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# Supplementary appendix

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# Supplementary Information

**Supplementary Methods**

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## 1. Search and data extraction

Data were extracted by two authors independently (G.H. and K.B.). Plot digitizer software (https://automeris.io/WebPlotDigitizer/) was used to extract data when only available in plot format.(1) If more than one dose or time-point was reported, the data for the maximum dose or the time-point associated with the highest mean symptom score was extracted since we aimed to determine the maximum possible effect. Variables extracted were author, year of publication, number of completed participants, mean age, proportion male, percentage current tobacco smokers, mean total lifetime cannabis exposures, details of control condition and randomisation procedure, inclusion and exclusion criteria, route and dose of THC, symptom measure used and subscales reported, timing of measure relative to administration of THC and mean and SD of symptom scales. If dose was presented as mg/kg, the mean dose delivered was calculated by multiplying the dose/kg by the mean weight in kg.

If total cannabis exposure was reported as a categorical variable with ranges, means were estimated by multiplying the midpoint of each range by the frequency within each range, summing the answer for each bin and dividing by the total number of participants. Since the largest category was often "$>z$", where $z$ represents a given number of total cannabis exposures, we used $1.5z$ as the equivalent of the midpoint for the main analysis and performed a sensitivity analysis substituting $1.5z$ with $z$ and $2z$ (see Appendices 6 and 7). As details regarding cannabis use were often reported with low precision, we also dichotomised this variable to reflect high and low frequency of cannabis use (frequent $\geq$ 100 mean total uses, infrequent $\leq$ 100 mean total uses), in line with previous literature.(2)

Although not included in the initial protocol, an additional search was made for alternative scales measuring similar constructs: the scale for the assessment of positive symptoms (SAPS), scale for the assessment of negative symptoms (SANS) and the community assessment of psychic experience scale (CAPE). The search terms were identical to the PANSS/BPRS search besides the scales themselves: MEDLINE (from 1 January 1946 to 21 May 2019), EMBASE (from 1 January 1974 to 21 May 2019) and PsychINFO (from 1 January 1806 to week 21 May 2019) were searched. The following keywords were used: (THC OR tetrahydrocannabinol OR 9THC OR 9tetrahydrocannabinol OR delta9THC OR d9THC OR delta9tetrahydrocannabinol OR dronabinol OR marinol OR bedrobinol OR anandamide OR methanandamide OR "WIN,55,212-2" OR ACPA OR CP55940 OR bedrocan OR spice OR JWH-018 OR AM251 OR SR161716A OR rimonabant OR cannabidiol OR CBD OR cannabinoid) AND (SAPS OR "scale for the assessment of positive symptoms" OR SANS OR "scale for the assessment of negative symptoms" OR CAPE OR "community assessment of psychic experience"). The findings from this search are summarised in Appendix 8, Supplementary Figure 11 and Supplementary Table 11.

## 2. Analysis of moderating variables

In order to evaluate potential modifiers of THCs effects on psychopathology, we conducted secondary subgroup analyses of the following variables thought to potentially modulate sensitivity to THC's pharmacodynamic action or the endocannabinoid system, or key methodological factors. In order to investigate the association between the effect size and continuous variables, meta-regression analyses were conducted. We conducted meta-regressions if n of studies >5. Variables included were mean age(3), percentage male gender(4), and percentage tobacco smokers(5) and Newcastle-Ottawa Scale score (study quality). We grouped studies by route of administration in the analysis of dose as there is currently no standardised method to calculate THC dose equivalence for different routes of administration. We conducted subgroup-analyses for categorical variables. We first conducted a random effects meta-analysis for each subgroup. We then compared subgroup estimates in a fixed effects model with a Wald-type test. Variables were selected on the basis of prior evidence that they might influence the effect of THC, and were current use (comparing studies where subjects had confirmed recent use with a positive urine drug screen for cannabis vs studies where subjects had confirmed abstinence from recent cannabis with a negative urine drug screen for cannabis at screening)(6), frequency of use (mean total exposures>100 vs mean total exposures<100)(6), route of administration (oral vs inhaled vs IV)(7), type of THC (purified vs synthetic), symptom scale (BPRS vs PANSS) and study author (D'Souza et al. or group vs other)(8).

## 3. Comparing effect of THC on positive, negative and general symptoms

To determine whether the effect of THC was greater on positive, negative or general symptoms a multivariate meta analytic approach was adopted using an unstructured variance-covariance matrix. As within study correlations for positive, negative and general symptom scores are not reported we estimated the correlation coefficient to be 0.5 based on prior studies (9). We performed a sensitivity analysis to evaluate the influence of this assumption on these results by re-fitting our model using $r$ values of 0.1 and 0.7 (See Appendix 6).

**Table 1**: Timepoints measured, timings at peak symptoms and timings at resolution of symptoms for studies included in meta-analysis. Resolution of symptoms determined by qualitative evaluation of graphs comparing THC score to placebo score at corresponding timepoint. Scale is PANSS unless otherwise stated. *Timepoints are taken from a graph. These timepoints do not correspond to timepoints described in the methods and the scale on the graph has varying intervals (i.e. is not linear).

| | Route | Symptom domains | Timepoints (mins) | Peak (mins) | Time at resolution of symptoms (mins) | Comment |
|---|---|---|---|---|---|---|
| **Bhattacharyya 2015** | Oral | Positive, total | 60, 120, 180 | 120 | Not resolved | |
| **Bhattacharyya 2012** | Oral | Positive, negative | 60, 120 | 120 | Not resolved | |
| **Bossong 2009** | Inhaled | BPRS Total | 21, 102 | 21 | Not resolved | |
| **Liem-Moolenaar 2010** | Inhaled | Positive, negative, general, total | 40 after last dose | 40 | Not resolved | Multiple THC doses |
| **Kleinloog 2012** | Inhaled | Positive, negative, general, total | 36 after last dose | 36 | Not resolved | Multiple THC doses |
| **Morgan 2018** | Inhaled | BPRS Positive, negative | Not recorded | N/a | N/a | |
| **D'Souza 2012** | IV | Positive, negative, general, total | 10, 80 | 10 | Not resolved | |
| **D'Souza 2004** | IV | Positive, negative, general, total | 10, 80, 200 | 10 (positive, general, total)<br>80 (negative) | 200 | |
| **D'Souza 2008** | IV | Positive, negative, general, total | 10, 80, 200 | 10 | 200 | |
| **D'Souza 2009a** | IV | Positive, negative, general, total | 15, 65 | 15 | Not resolved | |
| **D'Souza 2009b** | IV | Positive, negative, general, total | 15, 65 | 15 | Not resolved | |
| **Radhakrishnan 2015** | IV | Positive, negative, general, total | 70, 240 | 70 | 240 | |
| **Barkus 2011** | IV | Positive, negative, general | 30, 80, 120 | 30 | 240 (positive)<br>80 (negative and general) | |
| **Morrison 2009** | IV | Positive, CAPE negative | 30, 80, 120 | 30 | 120 | |
| **Morrison 2011** | IV | Positive, negative | 30, 90 | 30 | 90 (Negative)<br>Positive not resolved by 90 | |
| **Ranganathan 2012** | IV | Positive, negative | 10, 65, 120, 250 | 120 (positive)<br>65 (negative) | 250 | Timepoints unclear* |

**Supplementary Table 2**. Raw data used in positive BPRS and PANSS analysis for healthy participants

| author | year | time | n1i | m1i | sd1i | n2i | m2i | sd2i |
|---|---|---|---|---|---|---|---|---|
| Barkus | 2011 | 30 | 9 | 13.37 | 2.4 | 9 | 7.12 | 0 |
| Bhattacharyya | 2015 | 120 | 36 | 9.6 | 3.62367 | 36 | 7.26 | 0.582702 |
| D'Souza | 2012 | 10 | 26 | 12.65 | 3.19 | 26 | 7.96 | 2.18 |
| D'Souza | 2004 | 10 | 18 | 9.966837 | 2.71207595 | 18 | 6.813776 | 0.82992611 |
| D'Souza | 2008 | 10 | 20 | 10.52 | 2.61 | 20 | 8.05 | 1.5 |
| D'Souza | 2009a | 15 | 14 | 9.48755251 | 1.51 | 14 | 7.6335764 | 0.73450605 |
| D'Souza | 2009b | 15 | 9 | 8.54065211 | 1.27455069 | 9 | 7.991526 | 0.866052 |
| Morrison | 2009 | 30 | 21 | 10.41396 | 5.28399034 | 21 | 7.0005403 | 0 |
| Morrison | 2011 | 30 | 16 | 11.3133161 | 3.5703548 | 16 | 7.036427 | 0 |
| Ranganathan | 2012 | 120 | 26 | 9.68 | 1.93 | 26 | 7.726444 | 1.03775281 |
| Bhattacharyya | 2009 | 120 | 15 | 9.58847489 | 8.27122099 | 15 | 7.05801 | 0.24986901 |
| Morgan | 2018 | NR | 48 | 6.6870748 | 1.03687393 | 48 | 6.42857 | 1 |
| Liem-Moolenaar | 2010 | 40 | 11 | 10.63 | 3.96 | 11 | 7.72 | 1.27 |
| Kleinloog | 2012 | 36 | 32 | 9.07 | 2.29 | 32 | 7.47 | 0.9 |
| Radhakrishnan | 2015 | 70 | 23 | 10.87 | 2.44 | 23 | 8.04 | 1.46 |

