

## Supplementary Online Content

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**eMethods.** Supplementary Methods

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**eTable 1.** Overview of 69 Studies Included in the Meta-Analysis

**eTable 2.** Neurocognitive Tests Analyzed in the Meta-Analysis, by Cognitive Domain

**eFigure 1.** (A) Unadjusted and (B) trim-and-fill funnel plots with standardized mean difference effect sizes (d)

**eFigure 2.** Mean weighted effect sizes and 95% confidence intervals for age groups.

**eFigure 3.** Mean weighted effect sizes and 95% confidence intervals for year of publication.

This supplementary material has been provided by the authors to give readers additional information about their work.

## Supplementary Methods

### Search Strategies and Selection of Studies

Literature searches using the keywords cannabis or marijuana paired with adolescent or young adult and cogniti\*, neuropsycholog\*, or domain-specific keywords (e.g., memory) were independently conducted by two reviewers using four electronic databases: PubMed, PsycINFO, Academic Search Premier, and Scopus. As an example, the following electronic search was conducted in PubMed: (((cannabis[Title/Abstract] OR marijuana[Title/Abstract]) AND (adolescent OR "young adult")) AND (cognition OR cognitive OR neuropsycholog\* OR memory OR attention OR concentration OR working memory OR executive function\* OR inhibition OR planning OR shifting OR switching OR verbal fluency OR language OR speed of information processing OR processing speed OR psychomotor OR visuospatial)) NOT Review[ptyp] AND Humans[Mesh] AND English[lang]). The reference lists of relevant reviews were also hand searched to identify omissions in our literature search.

See Methods in main text for meta-analysis inclusion criteria. Because we were interested in heavy/frequent cannabis use during potentially sensitive neurodevelopmental periods, we included studies in which the cannabis group had a mean age of 26 or less (it should be noted that 30 studies had an upper age range that may have been older than 26, though age range was not commonly reported in young adult studies). Although there is variability in trajectories of brain gray and white matter development and debate about when significant neurodevelopment decelerates, age 25 or 26 is when the deceleration in most changes in structural brain measures appears to occur.<sup>1</sup> Because this estimate of neurodevelopmental age may be imprecise, we also examined the mean age, age range of the cannabis sample, early versus late onset of cannabis use, and age at first cannabis use as explanatory variables to examine whether age influenced the magnitude of effect sizes.

For studies that examined cognitive functioning in cannabis users with severe psychiatric disorders (e.g., schizophrenia), we only included groups without such disorders. Similarly, studies that identified cannabis use as a significant comorbidity to another drug of interest (e.g., methylenedioxymethamphetamine [MDMA]) were excluded. Studies that reported cognitive data only from tests administered during functional neuroimaging were excluded due to the varying characteristics of the tests and their typically unexplored validity as behavioral markers of cognitive dysfunction. When studies included more than one affected group (e.g., early and late users) with independent data available, we used data from both groups but halved the comparison group sample size to avoid oversampling, as previously recommended.<sup>2</sup> For studies reporting cognitive functioning data in both early and later abstinence periods from the same users,<sup>3,4</sup> we included data from later abstinence periods in order to have sufficient data to address questions regarding abstinence. When sufficient data to calculate effect sizes were unavailable, study authors were contacted in an attempt to obtain data. Studies with shared authors were carefully reviewed to minimize inclusion of overlapping data.

Studies varied in their inclusion criteria for cannabis user groups (see eTable 1). Some studies provided limited information regarding criteria for cannabis group inclusion, although their cannabis group reported frequency and/or quantity of use that was similar to those of other studies with more specific criteria, and such studies were therefore included. However, this variability created challenges in creating standards for meta-analytic study inclusion. We decided to be inclusive to provide a comprehensive overview of the literature examining frequent/heavy cannabis use and cognitive functioning in adolescents and young adults. In addition, studies were inconsistent in their classifications of early cannabis use, with classification of early age of initiation ranging from 15 to 18. Therefore, we used the authors' classification of early use in each individual study to define early cannabis use for analytic purposes (see below).

Meta-analysis data presented in this study and a corresponding data dictionary are available on the Open Science Foundation website (<http://osf.io/z2qwf>).

### Effect Size Calculation

We used the standardized mean difference statistic ( $d$ ) as the measure of effect size, which was calculated as  $d = (M_e - M_c) / S_p$ , where  $M_e$  and  $M_c$  are the mean scores on a neuropsychological test for the cannabis and comparison groups, respectively, and  $S_p$  is the pooled within-group standard deviation. For studies in which mean scores and standard deviations were not reported, standardized mean difference effect sizes were derived from  $t$ -values based on independent  $t$ -tests or  $F$ -ratios from a two-group one-way analysis of variance.<sup>5</sup> If standard error of the mean was reported instead of standard deviation, transformation to standard deviation was conducted by multiplying the standard error by the square root of the sample size. When values were only displayed in figures and the authors could not provide data,<sup>3</sup> numerical values were extracted from figures using WebPlotDigitizer version 3.12 (<http://arohatgi.info/WebPlotDigitizer/app/>). By convention,  $d$  values of .2, .5, and .8 correspond to small,

medium, and large effect sizes, respectively,<sup>6</sup> although it should be noted that these categorizations are broad and do not necessarily signify levels of practical significance.

Raters independently classified tests into domains based on evidence of construct validity. These domains were attention (e.g., Continuous Performance Test), learning (e.g., California Verbal Learning Test-Second Edition [CVLT-2] Trials 1–5), delayed memory (e.g., CVLT-2 Delayed Recall), speed of information processing (e.g., Wechsler Adult Intelligence Scale, Third Edition [WAIS-III] Digit Symbol), verbal/language (e.g., Verbal Fluency), visuospatial (e.g., Rey Complex Figure Copy), motor functioning (e.g., Grooved Pegboard), and three subdomains of executive functioning, including abstraction/shifting (e.g., Wisconsin Card Sorting Test), updating/working memory (e.g., *n*-back), and inhibition (e.g., Stop Signal Paradigm). Note that “learning” as identified here is synonymous with “immediate memory,” while “delayed memory” is synonymous with “delayed recall.” If a study included multiple outcomes from a single neurocognitive test that assessed the same construct (e.g., CVLT-2 Delayed Free Recall and Delayed Cued Recall), consensus was used to select the outcome with the greatest evidence of construct validity (e.g., Delayed Free Recall) to reduce the problem of multiple comparisons. We chose not to examine IQ specifically as an outcome since many studies used a measurement of IQ or IQ estimate to match groups, which would bias effect sizes.

