily  Ages 14-19	Any use Men 484 (66%) Women 448 (52%)	6 years  Maximum attrition 18%	Used CIS-R score $\geq 12$ for depression/anxiety at age 20-21  Total 259 (16.3%) Men 71 (9.7%) Women 188 (22%)	Alcohol use, antisocial behaviour, parental separation, parent education, and depression/anxiety at previous time points Other drug use not adjusted for	Cannabis use < weekly (all): Crude OR = 1.5 (1.1 to 2.1) Adjusted OR = 1.4 (0.9 to 2.0)  Cannabis use $\geq$ weekly (men) Crude OR = 0.6 (0.2 to 1.6) Adjusted OR = 0.5 (0.2 to 1.3) Cannabis use $\geq$ weekly (women) Crude OR = 2.6 (1.6 to 4.3) Adjusted OR = 1.9 (1.1 to 3.3)	Suggestive in women though no statistical test for trend done

\*Additional data kindly provided by authors; <sup>†</sup> 5 different analytical methods used – results presented, where available, are for logistic regression; <sup>‡</sup> Attrition based on proportion of subjects lost to study from baseline cannabis assessment to outcome assessment at follow-up; <sup>§</sup> Haynes J, personal communication.  $\beta$  = linear regression coefficient. ns = not significant. CES-D = Centre for Epidemiological Studies-Depression Scale. CIDI = Composite International Diagnostic Interview. CIS-R = Clinical Interview Schedule-Revised. DIS = Diagnostic Interview Schedule. DISC = Diagnostic Interview Schedule for Children. DSM = Diagnostic Schedule Manual of mental disorders. HSC = Hopkins Symptom Checklist. OR = odds ratio, 95% confidence intervals in parentheses. r = correlation coefficient. SCL = Symptom Checklist. NIMH = National Institute of Mental Health (USA). NIDA = National Institute of Drug Abuse (USA).