| author | year | route | thc_drob | dose | prev_cannabis_mean | frequent_use | current_use | tobacco_current | age_m | Male | panss_bprs |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Barkus | 2011 | 1 | 0 | 2.5 | 153 | 1 | 0 | | 26.3 | 100% | 1 |
| Bhattacharyya | 2015 | 0 | 1 | 10 | 10.8333 | 0 | 0 | 25% | 25.97 | 100% | 1 |
| D'Souza | 2012 | 1 | 1 | 2.133 | 318 | 1 | | 15.79% | 25.92 | 65.3846154% | 1 |
| D'Souza | 2004 | 1 | 1 | 5 | 60.77 | 0 | 0 | 23.81% | 29 | 63.6363636% | 1 |
| D'Souza | 2008 | 1 | 1 | 5 | 147.51 | 1 | 1 | | 24.8 | 70% | 1 |
| D'Souza | 2009a | 1 | 1 | 2.0774 | 48.86 | 0 | 0 | 0% | 25.85 | 78.5714286% | 1 |
| D'Souza | 2009b | 1 | 1 | 2.1125 | 141.72 | 1 | 1 | 11.11111111% | 22.66 | 100% | 1 |
| Morrison | 2009 | 1 | 0 | 2.5 | | | 0 | | 28 | 100% | 1 |
| Morrison | 2011 | 1 | 0 | 1.25 | 40 | 0 | 0 | | 26 | 43.75% | 1 |
| Ranganathan | 2012 | 1 | 1 | 1.89 | | | | 26.66666667% | 27.14 | 86.6666667% | 1 |
| Bhattacharyya | 2009 | 0 | 1 | 10 | 8 | 0 | 0 | 46.66666667% | 26.7 | 100% | 1 |
| Morgan | 2018 | 2 | 1 | 8 | | | 1 | 70.83333333% | 21.705 | 70.83% | 0 |
| Liem-Moolenaar | 2010 | 2 | 1 | | | | 0 | | 24.1 | 100% | 1 |
| Kleinloog | 2012 | 2 | 1 | | 292.2 | 1 | 0 | 0% | 22.3 | 100% | 1 |
| Radhakrishnan | 2015 | 1 | 1 | 1.2147 | 296.75 | 1 | | 14.8148148% | 26.26 | 100% | 1 |

**Supplementary Table 3.** Raw data used in negative BPRS and PANSS analysis for healthy participants

| author | year | time | n1i | m1i | sd1i | n2i | m2i | sd2i | route | thc_drob | Dose |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Barkus | 2011 | 30 | 9 | 8.57 | 0.54 | 9 | 6.99 | 0 | 1 | 0 | 2.5 |
| D'Souza | 2012 | 10 | 26 | 11.73 | 3.56 | 26 | 7.58 | 2.3 | 1 | 1 | 2.133 |
| D'Souza | 2004 | 80 | 18 | 10.54235 | 6.31486836 | 18 | 5.29539162 | 1.06846315 | 1 | 1 | 5 |
| D'Souza | 2008 | 10 | 20 | 8.44 | 2.14 | 20 | 6.5 | 0.74 | 1 | 1 | 5 |
| D'Souza | 2009a | 15 | 14 | 8.43 | 1.99 | 14 | 7.29 | 2.08 | 1 | 1 | 2.0774 |
| D'Souza | 2009b | 15 | 9 | 7.78 | 1.23 | 9 | 7.22 | 0.91 | 1 | 1 | 2.1125 |
| Morrison | 2011 | 30 | 16 | 9.980617 | 2.55898846 | 16 | 6.986849 | 0 | 1 | 0 | 1.25 |
| Ranganathan | 2012 | 65 | 26 | 7.28 | 1.2 | 26 | 6.306244 | 0.80076204 | 1 | 1 | 1.88988636 |
| Bhattacharyya | 2012 | 120 | 15 | 9.3956442 | 2.17196325 | 15 | 7.272232 | 0.59043631 | 0 | 1 | 10 |
| Morgan | 2018 |  | 48 | 4.6870748 | 1.69670242 | 48 | 4.047619 | 1.31965776 | 2 | 1 | 8 |
| Liem-Moolenaar | 2010 | 40 | 11 | 11.63 | 2.91 | 11 | 10.45 | 5.59 | 2 | 1 |  |
| Kleinloog | 2012 | 36 | 32 | 9.89 | 3.18 | 32 | 7.79 | 1.24 | 2 | 1 |  |
| Radhakrishnan | 2015 | 70 | 23 | 10.87 | 2.44 | 23 | 8.04 | 1.46 | 1 | 1 | 1.2147 |

| author | year | prev_cannabis_mean | frequent_use | current_use | tobacco_current | age_m | male | panss_bprs |
|---|---|---|---|---|---|---|---|---|
| Barkus | 2011 | 153 | 1 | 0 |  | 26.3 | 100% | 1 |
| D'Souza | 2012 | 318 | 1 |  | 15.79% | 25.92 | 65.3846154% | 1 |
| D'Souza | 2004 | 60.77 | 0 | 0 | 23.81% | 29 | 63.6363636% | 1 |
| D'Souza | 2008 | 147.51 | 1 | 1 |  | 24.8 | 70% | 1 |
| D'Souza | 2009a | 48.86 | 0 | 0 | 0% | 25.85 | 78.5714286% | 1 |
| D'Souza | 2009b | 141.72 | 1 | 1 | 11.1111111% | 22.66 | 100% | 1 |
| Morrison | 2011 | 40 | 0 | 0 |  | 26 | 43.75% | 1 |
| Ranganathan | 2012 |  |  |  | 26.6666667% | 27.14 | 86.6666667% | 1 |
| Bhattacharyya | 2012 | 8 | 0 | 0 | 46.6666667% | 26.7 | 100% | 1 |
| Morgan | 2018 |  |  | 1 | 70.8333333% | 21.705 | 70.833333% | 0 |
| Liem-Moolenaar | 2010 |  |  | 0 |  | 24.1 | 100% | 1 |
| Kleinloog | 2012 | 292.2 | 1 | 0 |  | 22.3 | 100% | 1 |
| Radhakrishnan | 2015 | 296.75 | 1 |  | 14.8148148% | 26.26 | 100% | 1 |

**Supplementary Table 4** Raw data used in general PANSS analysis for healthy participants

| author | year | time | n1i | m1i | sd1i | n2i | m2i | sd2i | route | thc_drob | dose |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Barkus | 2011 | 30 | 9 | 23.87 | 0.9 | 9 | 16.03 | 0 | 1 | 0 | 2.5 |
| D'Souza | 2012 | 10 | 26 | 25.65 | 6.3 | 26 | 17.12 | 2.92 | 1 | 1 | 2.133 |
| D'Souza | 2004 | 10 | 18 | | | 18 | | | 1 | 1 | 5 |
| D'Souza | 2008 | 10 | 20 | 19.96 | 4.44 | 20 | 16.45 | 2.42 | 1 | 1 | 5 |
| D'Souza | 2009a | 15 | 14 | | | 14 | | | 1 | 1 | 2.0774 |
| D'Souza | 2009b | 15 | 9 | | | 9 | | | 1 | 1 | 2.1125 |
| Liem-Moolenaar | 2010 | 40 | 11 | 24.82 | 4.51 | 11 | 19 | 3 | 2 | 1 | |
| Kleinloog | 2012 | 36 | 32 | 19.56 | 3.45 | 32 | 17.02 | 1.73 | 2 | 1 | |
| Radhakrishnan | 2015 | 70 | 23 | 20.91 | 4.1 | 23 | 18 | 3.97 | 1 | 1 | 1.2147 |

| author | year | prev_cannabis_mean | frequent_use | current_use | tobacco_current | age_m | male | panss_bprs |
|---|---|---|---|---|---|---|---|---|
| Barkus | 2011 | 153 | 1 | 0 | | 26.3 | 100% | 1 |
| D'Souza | 2012 | 318 | 1 | | 15.79% | 25.92 | 65.3846154% | 1 |
| D'Souza | 2004 | 60.77 | 0 | 0 | 23.81% | 29 | 63.6363636% | 1 |
| D'Souza | 2008 | 147.51 | 1 | 1 | | 24.8 | 70% | 1 |
| D'Souza | 2009a | 48.86 | 0 | 0 | 0% | 25.85 | 78.5714286% | 1 |
| D'Souza | 2009b | 141.72 | 1 | 1 | 11.1111111% | 22.66 | 100% | 1 |
| Liem-Moolenaar | 2010 | | | 0 | | 24.1 | 100% | 1 |
| Kleinloog | 2012 | 292.2 | 1 | 0 | 0% | 22.3 | 100% | 1 |
| Radhakrishnan | 2015 | 296.75 | 1 | | 14.8148148% | 26.26 | 100% | 1 |