The following information was extracted from each study: (a) participant demographic variables (e.g., mean age), (b) cannabis use characteristics (e.g., mean age of cannabis use onset, frequency of cannabis use), (c) other clinical characteristics (e.g., comorbid alcohol use, length of cannabis abstinence), (d) study inclusion/exclusion criteria, (e) sample size, and (f) summary statistics for the calculation of effect sizes.

### **Additional Explanatory Variables**

We examined a number of predetermined additional study-level variables as explanatory variables based on prior research, including mean hours of reported abstinence, study abstinence criteria, the between-groups standardized mean difference of a study’s reported depression measure, time period of publication, whether groups in a study were matched on alcohol use, and whether the sample was a community-based or clinical sample. Given the multiple variables examined, we defined a Bonferroni correction level of  $p = 0.008$  and also reported results unadjusted for multiple comparisons.

We examined the age of a sample as a categorical variable, representing adolescent (age 10 to 18;  $k = 15$ ,  $N = 790$ ), young adult (age 19 to 26;  $k = 41$ ,  $N = 3457$ ), or mixed adolescent and young adult ( $k = 13$ ,  $N = 4480$ ) sample. Similarly, we examined age at first use (available for  $k = 45$  studies) as a categorical variable for subgroup analyses, representing early use of cannabis ( $k = 13$ ,  $N = 817$ ) and late use or nonspecific onset of cannabis use ( $k = 56$ ,  $N = 7910$ ).

Mean hours of reported abstinence was positively skewed and log transformed for further analysis. To examine clinically relevant cannabis abstinence criteria, we also divided study abstinence criteria into a three-level variable representing: (1) none or no specificity in abstinence criteria ( $k = 22$ ,  $N = 5768$ ); (2) equal to or less than 72 hours of abstinence ( $k = 32$ ,  $N = 2031$ ); and (3) greater than 72 hours of abstinence ( $k = 15$ ,  $N = 928$ ). Seventy-two hours was chosen as a cutoff to correspond to the post-peak period for most cannabis withdrawal symptoms.<sup>7</sup> Subgroup analyses combined groups 1 and 2 above to compare to group 3. However, we present data in Figure 3 in the main text to show that the subgroup with unknown or zero abstinence levels were not the primary contributor to these differences.

Given increasing levels of THC in cannabis, some have proposed the potential for increased cannabis-associated deficits in recent years due to this increased potency. We present estimated effect sizes for each year of publication across studies in eFigure 3 so that readers can visually examine whether cannabis is associated with any trends in effect size magnitude by year. Further, we also created a three-level variable, representing studies published before the year 2000 ( $k = 6$ ,  $N = 376$ ), from 2000–2009 ( $k = 17$ ,  $N = 882$ ), and after 2010 ( $k = 46$ ,  $N = 7469$ ) to test in subgroup analyses whether associations between frequent cannabis use and cognitive functioning were different in older vs. more recent studies.

A depression measure for both groups, necessary to construct between-groups standardized mean differences, was available for  $k = 24$  studies ( $N = 1408$ ). Only  $k = 23$  studies ( $N = 1708$ ) matched groups by alcohol use characteristics.

We also conducted secondary analyses to examine the consistency of results and protect against concerns regarding variable selection. To this end, we examined whether analyses of continuous variables representing early use of cannabis (i.e., mean age at first cannabis use, available for  $k = 45$ ,  $N = 6454$ ) sample age (i.e., mean age of each cannabis sample, available for  $k = 68$ ,  $N = 8675$ ), and abstinence criteria (e.g., required hours of abstinence, available for  $k = 69$ ,  $N = 8727$ ) were consistent with analyses of the categorical variables described above. Required

hours of abstinence was coded as zero if no information on abstinence was reported. This variable was positively skewed and log transformed for further analysis.

It was not possible to code a number of factors that could affect the interpretation of results. No studies reported the use of neuropsychological performance validity tests to examine the influence of effort on neuropsychological test performance, despite the relevance of such measures for predicting cognitive performance in individuals with psychiatric disorders.<sup>8</sup> There were also limited means for classifying cannabis use severity, as there was heterogeneity in the measurement and reporting of cannabis use parameters.

## **Analyses**

### **Analysis of Bias**

It is well known that studies with small sample sizes that are published in the research literature are likely to show larger effects than studies with larger samples, which can lead to small study effects in meta-analyses.<sup>9</sup> To examine potential small study bias in the literature, funnel plot tests and exploratory analyses were conducted. These procedures included visual inspection of the funnel plot, the method of Egger and colleagues<sup>9</sup> to test for small study effects, and the trim-and-fill method of Duval and Tweedie<sup>10</sup> to fill potentially missing effect sizes. We interpreted significant funnel plot asymmetry as potentially indicative of publication bias across the literature. This asymmetry often occurs when smaller studies with low precision and null or unexpected effects are systematically missing from the published literature. The trim-and-fill method is a sensitivity analysis to follow up on potentially asymmetrical funnel plots. The method estimates the number of potentially missing effect sizes from a meta-analysis and examines the effects of imputing the missing effect sizes. Since, to our knowledge, there is no trim-and-fill method for mixed effects meta-analysis, we ran a random effects meta-analysis on all data and adjusted using the standard trim-and-fill method. Given that this analysis was not identical to our primary mixed effects analyses, the exact reduction in effect size magnitude and the number of filled effect sizes generated from this analysis should be interpreted with caution.

### **Statistical Analyses**

Our analyses used a multivariate mixed-effects model for several theoretical and practical reasons. First, this method was chosen to allow for multiple outcomes per study. Most studies of neurocognitive functioning report multiple cognitive outcomes since multiple tests are typically required to have reliable data that assesses cognitive functioning across several ability areas. Although some meta-analyses conduct multiple, separate univariate meta-analyses when encountering multiple outcomes per study, this approach unfortunately does not allow the comparison and synthesis of effect sizes within studies and can lead to partially redundant analyses. Some meta-analyses simply allow a single study to contribute more than one effect size estimate when multiple outcome measures are reported. However, effect sizes within such studies are likely non-independent. Riley<sup>11</sup> has demonstrated that treating multiple effect sizes within studies as though they were statistically independent may lead to biased estimates and invalid conclusions, unless the within-study variance is small relative to the between-study variance and the within-study covariances differ little across studies. Although some meta-analyses simply average data across domains or select a single measure to represent a functional domain, this process ignores the richness of data and could introduce significant biases.

