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**Assessing Undertreatment and Overtreatment/Misuse of ADHD medications in children and adolescents across continents: a systematic review and meta-analysis**

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**Author contributions:**

RM had full access to the aggregate analysis data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. CRMM, SC, GP and LAR were responsible for the study concept, and RM, CRMM, GP, SC and LAR were responsible for the study design. RM, CRMM, FC, MS, JA, LT and GCAM were involved in the acquisition of data. RM and LAR were involved in statistical analysis and interpretation of data. RM, LAR, SC, and GP drafted the manuscript. All authors critically revised the manuscript for important intellectual content.

**ABSTRACT**

A controversy exists on whether there is an over or underuse of medications for Attention-Deficit/Hyperactivity Disorder (ADHD). We conducted the first meta-analysis to estimate the rate of ADHD pharmacological treatment in both diagnosed and undiagnosed individuals. Based on a pre-registered protocol (CRD42018085233), we searched a broad set of electronic databases and grey literature. After screening 25,676 abstracts, we retained 36 studies including 104,305 subjects, from which 18 studies met our main analysis criteria. The pooled pharmacological treatment rates, estimated with the DerSimonian and Laird method for random-effect model in R, were 19.1% and 0.9% in school-age children/adolescents with and without ADHD, respectively. We estimated that for each individual using medication without a formal ADHD diagnosis, there are three patients with a formal diagnosis who might benefit from medication but do not receive it in the US. Our results indicate both overtreatment/misuse of medication in individuals without ADHD and pharmacological undertreatment in youths with the disorder. Our findings reinforce the need for public health policies improving education on ADHD and discussions on the benefits and limitations of ADHD medications.

Keywords: ADHD, prevalence, treatment, stimulants, pharmacological interventions

**INTRODUCTION**

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most common neurodevelopmental disorders, characterized by developmentally-inappropriate and impairing inattention and/or hyperactivity-impulsivity.1 The worldwide prevalence of the disorder is estimated at around 5-7% among children/adolescents and 2.5% in adults.2,3 Individuals diagnosed with ADHD are at higher risks of several negative outcomes (e.g., substance misuse,4 car accidents,5 unintentional injuries,6 emergency department visits,7 depression,8 criminality9 and suicide10). They also present a mortality rate of 2.64-fold higher than the one in non-affected individuals,11 although Sun et al. (2019) found that such high mortality rates are mostly but not exclusively driven by comorbidities. (REF) All these consequences, and the substantial economic impact associated with them,12 turn ADHD into a relevant public health problem. However, ADHD diagnosis continues to be controversial in lay media.13,14 In the scientific community, one of the most intense controversies is whether the disorder is under or over-diagnosed,15 and, more importantly, under or over-treated with medications.16–18

Pharmacotherapy for ADHD is supported by meta-analytic evidence, at least in the short-term,19 and recommended as the first-line treatment in most of the international guidelines/practice parameters.20–24 In some of them, pharmacological treatment is reserved for severe cases,25 or as a treatment strategy for patients who have not responded to non-pharmacological interventions.25,26 There has been an increase in the prescription rates of ADHD medications over the last decades, leading to concerns of overdiagnosis and overtreatment.16–18 A large study on the prevalence of ADHD treatment worldwide relied on data referring to treatment-seeking populations. 27 Thus, this investigation could not establish prescription rates of medication for affected and non-affected individuals in the community. As a result, it remains unclear which proportion of patients with ADHD, who may benefit from pharmacological treatment, indeed do receive it and which proportion of non-affected individuals are potentially misusing ADHD medication.

In this systematic review and meta-analysis, we aimed to estimate the pooled rates of ADHD medication use in both children and adolescents with and without ADHD across continents, filling this critical gap in the literature. To our knowledge, no previous meta-analysis with this objective has been conducted. We hypothesized that global pooled estimates in affected individuals would suggest overall undertreatment of ADHD.

**METHODS**

We followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA),28 and the Meta-Analysis of Observational Studies in Epidemiology (MOOSE).29 The MOOSE checklist is reported in supplemental materials, page 4. The protocol for this study is registered in the International Prospective Register of Systematic Reviews (PROSPERO), CRD42018085233, and is published elsewhere.30

**Selection criteria**

We searched for population-based, cross-sectional or longitudinal studies published since inception up to April 30th, 2020, with no language or age restrictions. Studies had to report data on participants primarily diagnosed with ADHD or Hyperkinetic Disorder (HKD) and/or on non-affected individuals. We accepted all the following definitions of ADHD: a) medical diagnosis according to any DSM versions (II, III, IV(-TR), 5), ICD- 9 or ICD-10, confirmed by validated diagnostic instruments (Supplemental materials, Table S1) or clinical interviews; b) diagnosis using a validated ADHD symptom scales with a pre-specified threshold (Supplemental materials, Table S1); or c) diagnosis reported by participants/caregivers (e.g., an affirmative answer to the question “did any doctor diagnosed you [or your familiar] with ADHD?”). We included studies presenting information on stimulants (methylphenidate, dexmethylphenidate, amphetamines), and atomoxetine, which are recommended by the majority of the international guidelines.20–25 We also retained studies with ADHD medication use reported by participants/caregivers (e.g., an affirmative answer to the question: “Are you [or your familiar] currently taking medication for ADHD?”).