**Supplementary Table 5**. Raw data used in total BPRS and PANSS analysis for healthy participants

| author | year | time | n1i | m1i | sd1i | n2i | m2i | sd2i | route |
|---|---|---|---|---|---|---|---|---|---|
| Bhattacharyya | 2015 | 120 | 36 | 40.17 | 9.53892 | 36 | 31.67 | 3.17964 | 0 |
| D'Souza | 2012 | 10 | 26 | 50.04 | 10.52 | 26 | 32.65 | 5.38 | 1 |
| D'Souza | 2004 | 10 | 18 | 41.94 | 12.71 | 18 | 30.28 | 2.16 | 1 |
| D'Souza | 2008 | 10 | 20 | 38.92 | 7.35 | 20 | 31 | 3.48 | 1 |
| D'Souza | 2009a | 15 | 14 | 36.29 | 3.92 | 14 | 30.64 | 2.32 | 1 |
| D'Souza | 2009b | 15 | 9 | 33.44 | 2.71 | 9 | 31.11 | 2.47 | 1 |
| Radhakrishnan | 2015 | 70 | 23 | 40.83 | 7.69 | 23 | 33.26 | 6.33 | 1 |
| Bossong | 2009 | 21 | 7 | 23.43 | 3.41 | 7 | 18.14 | 0.38 | 2 |
| Liem-Moolenaar | 2010 | 40 | 11 | 47.09 | 8.99 | 11 | 36.91 | 7.85 | 2 |
| Kleinloog | 2012 | 36 | 32 | 38.52 | 7.7 | 32 | 32.28 | 3.1 | 2 |

| author | year | thc_drob | dose | prev_cannabis_m | freq_use | current_use | tobacco_current | age_m | male | panss_bprs |
|---|---|---|---|---|---|---|---|---|---|---|
| Bhattacharyya | 2015 | 1 | 10 | 10.83 | 0 | 0 | 25% | 25.97 | 100% | 1 |
| D'Souza | 2012 | 1 | 2.133 | 318 | 1 |  | 15.79% | 25.92 | 65.3846154% | 1 |
| D'Souza | 2004 | 1 | 5 | 60.77 | 0 | 0 | 23.81% | 29 | 63.6363636% | 1 |
| D'Souza | 2008 | 1 | 5 | 147.51 | 1 | 1 |  | 24.8 | 70% | 1 |
| D'Souza | 2009a | 1 | 2.0774 | 48.86 | 0 | 0 | 0% | 25.85 | 78.5714286% | 1 |
| D'Souza | 2009b | 1 | 2.1125 | 141.72 | 1 | 1 | 11.1111111% | 22.66 | 100% | 1 |
| Radhakrishnan | 2015 | 1 | 1.2147 | 296.75 | 1 |  | 14.8148148% | 25.44 | 100% | 1 |
| Bossong | 2009 | 1 | 8 |  |  | 0 |  | 21.9 | 100% | 0 |
| Liem-Moolenaar | 2010 | 1 |  |  |  | 0 |  | 24.1 | 100% | 1 |
| Kleinloog | 2012 | 1 |  | 292.2 |  | 0 |  | 22.3 | 100% | 1 |

**Supplementary Table 6.** Summary of Study Characteristics: within person studies examining acute administration of THC in healthy controls

Exclusion criteria:
1 = Past or present psychiatric history (excluding cannabis use disorder)
2 = Recent history of substance abuse (excluding cannabis and nicotine)
3 = Family history of psychosis
4 = Major medical or neurological disorder
5 = Concurrent psychotropic medication use

| Study | Blinded | Randomised | THC method of administration/dose | Placebo condition | Symptoms (BPRS/PANSS) | Exclusion Criteria |
|---|---|---|---|---|---|---|
| **Barkus 2011** | Double | Yes | IV bolus<br>2.5mg dronabinol<br><br>Timing: >24 hours<br><br>Fasting: not known | 2.5% ethanol + saline | PANSS:<br>Positive<br>Negative<br>General<br><br>Timing: 30 mins after bolus | 1,3,4,5 |
| **Bhattacharyya 2015** | Double | Yes | Oral capsule<br>10mg purified THC<br><br>Timing: 1 month<br><br>Fasting: Overnight fasting, light standardised breakfast | Matched placebo capsule | PANSS:<br>Total<br>Positive<br><br>Timing: 120 minutes after administration | 1,2,3 |
| **D'Souza 2012** | Double | Yes | IV bolus<br>0.03mg/kg purified THC<br><br>Timing: Not given<br><br>Fasting: Overnight fasting, light standardised breakfast | Ethanol | PANSS: Total, positive, negative<br><br>Timing: 10 mins after bolus | 1,2,3,5 |
| **D'Souza 2004** | Double | Yes | IV over 2minutes<br>5mg purified THC<br><br>Timing: >1 week<br><br>Fasting: Overnight fasting + standardised breakfast | Ethanol | PANSS:<br>positive and negative<br><br>Timing 10 mins after bolus for positive, 80 mins for negative | 1,2,3 |
| **D'Souza 2008** | Double | Yes | IV over 20 minutes<br>0.0286mg/kg purified THC<br><br>Timing: 125 mins<br><br>Fasting: Overnight fasting + standardised breakfast | Ethanol | PANSS: Total<br>Positive<br><br>Timing: 15 mins after bolus | 1,2,3,5 |
| **D'Souza 2009** | Double | No | IV over 20 minutes<br>0.0286mg/kg purified THC<br><br>Timing: 125 minutes<br><br>Fasting: Overnight fasting + standardised breakfast | Matched vehicle | PANSS:<br>positive<br><br>Timing: 15 mins bolus | 1,2,3,5 |
| **Morrison 2009/2011** | Double | Yes | IV over 5 minutes<br>2.5mg dronabinol<br><br>Timing: >2 weeks<br><br>Fasting: Not known | Normal saline | Positive (1)<br>Negative<br><br>Timing: 30mins after bolus | 1,2,3,4 |
| **Morrison 2011** | Double | Yes | IV over 5 minutes<br>1.25 mg synthetic THC<br><br>Timing: >2 weeks<br><br>Fasting: Not known | Normal saline | PANSS:<br>positive and negative<br><br>Timing: 30 mins after bolus | 1,2,3,4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Ranganathan 2012** | Double | No | IV over 20 minutes<br>0.025mg/kg<br><br>Timing: 120 minutes<br><br>Fasting: Standard light breakfast | Vehicle | PANSS: Positive and negative<br><br>Timing: 65 mins after bolus | 1,2,3,5 |
| **Bhattacharyya 2009&2012/Fusar Poli 2009** | Double | Yes | Oral<br>10mg purified THC<br><br>Timing: Not known<br><br>Fasting: Light standardised breakfast | Flour capsule | PANSS: Positive and negative<br><br>Timing: 120 mins after capsule | 2 |
| **Rhadakrishnan 2015** | Double | Yes | IV over 10 minutes<br>0.015mg/kg purified THC<br><br>Timing: 1 day<br><br>Fasting: Overnight fasting + light standardised breakfast | Placebo THC | PANSS: Positive, negative, general and total<br><br>Timing: 70 mins after bolus | 1,2,3,5 |
| **Liem-Moolenaar 2010** | Double | Yes | Inhaled using volcano vaporizer<br>Consecutive doses of 2mg, 4mg, 6mg purified THC<br><br>Timing: 2 weeks<br><br>Fasting: Light standardised breakfast | Matching placebo | PANSS: Total<br>Positive (1)<br>Negative<br><br>Timing: 40 mins after last dose administered | 5 |
| **Kleinloog 2012** | Double | Yes | Inhaled using Volcano vaporizer<br>Consecutive doses of 2mg, 4mg and 6mg purified THC<br><br>Timing: 2 weeks<br><br>Fasting: Not known | Placebo THC | PANSS: total, positive and negative<br><br>Timing: 36 minutes after last dose administered | 1,2,3,5 |
| **Bossong 2009** | Double | Yes | Inhaled using Volcano vaporizer<br>8mg purified THC<br><br>Timing: 2 weeks<br><br>Fasting: 4 hours fasting + standardised meal | Ethanol vehicle | BPRS: Total<br><br>Timing: 21 minutes after inhalation | 1,3,2,4,5 |
| **Morgan 2018** | Double | Yes | Inhaled using Volcano vaporizer<br>8mg THC<br><br>Timing: 1 week<br><br>Fasting: Not known | Ethanol vehicle | BPRS: Positive and negative<br><br>Scales items not defined.<br><br>Timing not provided | 2,4 |