The statistically and substantively more sound approach is a multivariate model that allows for multiple correlated within-study effect sizes, takes the hierarchical (clustered) data structure into account, and permits different cluster sizes (i.e., different number of effect sizes per study). A multivariate mixed-effects model for meta-analysis also allows us to increase generalizability instead of allowing inferences only about this particular set of studies. To apply this model to meta-analytic data, we first calculated  $d$  and determined the sampling variance of each effect size, and we defined a two-level mixed effects model, where level 1 is represented by multiple effect sizes within studies, and level 2 is represented by the different studies. The model considers the level-1 effect size variances as fixed/known (as calculated).

## **eResults. Results.**

### **Preliminary Analyses**

eFigure 1A displays a funnel plot of effect size estimates against their standard error across the 69 studies, revealing asymmetry. We applied the trim and fill method of Duval and Tweedie<sup>10</sup> to examine the effect of filling the funnel plot with potentially missing effect sizes. As shown in eFigure 1B, this method filled an additional 44 studies, with the effect size (reported as mean [95% CI]) being reduced from  $d = -.206$  [-0.24, -0.16] to  $d = -.128$  [-0.17, -.09], although this adjusted mean effect size was still significant ( $p < .001$ ).

## Follow-up Analyses

As shown in eFigure 2, subgroup analyses showed no differences in effect size magnitude between studies that only included adolescents (18 years old and under;  $d=-.19$ ), only included young adults ( $d=-.26$ ), or included mixed adolescent/adult samples ( $d=-.26$ ) ( $\chi^2(2)=0.37, p=.83$ ). Secondary analyses showed no significant differences in effect size magnitudes by mean age ( $\beta=-.01; p=.29$ ).

In subgroup analyses, no significant differences in effect size magnitudes were found between studies examining early use ( $d=-.28$ ) versus late use or nonspecific samples ( $d=-.24; \chi^2(1)=0.15, p=0.70$ ). Secondary analyses of age at first use showed that this variable was also not associated with variability in effect sizes ( $\beta=.003, p=.92$ ).

There was no effect of between-groups discrepancy (i.e., standardized mean difference) in depression scores ( $\beta=.14; p=.54$ ) on the magnitude of effect sizes. There was also no effect of whether groups were matched on alcohol use in a study ( $\chi^2(1)=0.84; p=.36$ ). Effect size magnitude also did not significantly differ by time period of publication (pre-2000  $d = -.34$ ; 2000-2009  $d = -.34$ ; 2010-2017  $d = -.19; \chi^2(2)=3.62; p=.16$ ).

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**eTable 1.**  
**Overview of 69 Studies Included in the Meta-Analysis**

Study	Cannabis <i>n</i>	Comparison <i>n</i>	Cognitive Domains Assessed	Age Range	Cannabis Group Inclusion Criteria	Cannabis Quantity or Frequency <i>M</i>	Required Abstinence (minimum hours)
Ashtari et al. (2011)	14	14	Learning, Delayed Memory	18-20	Cannabis as drug of choice; DSM-IV criteria for cannabis dependence; 3 or more joints per day for at least 1 year prior to commencement of treatment	5.8 joints/ day; 5.3 years of use	720
Becker et al. (2014)	35	35	Attention, Learning, Delayed Memory, SIP, EF – Updating/ Working Memory, EF – Abstraction/ Shifting, Verbal/ Language, Motor	18-20	Cannabis use $\geq$ 5 times per week over past year; use onset before age 17	333.4 days/ past year; 25.9 days/ past 30 days; 10.2 hits per day in past 30 days	12
Brown et al. (2010)	32	33	Learning, Delayed Memory	18+	Not well specified	1208 lifetime cannabis uses	48
Churchwell et al. (2010)	18	18	Verbal/Language	16-19	DSM cannabis abuse	9.1 times/ week; 1351.9 lifetime cannabis uses	0
Cousijn et al. (2013)	17	26	EF – Inhibition	18-30	Weekly cannabis use for the past 2 years; $\geq$ 200 lifetime use occasions; never sought treatment for cannabis use; does not meet criteria for cannabis dependence	5.2 days/ week; 4.3 grams weekly	0
Cousijn et al. (2013)	10	26	EF – Inhibition	18-30	Weekly cannabis use for the past 2 years; $\geq$ 200 lifetime use occasions; never sought treatment for cannabis use; meets criteria for cannabis dependence	5.0 days/ week; 3.0 grams weekly	0
Croft et al. (2001)	18	31	Learning, Delayed Memory SIP, EF – Inhibition, EF –	18+	Not well specified	7762.4 joints lifetime	48

			Updating/ Working Memory, Verbal/Language , Motor				
Cuttler et al. (2012)	48	48	Learning, EF – Updating/ Working Memory	17-33	Cannabis use $\geq 3$ times per week for at least 1 year	N/A	0
Cuyàs et al. (2011)	110	93	Delayed Memory, Learning, Visuospatial, SIP, Verbal/Language	18+	Not well specified	6.1 years of cannabis use	72
Dougherty et al. (2013)	45	48	Attention, EF – Updating/ Working Memory, EF – Abstraction/Shifting, EF – Inhibition, Learning	14-17	Cannabis use minimum of 4 days per week for $\geq 6$ months	5.2 days/ week; 2.8 years of cannabis use	18
Ehrenreich et al. (1999)	48	49	Attention, EF – Updating/ Working Memory, EF – Abstraction/Shifting	18+	Cannabis use once per week for $\geq 6$ months; age of onset $< 16$ (early use group)	3.9 days/ week; 1087.5 lifetime days of use	24
Ehrenreich et al. (1999)	51	49	Attention, EF – Updating/ Working Memory, EF – Abstraction/ Shifting	18+	Cannabis use once per week for $\geq 6$ months; age of onset $> 16$ (late use group)	3.2 days/ week; 709.8 lifetime days of use	24
Epstein & Kumra (2014)	29	53	Attention, EF – Inhibition	10-23	Cannabis as drug of choice; significant cannabis exposure by age 17 years; $> 50$ exposures	934 lifetime uses	0
Filbey et al. (2015)	36	16	Learning, Delayed Memory	18-50	Cannabis use $\geq 4$ times/week over the past 6 months	80.6 days of cannabis use in past 90 days; 5565 lifetime cannabis uses	72
Filbey et al. (2015)	19	16	Learning, Delayed Memory	18-50	Cannabis use $\geq 4$ times/week over the past 6 months; nicotine use $\geq 10$ times daily	82.2 days of cannabis use in past 90 days; 6704 lifetime cannabis uses	72
Flavel et al. (2013)	10	10	Motor	18+	$\geq 30$ lifetime uses	1067 lifetime cannabis use	12
Fried et al. (2005)	35	59	Attention, Learning, Delayed Memory, SIP, EF – Updating/ Working Memory, EF –	17-21	Current cannabis use $\geq 5$ joints/week	12.4 joints/ week; 1884 joints lifetime;	2160

