**Supplementary material**

**Supplementary Table 1. Table of search terms**

|  |  |
| --- | --- |
| **Areas of Interest** | **Full Search Terms (as title, abstract, or keyword terms)** |
| ADHD subjects in all countries | ADHD OR ADD OR attention deficit OR hyperkinetic OR hyperkinesis OR TDAH OR DAH OR DAA OR ADHS |
| Concerta | Concerta OR extended release methylphenidate OR methylphenidate extended release OR methylphenidate ER OR methylphenidate XR OR MPH ER OR MPH XR OR osmotic-release oral system methylphenidate OR OROS MPH OR OROS methylphenidate OR osmotic-release oral system MPH OR long acting methylphenidate OR methylphenidate LA OR MPH LA OR methylphenidate long acting |
| Strattera | Strattera OR atomoxetine OR tomoxetine |
| Vyvanse | Vyvanse OR lisdexamphetamine OR lisdexamfetamine OR LDX OR Elvanse OR Venvanse |

For PubMed:

((((((((ADHD[Title/Abstract] OR ADD[Title/Abstract]) OR attention deficit[Title/Abstract]) OR hyperkinetic[Title/Abstract]) OR hyperkinesis[Title/Abstract]) OR TDAH[Title/Abstract]) OR DAH[Title/Abstract]) OR DAA[Title/Abstract]) OR ADHS[Title/Abstract]) AND (((((((((((((((((Concerta[Title/Abstract] OR extended release methylphenidate[Title/Abstract]) OR methylphenidate extended release[Title/Abstract]) OR MPH ER[Title/Abstract]) OR osmotic-release oral system methylphenidate[Title/Abstract]) OR OROS MPH[Title/Abstract]) OR OROS methylphenidate[Title/Abstract]) OR osmotic-release oral system MPH[Title/Abstract]) OR long acting methylphenidate[Title/Abstract]) OR MPH LA[Title/Abstract]) OR Strattera[Title/Abstract]) OR atomoxetine[Title/Abstract]) OR tomoxetine[Title/Abstract]) OR Vyvanse[Title/Abstract]) OR Venvanse[Title/Abstract]) OR lisdexamphetamine[Title/Abstract]) OR lisdexamfetamine[Title/Abstract]) OR LDX[Title/Abstract])

For CENTRAL (as title or abstract or keyword terms):

ADHD OR ADD OR attention deficit OR hyperkinetic OR hyperkinesis OR TDAH OR DAH OR DAA OR ADHS

Concerta OR extended release methylphenidate OR methylphenidate extended release OR methylphenidate ER OR methylphenidate XR OR MPH ER OR MPH XR OR osmotic-release oral system methylphenidate OR OROS MPH OR OROS methylphenidate OR osmotic-release oral system MPH OR long acting methylphenidate OR methylphenidate LA OR MPH LA OR methylphenidate long acting OR Strattera OR atomoxetine OR tomoxetine OR Vyvanse OR lisdexamphetamine OR lisdexamfetamine OR LDX OR Elvanse OR Venvanse

For EMBASE (as title, original title, abstract, or keyword terms):

(ADHD or "attention deficit hyperactivity disorder$" or "attention deficit" or "attention deficit disorder$") or (hyperkinetic$ or hyperkinesis) or (TDAH or DAH or DAA or ADHS)

(vyvanse or lisdexamfetamine or lisdexamphetamine or LDX or elvanse or venvanse) or (concerta or strattera or atomoxetine or tomoxetine) or ((methylphenidate or MPH) adj ("extended release" or ER or XR or "long acting" or LA or OROS or "osmotic release"))

NOT (editorial or erratum or letter or note or "review")

**Supplementary Figure 1. Screening flow chart.**



ADHD, attention-deficit hyperactivity disorder; ADHD-RS, ADHD Rating Scale-IV; AISRS, Adult ADHD Investigator Symptom Report Scale; CAARS, Conners’ Adult ADHD Rating Scale; RCT, randomized controlled trial.

**Supplementary Figure 2.** Observed effect sizes (dots) and 95% confidence intervals (CIs) for each study stratum. Data included in the base-case analysis are in green and blue. Data included in the adults-only sensitivity analysis are in green. Data included in the non-standard pill-placebo sensitivity analysis are in red. The size of the dot indicates the statistical weight based on the study population size. Effect sizes are Cohen’s *d*. ATX, atomoxetine; LDX, lisdexamfetamine; OROS-MPH, osmotic-release oral system methylphenidate.



**Supplementary Table 2.** Comparison of placebo designs in European studies of adults reporting CAARS.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| First author, date | *n* | Mean pre–post difference | SD | Study design | Study location |
| Sobanski, 2012 [31] | 21 | −0.4 | 4.8 | Wait-list | EU |
| Medori, 2008 [23] | 95 | −7.6 | 9.93 | Pill | EU |
| Casas, 2013 [9] | 97 | −10.4 | 11.0 | Pill | EU |

CAARS, Conners’ Adult ADHD Rating Scale; EU, Europe; SD, standard deviation.

**Supplementary Information 1: Model Specifications**

Study stratum effect sizes were modeled by fitting a mixed-effects linear model with the following specification:

*Y* = *a* + *X* β + *e*;

where *Y* is the (k x 1) vector of effect sizes,

*X* (k x p) is the design matrix describing study arm characteristics (covariates) that influence the effect sizes,

β(p x 1) is the vector of fixed-effect parameters,

*a* (k x 1) is the vector of random intercepts or the residuals on the between-study level, and

*e* (k x k) is the matrix of residuals on the within-study level.

The effect sizes were assumed to be normally distributed. The random intercept vector *a* had a multivariate normal distribution with a zero mean vector and a covariance matrix τI (k x k) where I is the identity matrix. The chance error *e* was a multivariate normal with zero means and a diagonal covariance matrix R (k x k). The random intercept *a* and the random error *e* were assumed to be independent of each other. The within-study variances were considered known as the study strata sample sizes were large.

Using this model, the estimated overall average treatment effect (μ), and the between-study variance (τ), an estimate of the study-specific effect size for study i was normally distributed with mean:

Ci μ + ( 1 – Ci ) Yi;

where Ci = Si / (Si + τ),

Si were the known within-study variances for study i, and Yi were the observed effect sizes for study i. Thus, an estimate of the true study-specific effect size was a weighted average of the estimated overall effect size μ (averaged over all studies combined) and the observed effect size of a particular study. The weight was determined by the relative sizes of the between-study and within-study variances. Within-study variance estimates for studies contributing multiple strata to the analysis were pooled.