**Supplementary Table 7**. Newcastle-Ottawa quality assessment scale for cohort studies

| Study | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| Barkus 2011 | Male university staff | * | * | * | ** | * | * | * |
| Bhattacharyya 2015 | Male | * | * | * | ** | * | * | Not described |
| D'Souza 2012 | 18-35 years old | * | * | * | ** | * | * | Lacking detail of reasons for drop-outs |
| D'Souza 2004 | * | * | * | * | ** | * | * | Lacking detail of reasons for drop-outs |
| D'Souza 2008 | High cannabis use | * | * | * | ** | * | * | Lacking detail of reasons for drop-outs |
| D'Souza 2009a (Low cannabis use) | * | * | * | * | ** | * | * | * |
| D'Souza 2009b (High cannabis use) | High cannabis use | * | * | * | ** | * | * | * |
| Morrison 2009/2011 | Male university staff and students | * | * | * | ** | * | * | * |
| Morrison 2011 | University staff and students | * | * | * | ** | * | * | * |
| Ranganathan 2012 | * | * | * | * | ** | * | * | * |
| Bhattacharyya 2009/12 | Male | * | * | * | ** | * | Peak measurement at last timepoint | Not described |
| Rhadakrishnan 2015 | Male | * | * | * | ** | * | * | * |
| Liem-Moolenaar 2010 | Male | * | * | * | ** | * | * | * |
| Kleinloog 2012 | Male | * | * | * | ** | * | * | * |
| Morgan 2018 | Cannabis users, high and low schizotypy | * | * | * | ** | * | Single time point | Not described |
| Bossong 2009 | Male | * | * | * | ** | * | * | * |

1) **Representativeness of the exposed cohort:** * = "truly representative of average healthy individual in the community" or "somewhat representative of the average healthy individual in the community"
2) **Selection of the non-exposed cohort:** * = "Drawn from the same community as the exposed cohort" (within person design)
3) **Ascertainment of exposure:** * = "Secure record" or "Structured interview" (exposure provided as part of experiment)
4) **Demonstration that outcome of interest was not present at start of study**: * = "yes" i.e. SCID used to screen out people with significant psychopathology
5) **Comparability of cohorts on the basis of the design or analysis:**
    a. * = study controls for prior cannabis use
    b. * = study controls for any additional factor/factors
6) **Assessment of outcome**: * = "independent blind assessment" or "record linkage"
7) **Was follow-up long enough for outcomes to occur**: * = "yes" i.e. there were sufficient timepoints to show peak psychopathy
8) **Adequacy of follow-up cohorts**: * = "Complete follow-up – all subjects accounted for" or "subjects lost to follow-up unlikely to introduce bias – number lost - <20% or description provided of those lost"

**Table 8**: Table summarising studies evaluating CBD's effect on psychopathology compared to placebo

| Study | Sample size, n | Age. Mean (S.D) | M:F | Blind | Randomised group/ order | Route | Dose (mg) | Placebo condition | Scale | Effect |
|---|---|---|---|---|---|---|---|---|---|---|
| Bhatta-charyya 2009&2012, Fusar-Poli 2009 | 15 | 26.7 (5.7) | 15:0 | Double | Yes | Oral | 600 | Flour capsule | PANSS Total positive negative and general | → |
| Mueller 2016 (Confe-rence abstract) | 30 15 in each group Between person | NR | NR | Double | Yes | Oral | 800 | NR | PANSS Total and positive | → |
| Hundal 2017 | 32 Between person 16 in each group | 25 (8) placebo 26 (9) CBD | 8:8 both placebo and CBD | Double | Yes | Oral | 600 | Matched placebo | CAPE Total and positive | → |
| Morgan 2018 | 48 Within person | 21.7 (1.8) | 34:14 | Double | Yes | Inhaled | 16 | Ethanol vehicle | BPRS Positive and negative | → |

**Supplementary Table 9**: Summary of study characteristics – studies examining acute administration of THC and CBD in healthy controls

Exclusion criteria:
1 = Past or present psychiatric history (excluding cannabis use disorder)
2 = Recent history of substance abuse (excluding cannabis and nicotine)
3 = Family history of psychosis
4 = Major medical or neurological disorder
5 = Concurrent psychotropic medication use

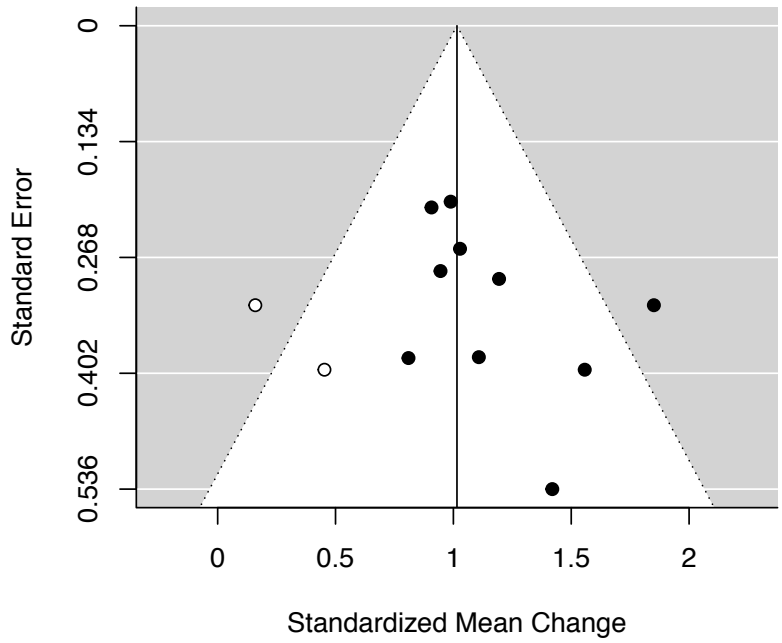
| Study | Design | Blinded | Randomised group/order | THC method of administration/ dose/timing | Placebo condition | Symptoms (BPRS/PANSS) | Exclusion Criteria |
|---|---|---|---|---|---|---|---|
| **Bhattacharyya 2010** | Within person | Double | Yes | IV over 5 minutes<br>1.25mg THC<br>5mg CBD<br><br>Timing: 2 weeks<br><br>Fasting: Not known | Ethanol vehicle | PANSS: positive<br><br>Timing: 30 and 60 minutes | Not provided |
| **Morgan 2018** | Within person | Double | Yes | Inhaled using Volcano vaporizer<br>8mg THC<br>16mg CBD<br><br>Timing: 1 week<br><br>Fasting: not known | Ethanol vehicle | BPRS: Positive and negative<br><br>Scales items not defined.<br><br>Timing not known | 2,4 |
| **Englund 2013** | Between person | Double | Yes | IV over 10 minutes<br>1.5mg synthetic THC<br>600mg CBD | Matching capsules (CBD) & Ethanol (THC) | PANSS: Positive<br><br>Timing: 10 mins after bolus | 1,3,4 |
| **Mueller 2016 (Conference abstract)** | Between person | Double | Yes | Oral<br>20mg THC<br>800mg CBD<br><br>Timing: NR<br><br>Fasting: NR | NR | PANSS: positive and total symptoms<br><br>Timing: not known | NR |

**Supplementary Table 10**: Study weights in meta-analysis (%)

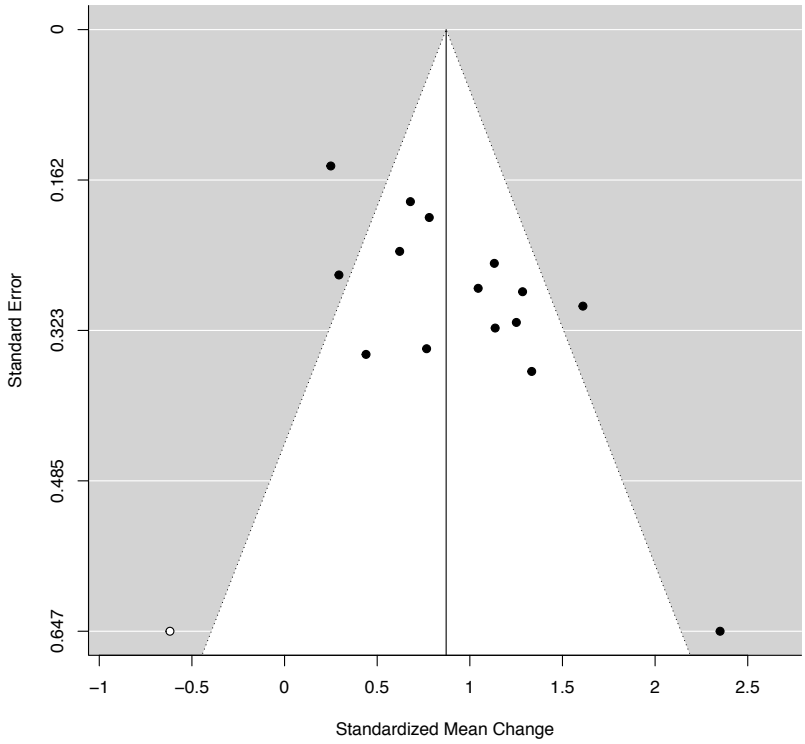
| Study | Total symptoms | Positive symptoms | Negative symptoms | General symptoms |
|---|---|---|---|---|
| Bhattacharyya 2015 | 20.32 | 8.65 | N/a | N/a |
| D'Souza 2012 | 8.05 | 6.49 | 7.97 | 12.53 |
| D'Souza 2004 | 10.45 | 6.18 | 7.60 | 13.98 |
| D'Souza 2008 | 9.81 | 6.84 | 7.69 | 14.11 |
| D'Souza 2009a | 5.32 | 5.34 | 7.28 | 8.28 |
| D'Souza 2009b | 5.70 | 5.62 | 5.49 | 7.87 |
| Radhakrishnan 2015 | 12.64 | 6.77 | 9.40 | 16.45 |
| Bossong 2009 | 2.93 | N/a | N/a | N/a |
| Liem-Moolenaar 2010 | 5.73 | 5.72 | 6.66 | 7.11 |
| Kleinloog 2012 | 19.05 | 8.31 | 10.82 | 18.95 |
| Barkus 2011 | N/a | 2.57 | 1.70 | 0.72 |
| Morrison 2009 | N/a | 7.59 | N/a | N/a |
| Morrison 2011 | N/a | 6.08 | 6.30 | N/a |
| Ranganathan 2012 | N/a | 7.34 | 9.29 | N/a |
| Morgan 2018 | N/a | 9.38 | 13.54 | N/a |
| Bhattacharyya 2012 | N/a | 7.11 | 6.25 | N/a |