			Abstraction/Shifting			2.6 years of regular cannabis use	
Fried et al. (2005)	35	59	Attention, Learning, Delayed Memory, SIP, EF – Updating/Working Memory, EF – Abstraction/Shifting	17-21	Former cannabis use $\geq$ 5 joints/week; no regular use for $\geq$ 3 months; $\leq$ 2 joints in past month	2203 joints lifetime; 2.2 years of regular cannabis use	0
Gonzalez et al. (2012)	65	65	EF – Inhibition, Learning	17-24	Cannabis as drug of choice; use of cannabis $>$ 200 times; $\geq$ 4 times per week during peak use; use in past 45 days	Median 270 lifetime joints; median 6 joints in past 30 days; 5.0 years of cannabis use	24
Gouzoulis-Mayfrank et al. (2000)	28	28	Attention, Learning, Delayed Memory, EF – Updating/ Working Memory, EF – Abstraction/ Shifting, EF – Inhibition, Verbal/Language	18-31	Cannabis use twice a month or more for 6 months or longer within the past 2 years	21.0 days/month; 35.1 months of regular cannabis use	24
Grant et al. (2012)	16	214	Attention, EF – Updating/ Working Memory, EF – Abstraction/ Shifting, EF – Inhibition	18-29	Used cannabis one or more times per week during the last 12 months	3.1 times/ week	0
Grant et al. (1973)	29	29	Learning, EF – Abstraction/ Shifting, SIP	18+	Used cannabis “one to three times a month” or more during the last 12 months; $>$ 50 lifetime uses	Median 4 years of cannabis use; median 3 times/ month	0
Gruber et al. (2012)	19	28	Attention, Learning, Delayed Memory, SIP, EF – Updating/ Working Memory, EF – Abstraction/ Shifting, EF – Inhibition, Visuospatial, Verbal/Language	18+	Used cannabis minimum 2,500 times; use at least 5 out of last 7 days; positive for urinary cannabinoids; DSM-IV criteria for abuse or dependence; onset before age 16	24.8 times/ week; 14.8 grams/ week; 8.7 years of use	12
Gruber et al. (2012)	15	28	Attention, Learning, Delayed Memory, SIP, EF – Updating/ Working Memory, EF – Abstraction/Shifting, EF – Inhibition, Visuospatial,	18+	Used cannabis minimum 2,500 times; use at least 5 out of last 7 days; positive for urinary cannabinoids; DSM-IV criteria for abuse or dependence;	12.2 times/ week; 5.9 grams/ week; 5.4 years of use	12

			Verbal/Language		onset after age 16		
Hadjiefthvoulou et al. (2011)	12	18	Learning, Delayed Memory	18+	Current cannabis abuser	1.9 times/ week; 22.3 joints in past 30 days; 2242.6 lifetime cannabis uses	24
Hanson et al. (2010)	19	21	Attention, EF – Updating/ Working Memory	15-19	200+ lifetime cannabis use episodes; >4 times past month cannabis use	16.0 cannabis use days in past month; 465.0 lifetime cannabis uses	504
Hanson et al. (2014)	24	34	Attention, EF – Updating/ Working Memory, EF – Abstraction/ Shifting, SIP, Verbal/Language	17-20	200+ lifetime cannabis use episodes; past month cannabis use	252.7 cannabis use days in past 18 months; 771.9 lifetime cannabis uses	336
Harvey et al. (2007)	34	36	Attention, Learning, Delayed Memory, EF – Updating/ Working Memory, EF – Abstraction/ Shifting, SIP	13-18	> once per week for past 28 days	Median 12 days in past 28 days; Median 11.3 joints in past 28 days	12
Hermann et al. (2007)	13	13	Attention, Learning, Delayed Memory, EF – Updating/ Working Memory, EF – Abstraction/ Shifting	18+	Current cannabis user; positive for urinary cannabinoids	25 days in past month; 719 grams lifetime	0
Herzig et al. (2014)	35	48	Delayed Memory, EF – Updating/Working Memory, EF – Abstraction/ Shifting	18+	Not well specified	11.1 joints/ week	2
Hooper et al. (2014)	33	43	Attention, Learning, Delayed Memory, EF - Inhibition, EF – Abstraction/ Shifting, EF – Updating/Working Memory	12-17	Cannabis use disorder in remission; no cannabis use for at least 1 month	18.1 joints/ week during regular use; 341.7 lifetime cannabis use episodes; 2029 lifetime joints	720

Houck et al. (2013)	36	33	EF – Updating/Working Memory	14-18	Score > 4 on Marijuana Use Scale	15.3 days in past 30 days	0
Jacobsen et al. (2004)	20	25	Attention	13-18	>= 60 episodes of cannabis use (lifetime)	282.8 lifetime cannabis uses	720
Jacobus et al. (2014)	24	30	Attention, Learning, Delayed Memory, EF – Inhibition, EF – Abstraction/Shifting, EF – Updating/Working Memory, Verbal/Language, Visuospatial, SIP, Motor	15-18	>200 lifetime cannabis use episodes	17.3 days in past month; 408.8 lifetime cannabis use days	672
Jacobus et al. (2015)	49	59	Attention, Learning, Delayed Memory, EF – Inhibition, EF – Abstraction/Shifting, EF – Updating/Working Memory, Verbal/Language, Visuospatial, SIP, Motor	15-18	>200 lifetime cannabis use episodes	15.5 days/month	672
Lamers et al. (2006)	15	15	EF - Inhibition, EF – Abstraction/Shifting, Learning, Delayed Memory, SIP, Visuospatial	21-42	>= 10 lifetime cannabis use episodes	1581.6 joints lifetime	0
Lane et al. (2007)	22	31	EF – Abstraction/Shifting	14-18	Cannabis use >= 4 days/week; positive for urinary cannabinoids; meet abuse or dependence criteria	3.3 years of cannabis use	0
Lisdahl & Price (2012)	23	36	Attention, Learning, Delayed Memory, EF – Inhibition, EF – Abstraction/Shifting, Verbal/Language	18-28	>= 10 joints in past year; >= 50 joints in lifetime	208 cannabis use episodes in past year; 1014 joints lifetime	168
de Sola Llopis et al. (2008)	23	34	Attention, EF - Inhibition, EF – Abstraction/Shifting, Learning, Delayed Memory, Verbal/Language , SIP	18+	Not well specified	12.7 days/month; 1670 joints lifetime	72
Mahmood et al. (2010)	65	65	Learning, Delayed Memory, Visuospatial	15-19	>= 60 lifetime cannabis use episodes	16.0 days/month; 500.7 cannabis use episodes lifetime	552
Medina et al. (2007)	31	34	Attention, Learning, Delayed Memory, EF – Abstraction/	16-18	>= 60 lifetime cannabis use episodes; past month cannabis	170.7 cannabis hits/	552