**Supplementary Table 11**: Table summarising study samples and designs involving healthy individuals receiving THC and placebo using CAPE as the outcome measure.

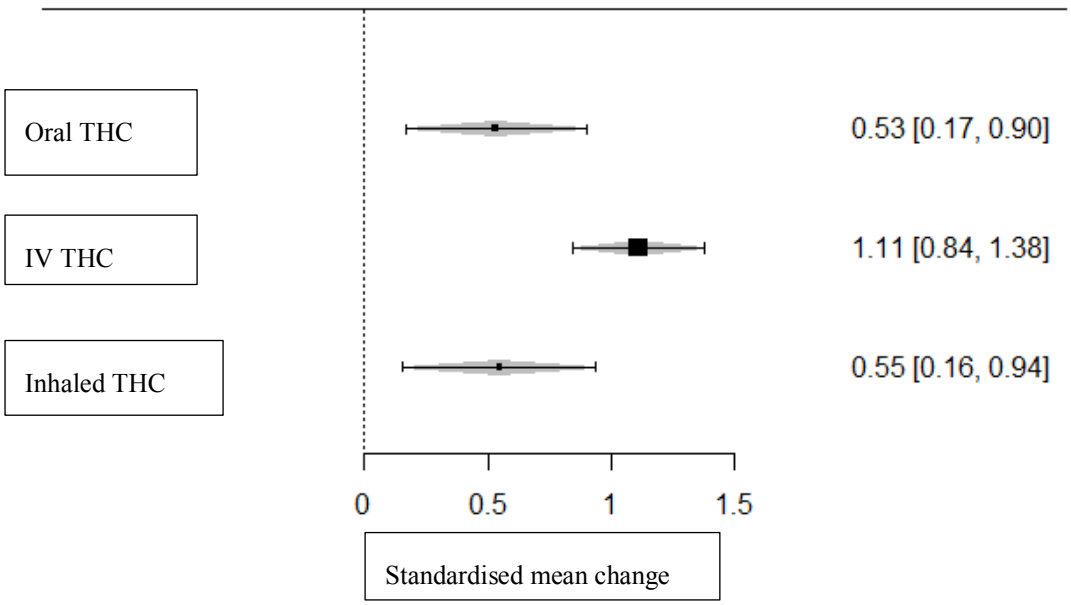
| Study | Sample size, n | Age. Mean (S.D) | M:F | Blind | Randomised group/ order | Route | Dose (mg) | Placebo condition | Scale | Effect |
|---|---|---|---|---|---|---|---|---|---|---|
| Morrison 2009 | 21 Within person | 28 (6) | 21:0 | Double | Yes | IV | 2.5 | Normal saline | PANSS: Positive | ↑ |
| Morrison 2011 | 19 Within person | NR | 19:0 | Double | Yes | IV | 2.5 | 2.5% ethanol | CAPE negative | ↑ |
| Freeman 2014 | 82 Between person 41 in each group | 30.3 (9.6) placebo, 30.8 (8.5) THC | 30:11 (placebo) 26:15 (THC) | Double | Yes | IV | 1.5 | Normal saline | CAPE Total | ↑ |
| Tunbridge 2015 | 78 Between person 39 in each group | NR (samples split according to COMT genotype) | 29:10 (Placebo) 25:14 (THC) | Double | Yes | IV | 1.5 | Saline | CAPE positive | ↑ |