			Shifting, EF – Updating/ Working Memory, SIP, Visuospatial, Verbal/Language		use	month; 540.6 lifetime cannabis uses; 2.9 years of weekly cannabis use	
Messinis et al. (2006)	20	24	Attention, Learning, Delayed Memory, EF – Abstraction/ Shifting, SIP, Verbal/Language	17-49	Use cannabis at least 4 days/ week currently; regular cannabis use >= 5 years	20.7 days/ month; 7.0 years of cannabis use	24
Morgan et al. (2012)	29	30	Attention, Learning, Delayed Memory, Verbal/Language	18-50	Frequent, heavy use of “skunk” cannabis; cannabis dependence (determined by severity score >3 on Severity of Dependence Scale)	28.7 days/ month; 7.0 grams/ day; 6.1 years of cannabis use	0
Murphy et al. (2011)	13	12	EF – Inhibition	18-30	Not well specified	877.2 lifetime cannabis use episodes; 51.2 months of cannabis use	168
Nestor et al. (2008)	35	38	Learning, Delayed Memory	18+	Cannabis use 5-7 days/week for past 2 years	23.1 days in past month; 5.7 years of cannabis use	0
Price et al. (2015)	27	32	EF – Inhibition, EF – Updating/Working Memory	18-25	>= 25 past year cannabis joints; >= 50 lifetime cannabis joints	391.4 joints in past year; 1944.5 joints lifetime	168
Pujol et al. (2014)	28	29	Attention, Learning, Delayed Memory	18-30	Cannabis use before age 16; cannabis use more than 14 times/ week for the past 2 years or more; positive for urinary cannabinoids	899 joints/ year; 5268 joints lifetime; 6.0 years of cannabis use	12
Quednow et al. (2006)	19	19	Attention, Learning, Delayed Memory	18+	"Chronic users of cannabis"	3.89 times/ week, 1033.4 lifetime cannabis use episodes	72

Rochford et al. (1977)	26	25	Learning, Visuospatial	18+	> 50 lifetime cannabis uses	N/A	0
Schwartz et al. (1989)	10	8	Learning, Delayed Memory	14-16	DSM-III criteria for cannabis dependence	5.9 days/ week; 18 grams/ week for at least 4 months	0
Schweinsburg et al. (2005)	15	19	Learning, Delayed Memory, EF – Updating/ Working Memory, EF – Abstraction/Shifting, SIP, Visuospatial	15-17	Current cannabis abuse or dependence DSM criteria; $\geq$ 100 lifetime cannabis uses; $\geq$ 10 days/month in 3 months before study	12.8 days/ month; 309.9 lifetime marijuana uses	48
Schweinsburg et al. (2010)	13	18	EF – Updating/Working Memory	15-18	Recent cannabis users; cannabis use within one week of testing	14.2 days/ month; 342.3 lifetime cannabis uses	48
Schweinsburg et al. (2010)	13	18	EF – Updating/Working Memory	15-18	Abstinent cannabis users; no cannabis use within 27 days	16.9 days/ month; 515.4 lifetime cannabis uses	648
Scott et al. (2017)	227	3401	Attention, EF – Updating/ Working Memory, EF – Abstraction/Shifting, Learning, Visuospatial	14-21	Used cannabis $\geq$ 3-4 times per week over the past year	N/A	0
Skosnik et al. (2008)	14	10	EF – Updating/Working Memory, SIP	18-35	At least 1 joint per week for the past 6 months; positive for urinary cannabinoids	9.7 joints/ week; 37.1 joints past month; 5.6 years of cannabis use	24
Smith et al. (2014)	10	44	EF – Updating/Working Memory	18+	History of cannabis abuse/dependence, but not during the past 6 months	N/A	0
Smith et al. (2015)	10	44	Delayed Memory	18+	History of cannabis abuse/dependence, but not during the past 6 months	N/A	0



Solowij et al. (2011)	52	62	Attention, Learning, Delayed Memory	16-20	Cannabis use at least twice/month for past 6 months OR a brief period of heavier use OR a longer history (> 18 months) of use that was less frequent	13.9 days/month; 17.5 joints/month; 2.4 years of regular cannabis use	12
Tait et al. (2011)	60	420	Learning, Delayed Memory, SIP, EF – Updating/ Working Memory	20-24	“Heavy” cannabis users, at least weekly at baseline	N/A	0
Tait et al. (2011)	60	420	Learning, Delayed Memory, SIP, EF – Updating/ Working Memory	20-24	“Heavy” cannabis users, at least weekly at baseline	N/A	0
Takagi et al. (2011)	19	19	EF – Inhibition	13-24	Daily or almost daily cannabis use for at least past 12 months	1.0 grams/day	24
Takagi et al. (2011)	21	21	Attention, Learning, Delayed Memory	13-24	Daily or almost daily cannabis use for at least past 12 months	1.0 grams/day	24
Takagi et al. (2014)	19	19	EF – Inhibition	13-24	Daily or almost daily cannabis use for at least past 12 months	1.0 grams/day	24
Tamm et al. (2013)	20	21	Learning, Delayed Memory, EF – Inhibition, EF – Updating/ Working Memory, EF – Abstraction/ Shifting	18+	Use of cannabis monthly or more frequently in the past year (majority reported weekly or daily use)	19.4 days/ last month	36
Varma et al. (1988)	26	26	SIP, Visuospatial, Learning, Delayed Memory	15-35	Regular consumption of cannabis for 5 years, use 20+ times/month, equivalent daily intake of 150 mg of THC	N/A	12
Verdejo-García et al. (2013)	86	58	EF – Updating/Working Memory, EF – Abstraction/ Shifting, SIP	18-30	Daily use of cannabis (>7 joints per week) for >= 3 years; DSM-IV criteria for cannabis abuse or dependence	1002.2 joints in past year; 5645.1 joints lifetime; 6.2 years of cannabis use	72
Vilar-López et al. (2013)	19	18	Attention, EF – Inhibition	12-25	Cannabis use daily or almost daily for at least 12 months	1.27 grams/day	24
Whitehurst et al. (2015)	17	13	EF – Inhibition, Learning, Delayed Memory, SIP	18+	Cannabis use 5-7 times per week; positive for urinary cannabinoids	83 cannabis uses during previous 21 days; 6.0 years of	0

						cannabis use	
Winward et al. (2014)	20	55	Learning, Delayed Memory, EF – Updating/Working Memory, EF – Abstraction/Shifting, SIP, Visuospatial	16-18	>100 cannabis use episodes	17.7 days/month; 500.5 lifetime cannabis uses	672

*Note.* DSM = Diagnostic and Statistical Manual of Mental Disorders; EF = Executive Functioning; SIP = speed of information processing; WM = working memory.

**eTable 2.**  
**Neurocognitive Tests Analyzed in the Meta-Analysis, by Cognitive Domain.**

Cognitive Domain		
<b>Attention</b>		
<i>Test</i>	<i>k</i>	<i>%</i>
WAIS-III/ WAIS-R/ WISC-III/ WMS Digit Span Forward	7	13.2
Rey Auditory Verbal Learning Test: Trial 1	6	11.3
CVLT/CVLT-II: Trial 1 Correct	4	7.5
D-KEFS Trail Making Test: Visual Scanning	3	5.7
Attention Network Test: Alerting	2	3.8
Attention Network Test: Orienting	2	3.8
CANTAB - Rapid Visual Information Processing Test: False Alarms	2	3.8
Ruff 2+7 Sustained Attention: Accuracy	2	3.8
Zimmerman Battery - Divided Attention	2	3.8
Zimmerman Battery - Phasic Alertness	2	3.8
Zimmerman Battery - Visual Scanning: Critical Stimulus	2	3.8
CalCAP - Choice RT: digits	1	1.9
CalCAP - Sequential RT2	1	1.9
CANTAB - Rapid Visual Information Processing Test: Correct Identifications	1	1.9
CANTAB - Rapid Visual Information Processing Test: Sensitivity	1	1.9
CANTAB - Rapid Visual Information Processing Test: Target Detection	1	1.9
Conner's Continuous Performance Test II: Variability	1	1.9
d2 Test of Attention: Total Items	1	1.9
Hamburg Wechsler Intelligenztest für Erwachsene Digits Forward	1	1.9
Hopkins Verbal Learning Test-Revised: Trial 1	1	1.9
Immediate Memory Test: Correct Detections	1	1.9
Letter Cancellation: Omissions	1	1.9
Penn Continuous Performance Test	1	1.9
Ruff 2+7 Sustained Attention: Speed	1	1.9
Stop Signal Reaction Time: Go Trials	1	1.9
Test of Attentional Performance - Divided Attention	1	1.9
Test of Attentional Performance - Intermodal Integration	1	1.9
Test of Attentional Performance - Phasic Alertness	1	1.9
Test of Attentional Performance - Visual Scanning: Critical Trial	1	1.9
VIG: Immediate Recall	1	1.9
<b>Total</b>	<b>53</b>	<b>100</b>
<b>Executive Functioning – Abstraction/Shifting</b>		
<i>Test</i>	<i>k</i>	<i>%</i>

Trailmaking Test Part B	8	17.0
D-KEFS Trail Making Test: Number-Letter Switching	7	14.9
D-KEFS Tower Test: Total Achievement	4	8.5
WCST: Perseverative Responses	4	8.5
CANTAB: Intradimensional Extradimensional Shift	3	6.4
Halstead Category Test: Total Errors	3	6.4
WCST: Total Categories	3	6.4
CANTAB - One Touch Stocking of Cambridge Task: Choices to Correct Solution	2	4.3
WCST: Perseverative Errors	2	4.3
WCST: Total Errors	2	4.3
Zimmerman Battery: Flexibility	2	4.3
D-KEFS Design Fluency: Total Correct	1	2.1
Penn Conditional Exclusion Test	1	2.1
Tower of London: % Perfect Solutions	1	2.1
Tower of London: Total Movements	1	2.1
Trail Making Test (B minus A)	1	2.1
Verbal Fluency: Alternating Criterion	1	2.1
WCST: % Conceptual Level Responses	1	2.1
<b>Total</b>	<b>47</b>	<b>100</b>
<b>Executive Functioning – Updating/Working Memory</b>		
<i>Test</i>	<i>k</i>	<i>%</i>
WAIS-R / WAIS-III/ WISC-R/ WMS Digit Span Backward	12	23.5
WAIS-III/WISC-III Digit Span	8	15.7
WAIS-III/ WISC-III/ WMS-III Letter-Number Sequencing	5	9.8
Paced Auditory Serial Addition Test	4	7.8
WAIS-III Arithmetic	4	7.8
WAIS-III Spatial Span Backward	2	3.9
Zimmerman Battery - Working Memory	2	3.9
Brown-Peterson Memory Test: Total Recall	1	1.9
CANTAB – <i>n</i> back ( <i>n</i> =2): Probability of a Hit	1	1.9
CANTAB – <i>n</i> back ( <i>n</i> =3): Probability of a Hit	1	1.9
CANTAB - Spatial Span	1	1.9
CANTAB - Spatial Working Memory	1	1.9
Corsi Block Tapping Test	1	1.9
Hamburg Wechsler Intelligenztest für Erwachsene Digits Backward	1	1.9
Letter <i>n</i> Back Test	1	1.9
<i>n</i> Back: Two Back % Correct	1	1.9
Self-Ordered Search: Total Between Search Errors	1	1.9
Spatial Delayed Response Task - Error: 8000-ms Delay	1	1.9