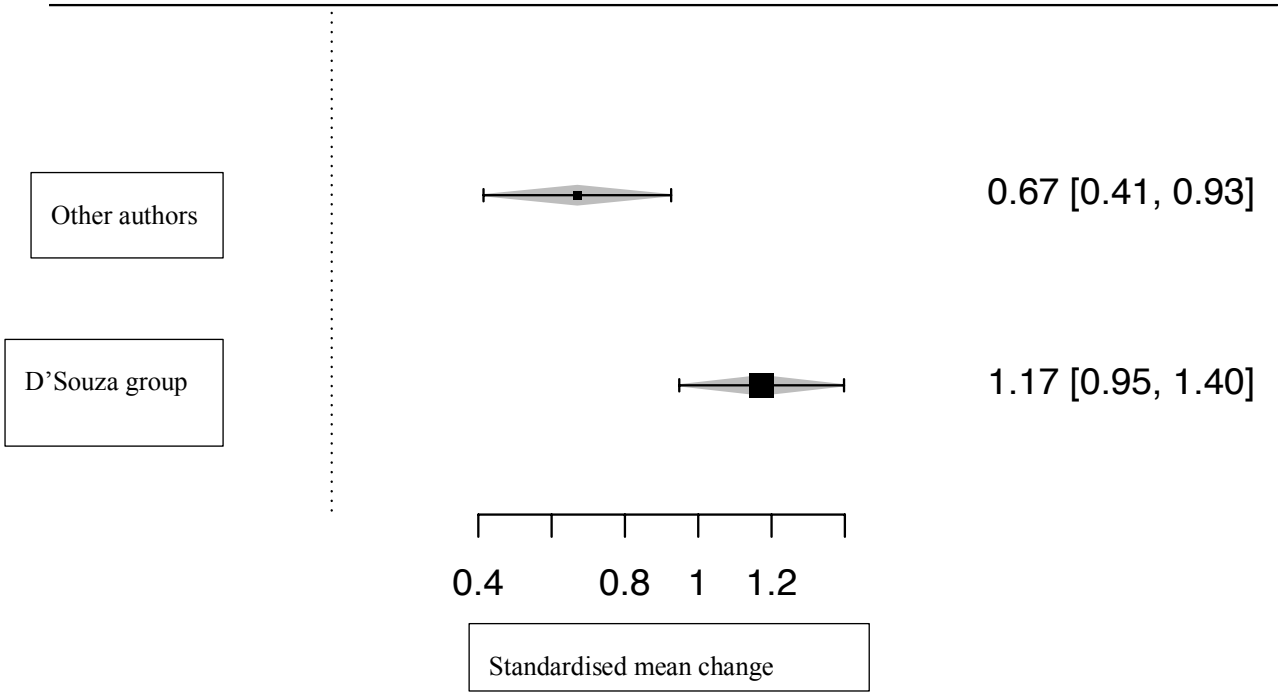

**Supplementary Figure 1.** Funnel Plot for total symptoms with 2 imputed missing studies



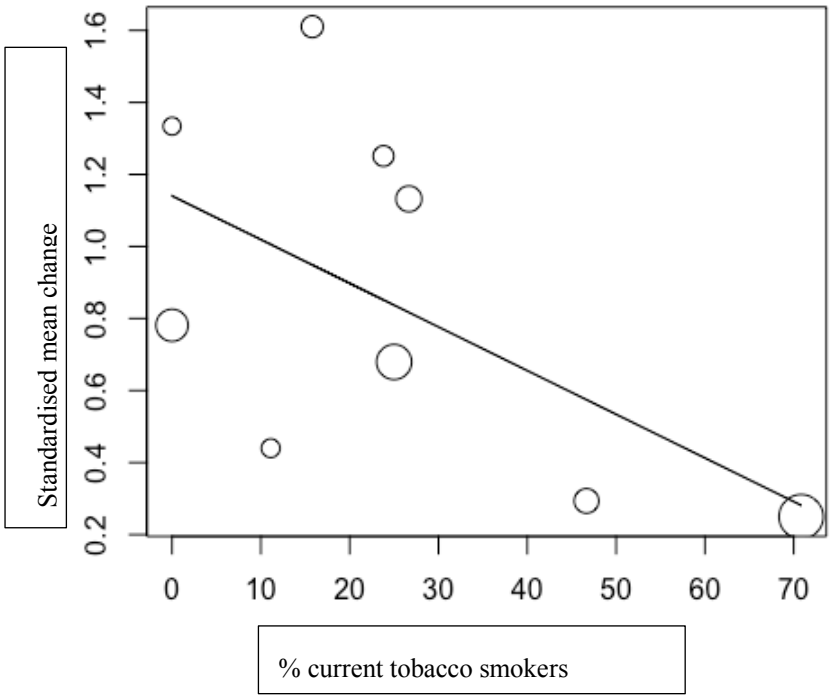

**Supplementary Figure 2.** Funnel Plot for positive symptoms with a single imputed missing study on the left hand-side



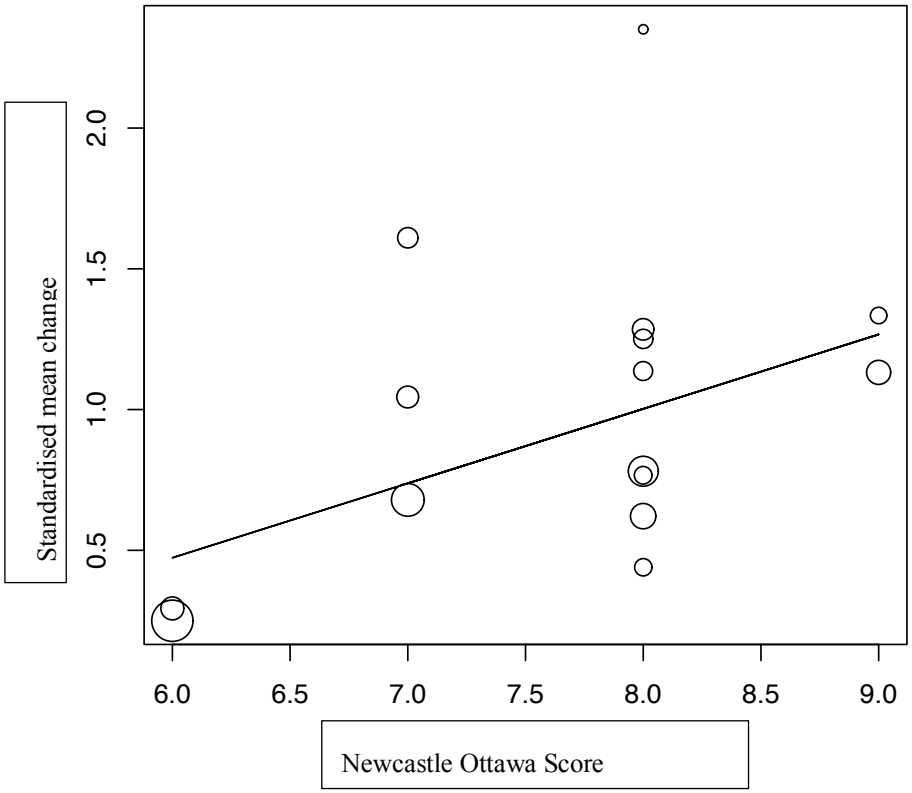

**Supplementary Figure 3.** Sub-group analysis of effect of route of administration on positive symptoms of schizophrenia.



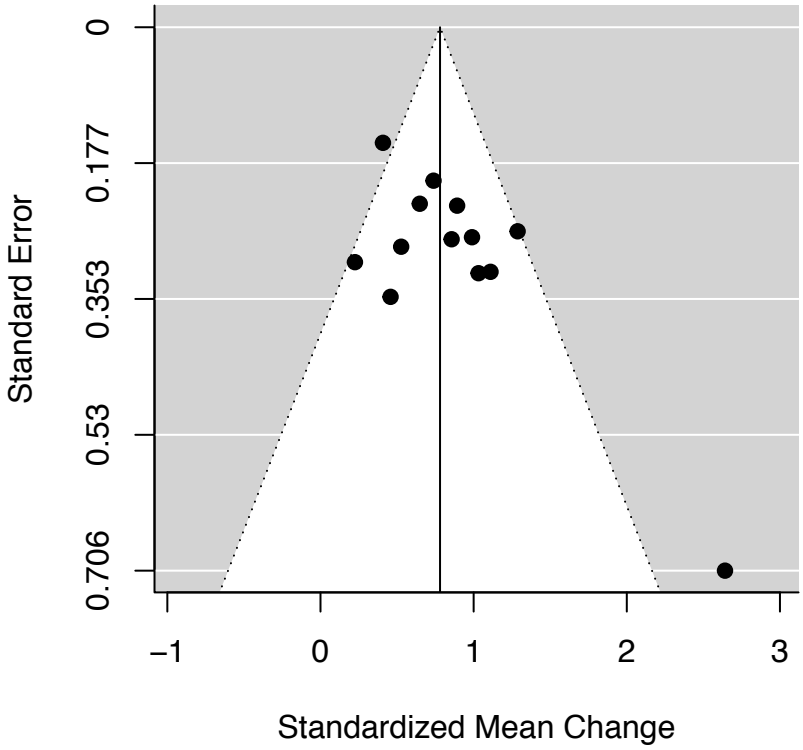

**Supplementary Figure 4.** Sub-group analysis of effect of study author (D'Souza group vs other) on positive symptoms of schizophrenia.



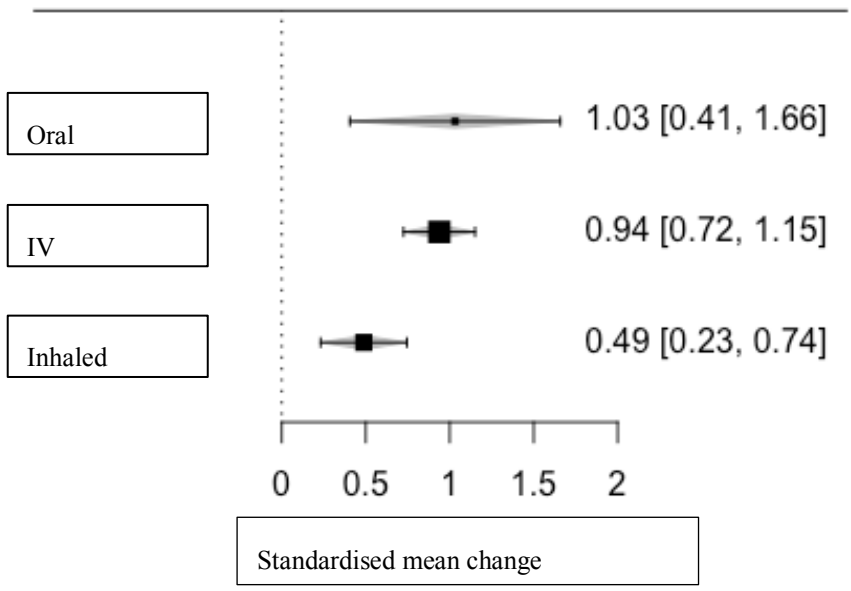

**Supplementary Figure 5.** Meta-regression showing a negative relationship between percentage current smokers and the induction of positive symptoms by THC (n=10, β=-0.013, p=0.019).



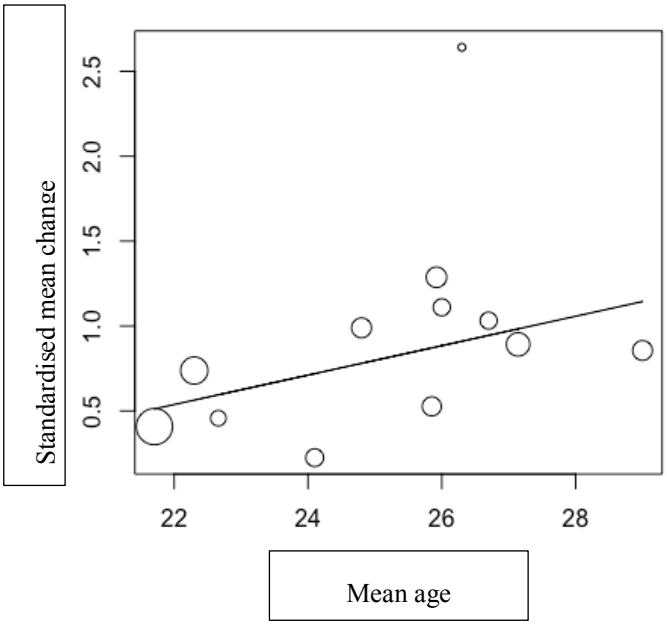

**Supplementary Figure 6.** Meta-regression showing a positive relationship between Newcastle Ottawa Score for study quality and the induction of psychotic symptoms by THC (n=15, β=0.26, p=0.011).



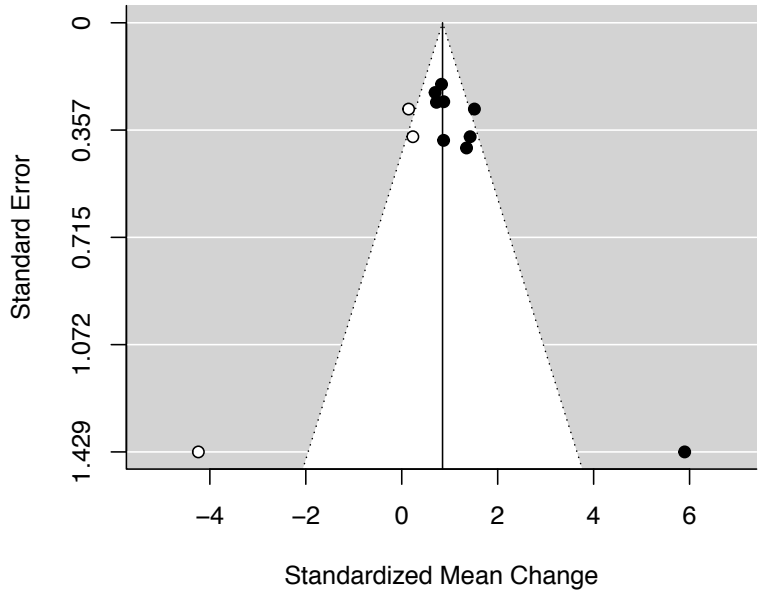

**Supplementary Figure 7.** Funnel Plot for negative symptoms



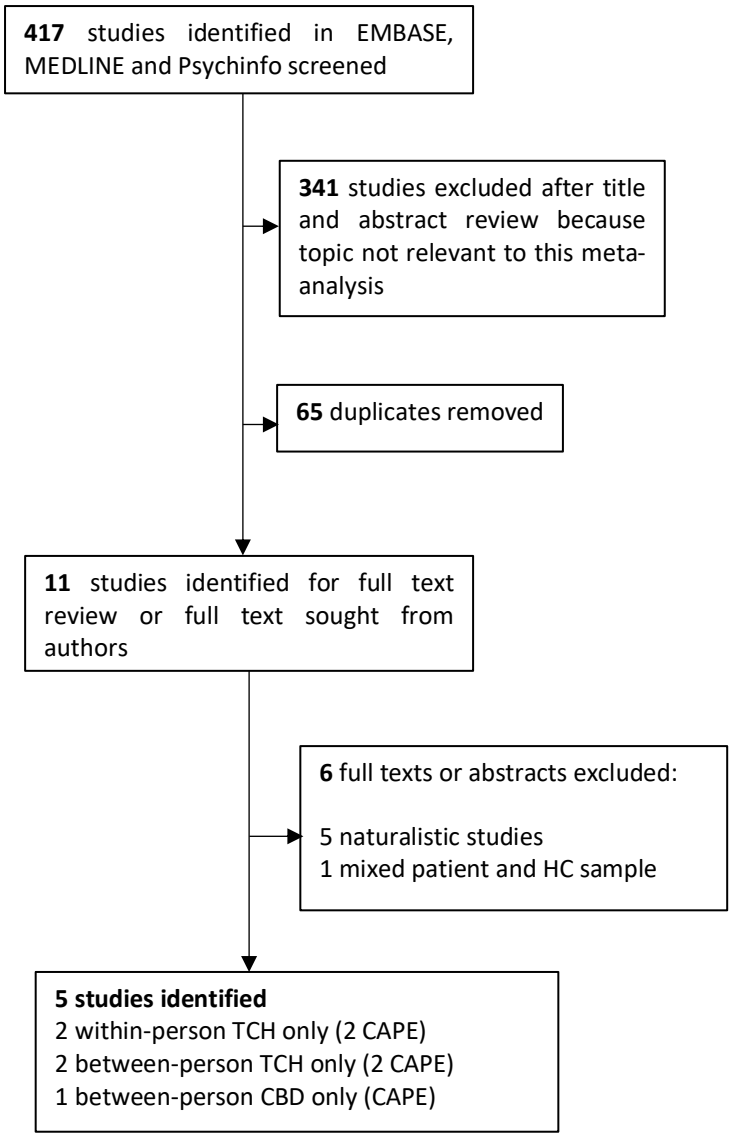

**Supplementary Figure 8.** Sub-group analysis of the moderating effect of route of administration on THC induced negative symptoms of schizophrenia.




**Supplementary Figure 9** Meta-regression showing a positive relationship between mean age and the induction of negative symptoms by THC (n=12, β=0.08, p=0.018).




**Supplementary Figure 10** Funnel Plot for general symptoms with 3 imputed missing studies




**Supplementary Figure 11:** Search process summarising the review and exclusion of papers for the CAPE/SANS/SAPS search.

**Appendix 1.** Re-fitting the model with $r = 0.1$

Acute administration of THC generated an increase in psychopathology in healthy participants, seen as a statistically significant increase in the positive symptoms (Standardised mean change score = 0.77, 95% CI, 0.57 to 0.96, P= <0.0001), negative symptoms (Standardised mean change score = 0.65, 95% CI, 0.48 to 0.83, p< 0.0001), general symptoms (Standardised mean change score = 0.81, 95% CI, 0.61 to 1.02, p< 0.0001) and total symptoms (Standardised mean change score =0.92, 95% CI, 0.75 to 1.09, P<0.0001) compared with a placebo condition.

**Appendix 2.** Re-fitting the model with $r = 0.7$

Acute administration of THC generated an increase in psychopathology in healthy participants, seen as a statistically significant increase in the positive symptoms (SMC = 1.03, 95% CI, 0.76 to 1.31 , P= <0.0001), negative symptoms (SMC= 0.89, 95% CI, 0.69 to 1.10, p< 0.0001), general symptoms (SMC = 1.17, 95% CI, 0.91 to 1.43, p< 0.0001) and total symptoms (SMC=1.29, 95% CI, 1.06 to 1.52, P<0.0001) compared with a placebo condition.

**Appendix 3.** Summary of timings of peak symptoms and duration of symptoms post THC administration (see Supplementary Table 1).

In both studies using orally administration, symptoms peaked at 120 mins for all domains reported (positive, negative, total) and had not fully resolved by the last timepoint reported (120mins and 180mins respectively).

Of 4 studies using inhaled THC, one did not report timings and two used multiple doses of THC, measuring a single time point per dose administered. In the only inhaled study reporting multiple timepoints, total symptoms peaked at 21 minutes and had not fully resolved at 102 minutes.

Finally, of 10 IV studies, symptoms peaked between 10-30 minutes in 8 studies. A single study peaked at 70 minutes although did not report earlier symptom measures. A final study reported mean positive symptoms peaking at 120 mins and negative symptoms at 65 minutes despite also measuring symptoms at 10 minutes, although the timings reported in this study are unclear. Regarding resolution of symptoms, negative and general symptoms resolved at a minimum of 80 minutes, positive symptoms at a minimum of 120 mins, and total symptoms at a minimum of 200 minutes, although total symptoms were not reported in several of the studies reporting earlier timepoints.

**Appendix 4.** Sensitivity analysis excluding potentially duplicated sample

Since we were unable to confirm that two of the samples included in the positive symptom analysis were independent,(10,11) we performed a sensitivity analysis excluding the study with the smaller sample.(10)

Positive symptoms were thus assessed in 13 studies (14 independent samples) involving a total of 309 participants. THC significantly increased positive symptom severity compared to placebo (SMC = 0.95, 95% CI: 0.72-1.19, p<0.0001). The result remained significant in all iterations of the leave-one-out-analysis (SMC = 0.89-1.01).

There was medium between-sample inconsistency ($I^2 = 63.75\%$, Cochran Q = 40.07, p<0.0001). Egger's test implied significant publication bias (p=0.0001). Trim-fill analysis did not identify any missing studies.

When comparing THC's effects on different symptom domains, THC's effect on positive symptoms remained significantly greater than on negative symptoms (z=2.29, p=0.022) but equivalent to its effect on general symptoms (z=0.23, p=0.82).

**Appendix 5.** Re-fitting the model comparing symptom domains with $r = 0.1$-$0.7$

When comparing positive and negative symptoms induced by the acute administration of THC, there was no significant difference when $r = 0.1$ (z=1.53, p=0.13) but the effect on positive symptoms was significantly greater when $r = 0.5$ (z=2.06, p=0.039) or $r = 0.7$ (z=2.31, p=0.02).

When comparing positive and general symptoms, there was no significant difference at either $r = 0.1$ (z=0.02, p=0.98), $r = 0.5$ (z=0.44, p=0.66) or $r = 0.7$ (z=0.72, p=0.47).

When comparing negative and general symptoms, there was no significant difference when $r$ = 0.1 (z=1.70, p=0.09) or $r$ = 0.5 (z=1.90, p=0.058) but the effect on general symptoms was significantly greater than negative symptoms when $r$ = 0.7 (z=2.01, p=0.044).

**Appendix 6.** Sensitivity analysis for lower estimation total cannabis exposures

There was no association found between frequent use and positive symptoms (z=1.57, p=0.12), negative symptoms (z=0.79, p=0.43), general symptoms (z=0.97, p=0.33) or total symptoms (z=0.53, p=0.59).