Strategy Scores on Spatial Working Memory Task	1	1.9
WJ-III Test of Cognitive Abilities - Auditory Working Memory	1	1.9
Working Memory Domain Score	1	1.9
<b>Total</b>	<b>51</b>	<b>100</b>
<b>Executive Functioning – Inhibition</b>		
<i>Test</i>	<i>k</i>	<i>%</i>
Stroop Color-Word: Interference	9	30.0
D-KEFS Color Word Interference: Inhibition	3	10.0
Attention Network Test: Executive Control	2	6.7
D-KEFS Color Word Interference - Inhibition/Switching	2	6.7
ANAM - Go/No Go: Number Correct	1	3.3
Conner's Continuous Performance Test II: Errors of Commission	1	3.3
D-KEFS Tower Test: Mean First Move Time	1	3.3
Go-Stop Task - Correct Inhibitions: Misses	1	3.3
Go-Stop Task - Inhibition Failures (150ms)	1	3.3
Go/No Go: Commission Errors	1	3.3
Go/No Go: d-prime	1	3.3
IMT: Total Commission Errors	1	3.3
Random Letter Generation Task: Alphabetical Sequences	1	3.3
Random Letter Generation Task: Repeated Sequences	1	3.3
Stop Signal Reaction Time	1	3.3
Stop Signal Reaction Time: Total Errors	1	3.3
Test of Attentional Performance: Go/No Go	1	3.3
Tower of London: Initiation Time	1	3.3
<b>Total</b>	<b>30</b>	<b>100</b>
<b>Learning</b>		
<i>Test</i>	<i>k</i>	<i>%</i>
CVLT/ CVLT-II: Trials 1-5 Total Recall	14	23.3
Rey Auditory Verbal Learning Test: Trials 1-5	10	16.7
WMS-III Logical Memory I	5	8.3
Benton Visual Retention Test - Immediate	2	3.3
Hopkins Verbal Learning Test-Revised: Total Recall	2	3.3
Tactual Performance Test: Memory	2	3.3
WMS-III Immediate Memory	2	3.3
ANAM - Code Substitution - Immediate: % Correct	1	1.7
Bender Gestalt Memory	1	1.7
Buschke Selective Reminding Test: Total Recall	1	1.7

Coughlan Design Learning: Design 1-5	1	1.7
Coughlan List Learning: List 1-5	1	1.7
CVLT - Child Version: List A Total	1	1.7
Face-Name Learning Task: Learning Performance Trials 1-5	1	1.7
Non-Spatial Associative Learning	1	1.7
Penn Face Memory Test	1	1.7
Penn Word Memory Test	1	1.7
PGI Memory Scale: Immediate Recall	1	1.7
Rey Auditory Verbal Learning Test: Trials 1-3	1	1.7
Rivermead Behavioral Memory Test - Prose Recall: Immediate	1	1.7
Spatial Associative Learning	1	1.7
Tempoleistung und Merkfähigkeit Erwachsener 1 Repeating Words	1	1.7
Verbal Paired Associates (Trial 1)	1	1.7
Verbal Triplet Associates: Immediate	1	1.7
VIG - Performance Over 5 Rehearsals	1	1.7
Visual Object Learning Test	1	1.7
Warrington Faces	1	1.7
Warrington Words	1	1.7
WMS Prose Passages: Immediate Recall	1	1.7
WMS-R Story Recall (Immediate) % Correct	1	1.7
<b>Total</b>	<b>60</b>	<b>100</b>
<b>Delayed Memory</b>		
<i>Test</i>	<i>k</i>	<i>%</i>
CVLT/ CVLT-II: Long Delay Free Recall	14	22.6
Rey-O Complex Figure: Delayed Recall	12	19.4
Rey Auditory Verbal Learning Test: Delayed Recall	8	12.9
WMS-III Logical Memory II	6	9.7
Hopkins Verbal Learning Test-Revised: Delayed Recall	2	3.2
WMS-III General Memory	2	3.2
ANAM - Code Substitution: Delayed Recall (% correct)	1	1.6
ANAM - Memory Search (% correct)	1	1.6
Benton Visual Retention Test: Delayed	1	1.6
Coughlan List Learning: List 6	1	1.6
Coughlin Design Learning: Design 6	1	1.6
CVLT-Child Version: Delayed Recall Scaled Score	1	1.6
Face-Name Learning Task: Long Delay Recall	1	1.6
Hopkins Verbal Learning Test-Revised: Percent Retention	1	1.6
PGI Memory Scale: Delayed Recall	1	1.6
PGI Memory Scale: Retention for Dissimilar Pairs	1	1.6

PGI Memory Scale: Retention for Similar Pairs	1	1.6
PGI Memory Scale: Visual Retention	1	1.6
Rey Auditory Verbal Learning Test - Decay	1	1.6
Rivermead Behavioral Memory Test - Prose Recall: Delayed	1	1.6
Spatial Recognition: % correct recall	1	1.6
Tempoleistung und Merkfähigkeit Erwachsener 2	1	1.6
Wide Range Assessment of Memory and Learning-2 - Verbal Memory	1	1.6
Wide Range Assessment of Memory and Learning-2 - Visual Memory	1	1.6
<b>Total</b>	62	100
<b>Speed of Information Processing</b>		
<i>Test</i>	<i>k</i>	<i>%</i>
WAIS-III Digit Symbol Coding	7	23.3
Trailmaking Test Part A	6	20.0
D-KEFS Trail Making Test: Number Sequencing	5	16.7
Symbol Digit Modalities Test	4	13.3
Stroop Color-Word - Color Naming	2	6.7
WAIS-III Processing Speed Index	2	6.7
ANAM - Procedural Reaction Time	1	3.3
CANTAB - Rapid Visual Information Processing Test: Probability of a Hit	1	3.3
Letter Cancellation: Time	1	3.3
Stroop Color-Word: Word Reading	1	3.3
<b>Total</b>	30	100
<b>Verbal/Language Processing</b>		
<i>Test</i>	<i>k</i>	<i>%</i>
Category Fluency	7	33.3
Letter Fluency (COWAT)	6	28.6
D-KEFS Verbal Fluency Test: Letter Fluency	5	23.8
Verbal Fluency (measure not specified)	2	9.5
Boston Naming Test	1	4.8
<b>Total</b>	21	100
<b>Visuospatial Functioning</b>		
<i>Test</i>	<i>k</i>	<i>%</i>
Rey-O Complex Figure: Copy Accuracy	10	66.7
Bender Gestalt - Hutt Adaptation	1	6.7
Bender Visual-Motor Gestalt Test	1	6.7