**Appendix 7.** Sensitivity analysis for higher estimation of total cannabis exposures

There was no association found between frequent use and positive symptoms (z=0.87, p=0.38), negative symptoms (z=0.23, p=0.82), general symptoms (-0.07, p=0.95) or total symptoms (z=-0.35, p=0.73).

**Appendix 8.** Supplementary analysis including studies using the CAPE scale

We identified two within person studies that had used the CAPE and two between person studies (Supplementary Figure 11.(12,13) All four reported a significant increase in symptoms following administration of THC compared to placebo (Supplementary Table 11)."

Of the within-person studies, one study reported PANSS positive scores in addition to CAPE positive scores and so was already included in the positive symptoms meta-analysis.(12) The second study only reported CAPE negative scores (PANSS negative subscale was also measured but the results are not reported in the text and the author did not respond to requests for data).(13) As there are marked differences between the rating procedure for CAPE relative to the other instruments (the CAPE is a self-reported measure, whereas the PANSS and BPRS are rated by a trained researcher using semi-structured interviews) we excluded the CAPE from our main analysis of negative symptoms. However, we performed a sensitivity analysis including this study for completeness.

Negative symptoms were thus assessed in 13 studies (14 independent samples) involving a total of 286 participants. THC significantly increased negative symptom severity compared to placebo (SMC = 0.75, 95% CI: 0.58-0.93, p<0.0001). The result remained significant in all iterations of the leave-one-out-analysis (SMC = 0.70-0.80).

There was medium between-sample inconsistency ($I^2$ = 38.52%, Cochran Q = 25.39, p=0.02). Egger's test implied significant publication bias (p=0.0061). Trim-fill analysis identified one putative missing study on the left side. On imputation of the putative missing study, the effect of THC remained highly significant (SMC = 0.73, 95% CI: 0.54-0.91, p<0.0001).

When comparing THC's effects on different symptom domains, THC's effect on positive symptoms remained significantly greater than on negative symptoms (z=2.38, p=0.018). However, its effect on general symptoms became significantly greater when compared to negative symptoms with the additional study included (z=2.14, p=0.032).

**Appendix 9.** Leave one-out analysis full results

**Total symptoms**

| | estimate | se | zval | pval | ci.lb | ci.ub |
|---|---|---|---|---|---|---|
| Bhattacharyya, 2015 | 1.1427 | 0.1118 | 10.2195 | 0.0000 | 0.9235 | 1.3618 |
| D'Souza, 2012 | 1.0371 | 0.0956 | 10.8491 | 0.0000 | 0.8498 | 1.2245 |
| D'Souza, 2004 | 1.1300 | 0.1032 | 10.9510 | 0.0000 | 0.9278 | 1.3322 |
| D'Souza, 2008 | 1.0974 | 0.1000 | 10.9715 | 0.0000 | 0.9013 | 1.2934 |
| D'Souza, 2009a | 1.0771 | 0.0942 | 11.4339 | 0.0000 | 0.8925 | 1.2617 |
| D'Souza, 2009b | 1.1235 | 0.0964 | 11.6548 | 0.0000 | 0.9346 | 1.3124 |
| Radhakrishnan, 2015 | 1.1257 | 0.1071 | 10.5109 | 0.0000 | 0.9158 | 1.3356 |
| Bossong, 2009 | 1.0931 | 0.0930 | 11.7485 | 0.0000 | 0.9107 | 1.2754 |
| Liem-Moolenaar, 2010 | 1.1050 | 0.0964 | 11.4644 | 0.0000 | 0.9161 | 1.2939 |
| Kleinloog, 2012 | 1.1494 | 0.1025 | 11.2132 | 0.0000 | 0.9485 | 1.3502 |

**Positive symptoms**

| | estimate | se | zval | pval | ci.lb | ci.ub |
|---|---|---|---|---|---|---|
| Barkus, 2011 | 0.8661 | 0.1144 | 7.5736 | 0.0000 | 0.6420 | 1.0902 |
| Bhattacharyya, 2015 | 0.9342 | 0.1289 | 7.2492 | 0.0000 | 0.6816 | 1.1868 |
| D'Souza, 2012 | 0.8493 | 0.1133 | 7.4953 | 0.0000 | 0.6273 | 1.0714 |
| D'Souza, 2004 | 0.8865 | 0.1236 | 7.1720 | 0.0000 | 0.6443 | 1.1288 |
| D'Souza, 2008 | 0.9021 | 0.1270 | 7.1009 | 0.0000 | 0.6531 | 1.1511 |
| D'Souza, 2009a | 0.8841 | 0.1221 | 7.2430 | 0.0000 | 0.6449 | 1.1234 |
| D'Souza, 2009b | 0.9377 | 0.1237 | 7.5812 | 0.0000 | 0.6953 | 1.1801 |
| Morrison, 2009 | 0.9353 | 0.1272 | 7.3540 | 0.0000 | 0.6861 | 1.1846 |
| Morrison, 2011 | 0.8960 | 0.1252 | 7.1539 | 0.0000 | 0.6505 | 1.1415 |
| Ranganathan, 2012 | 0.8935 | 0.1264 | 7.0703 | 0.0000 | 0.6458 | 1.1412 |
| Bhattacharyya, 2009 | 0.9515 | 0.1198 | 7.9425 | 0.0000 | 0.7167 | 1.1863 |
| Morgan, 2018 | 0.9636 | 0.1084 | 8.8904 | 0.0000 | 0.7512 | 1.1761 |
| Liem-Moolenaar, 2010 | 0.9209 | 0.1264 | 7.2855 | 0.0000 | 0.6732 | 1.1687 |
| Kleinloog, 2012 | 0.9251 | 0.1296 | 7.1385 | 0.0000 | 0.6711 | 1.1792 |
| Radhakrishnan, 2015 | 0.8809 | 0.1230 | 7.1601 | 0.0000 | 0.6397 | 1.1220 |

**Negative symptoms**

| | estimate | se | zval | pval | ci.lb | ci.ub |
|---|---|---|---|---|---|---|
| Barkus, 2011 | 0.7444 | 0.0911 | 8.1703 | 0.0000 | 0.5658 | 0.9230 |
| D'Souza, 2012 | 0.7236 | 0.0896 | 8.0772 | 0.0000 | 0.5480 | 0.8991 |
| D'Souza, 2004 | 0.7791 | 0.1046 | 7.4463 | 0.0000 | 0.5740 | 0.9842 |
| D'Souza, 2008 | 0.7653 | 0.1022 | 7.4856 | 0.0000 | 0.5649 | 0.9657 |
| D'Souza, 2009a | 0.8044 | 0.1034 | 7.7815 | 0.0000 | 0.6018 | 1.0070 |
| D'Souza, 2009b | 0.8023 | 0.1015 | 7.9055 | 0.0000 | 0.6034 | 1.0013 |
| Morrison, 2011 | 0.7579 | 0.0990 | 7.6571 | 0.0000 | 0.5639 | 0.9519 |
| Ranganathan, 2012 | 0.7743 | 0.1057 | 7.3258 | 0.0000 | 0.5671 | 0.9815 |
| Bhattacharyya, 2012 | 0.7650 | 0.1007 | 7.5985 | 0.0000 | 0.5677 | 0.9624 |
| Morgan, 2018 | 0.8305 | 0.0868 | 9.5637 | 0.0000 | 0.6603 | 1.0007 |
| Liem-Moolenaar, 2010 | 0.8164 | 0.0969 | 8.4274 | 0.0000 | 0.6265 | 1.0063 |
| Kleinloog, 2012 | 0.7932 | 0.1089 | 7.2863 | 0.0000 | 0.5798 | 1.0065 |
| Radhakrishnan, 2015 | 0.8003 | 0.1068 | 7.4945 | 0.0000 | 0.5910 | 1.0096 |

**General symptoms**

| | estimate | se | zval | pval | ci.lb | ci.ub |
|---|---|---|---|---|---|---|
| Barkus, 2011 | 0.9662 | 0.1124 | 8.5991 | 0.0000 | 0.7459 | 1.1864 |
| D'Souza, 2012 | 0.9020 | 0.1050 | 8.5928 | 0.0000 | 0.6963 | 1.1077 |
| D'Souza, 2004 | 1.0724 | 0.1422 | 7.5409 | 0.0000 | 0.7937 | 1.3512 |
| D'Souza, 2008 | 1.0586 | 0.1500 | 7.0557 | 0.0000 | 0.7645 | 1.3526 |
| D'Souza, 2009a | 0.9660 | 0.1212 | 7.9721 | 0.0000 | 0.7285 | 1.2036 |
| D'Souza, 2009b | 1.0402 | 0.1396 | 7.4513 | 0.0000 | 0.7666 | 1.3138 |
| Liem-Moolenaar, 2010 | 0.9850 | 0.1268 | 7.7707 | 0.0000 | 0.7366 | 1.2335 |
| Kleinloog, 2012 | 1.0746 | 0.1522 | 7.0611 | 0.0000 | 0.7763 | 1.3729 |
| Radhakrishnan, 2015 | 1.0789 | 0.1381 | 7.8114 | 0.0000 | 0.8082 | 1.3496 |

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