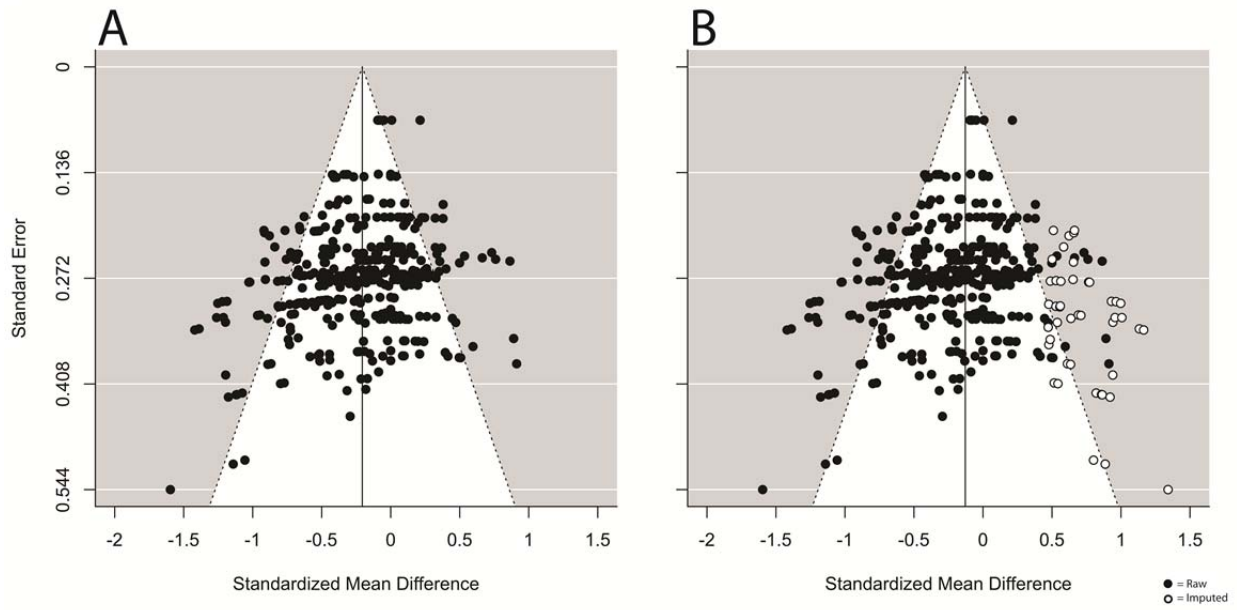
Minnesota Percepto-Diagnostic Test	1	6.7
Nahor-Benson Test: Error Score	1	6.7
Penn Line Orientation Test	1	6.7
<b>Total</b>	15	100
<b>Motor</b>		
<i>Test</i>	<i>k</i>	<i>%</i>
D-KEFS Trail Making Test: Motor Speed	2	22.2
Grooved Pegboard: Dominant	2	22.2
Grooved Pegboard: Non-Dominant	2	22.2
Finger Tapping Test: number of taps in 5 seconds	1	11.1
Finger Tapping Test: Dominant	1	11.1
Finger Tapping Test: Non-Dominant	1	11.1
<b>Total</b>	9	100

Note. % = Percent of studies within each domain that included the neuropsychological test in the primary source; *k* = number of studies. ANAM = Automated Neuropsychological Assessment Metrics; CalCAP = California Computerized Assessment Package; CANTAB = Cambridge Neuropsychological Test Automated Battery; CVLT = California Verbal Learning Test; COWAT = Controlled Oral Word Association Test; D-KEFS = Delis-Kaplan Executive Functioning System; PASAT = Paced Auditory Serial Addition Test; RAVLT = Rey Auditory Verbal Learning Test; Rey-O = Rey-Osterrieth; RT = Reaction Time; VIG = Visuelles Gedächtnis; WAIS = Wechsler Adult Intelligence Test; WCST = Wisconsin Card Sorting Test; WMS = Wechsler Memory Scale.

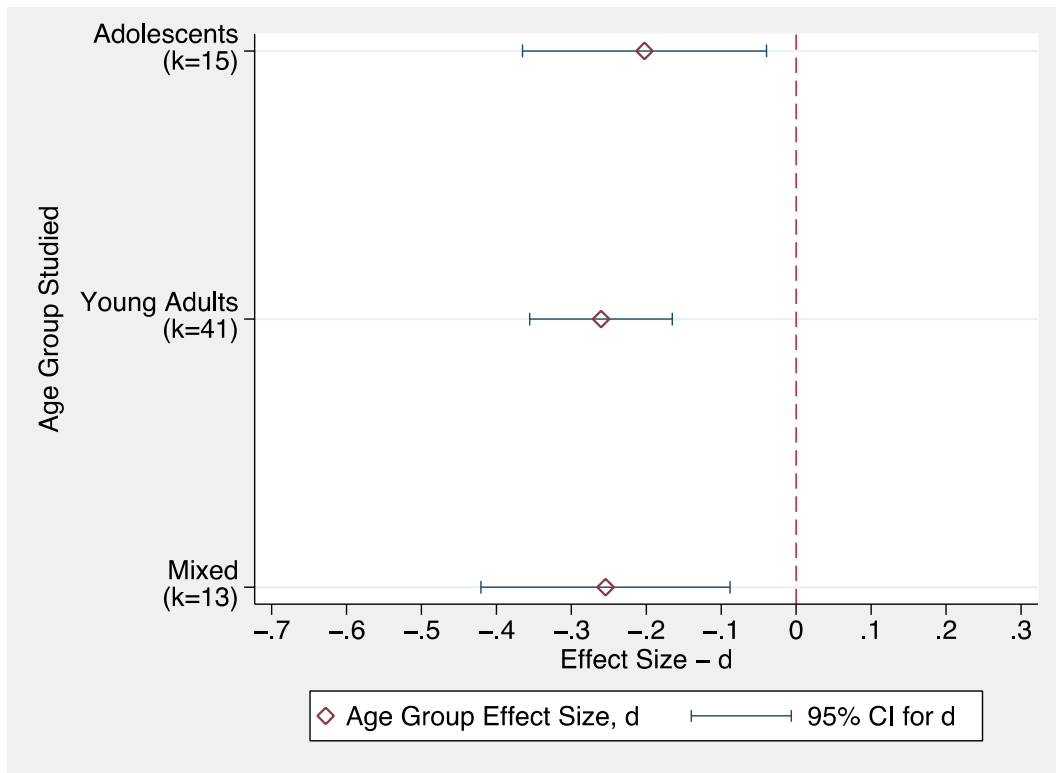


**eFigure 1.**

**(A) Unadjusted and (B) trim-and-fill funnel plots with standardized mean difference effect sizes (*d*).**



**eFigure 2.**  
**Mean weighted effect sizes and 95% confidence intervals for age groups.**  
**CI = confidence interval; d = standardized mean difference.**



**eFigure 3.**  
**Mean weighted effect sizes and 95% confidence intervals for year of publication.**  
**CI = confidence interval; d = standardized mean difference.**