We excluded studies: a) based on clinical samples, including those relying on insurance health system and third-party reimbursement data sets, as our research question was on the rates of ADHD treatment use in the population and not in individuals searching for treatment; b) with no clear description of the diagnostic process; and c) using solely ADHD pharmacological treatment as an indication (proxy) for ADHD diagnosis (without proper confirmation of the diagnosis), thus avoiding a tautological approach. Before exclusion, we systematically contacted all the authors of studies lacking relevant information via e-mail to request missing information, making at least three attempts to gather missing information/data.

**Search strategy and data extraction**

The search strategies/syntaxes were developed with the support of a librarian at the University of Southampton, UK. The following main databases were searched: Medline, Embase, CINAHL, PsychINFO, Web of Science, and Scopus. Details on search strategy/syntax and a list of additional databases and websites searched, including sources of conference abstracts, are described in supplemental material (pages 10-16). Papers selected for full-text reading and relevant systematic reviews were hand-searched for references of interest. The first author of each included study and experts in the field were contacted to retrieve gray literature. However, no unpublished studies of interest were found.

Data extraction followed standard procedures (see supplemental material, page 17). We extracted the following data: a) Study author, year of publication, country, year of data collection, name of the sample (if any), study design and response/completion rates (if reported); b) Patient age range, age mean, gender, method of ADHD diagnosis, diagnostic criteria, comorbidities, co-medication, name of diagnostic instrument and/or rating scale (if described), socioeconomic status, level of care (primary, secondary, or tertiary); c) Medication class and formulation, dose range, mean dose, length of treatment and medication assessment method (e.g., only question exploring if the individual was using or not ADHD medication, request for showing the container of the medication, or confirmation of the of ADHD medication prescription in medical records).

**Study outcome measure and quality of the studies**

The primary outcomes of our meta-analyses were the rates of ADHD medication use by children and adolescents with a clinical diagnosis of ADHD or HKD, and the prevalence rates of ADHD medication use in non-affected individuals.

We assessed the quality of studies using a modified version of the Newcastle–Ottawa scale (NOS)31 (see details in supplementary materials, page 17 to 19).

**Data Analysis**

A meta-analysis of proportions was performed with the *“meta”* package in R software. The Metaprop function was used to compute the independent pooled prevalence and 95% confidence interval (95% CI) of medication use in pharmacologically treated and untreated individuals, both with and without a diagnosis of ADHD.32 Normality tests of study rates were performed using Log, Logit, and Freeman-Tukey Double Arcsine transformations, and the Logit transformation was the most appropriate. The confidence intervals were computed using the Clopper-Pearson exact method with continuity correction, a proper method for small proportions.33 We used the DerSimonian and Laird method for random-effect model due to expected heterogeneity among studies.34 Heterogeneity was evaluated with the Cochran's chi-squared test (Cochran's Q), and the *I*².35 Publication bias was explored through the visual inspection of the funnel plot asymmetry and the Egger's linear regression test.36 The jackknife sensitivity analysis was used to explore the effect of individual studies in both prevalence and heterogeneity.37 Additionally, individual random-effect meta-regression analyses were conducted exploring the impact of following covariates (individually entered in the model): year, quality of the study, continent, country, method of diagnosis, type of medication, method of medication assessment and study design.

Any deviation of the published protocol is reported in the supplementary materials, page 20.

**RESULTS**

As presented in Figure 1, 25,676 records were screened, and 36 studies from 10 countries were retained, including a total of 104,305 participants.38–73 The list of studies excluded after the full-text screening with reasons of exclusions can be found in Supplemental Material, Table S4. We found 5 studies with adult samples (n = 6,620), the majority being restricted to university students. In addition, we found two studies exclusively on preschoolers (5 years old or younger, n = 20,174). Adult and preschooler analyses are reported separately in Supplemental materials (Tables S5 and S6, Figures S1 and S2).

Most of the studies with samples of children and adolescents included in our analyses were cross-sectional with ADHD diagnosis according to DSM criteria (see Table 1). The population included in these studies encompassed youth mostly from Western developed countries, predominantly from the United States of America. The few control samples that described other psychiatric diagnoses had lower rates of mental disorders than ADHD samples. The mean response/completion rate of the studies included in the main analysis was 68%.

Our main analyses were restricted to studies where the diagnosis was made either according to DSM/ICD criteria or to validated scales. The pooled pharmacological treatment rate for the DSM/ICD ADHD diagnosis group (18 studies; n = 3,311) was 0.191 (95% CI: 0.115-0.299; Figure 2). Regarding the non-ADHD group (14 studies; n = 29,559), the pooled ADHD medication use rate was 0.009 (95% CI: 0.005-0.017; Figure 3).

The mean NOS score was 3.7 for studies included in our main analyses, and the most critical item affecting total scores was comparability (see Table 1). Funnel plots for both groups are shown in supplemental material (Figures S3 and S4). Egger’s test was non-significant for both diagnosed and undiagnosed groups (p-values of 0.29 and 0.10, respectively), not suggesting a significant risk of publication bias.

We identified high heterogeneity in our main analyses involving both diagnosed and undiagnosed groups. Jackknife sensitivity analyses demonstrated that, in no instance, single study exclusion significantly modified the heterogeneity (Supplemental material, Figures S5 and S6). When exploring the impact of covariates (e.g., year, quality of the study, continent, country, medication assessment method, type of medication and study design) on heterogeneity and estimates of our main analyses, we observed that heterogeneity was reduced when the studies were grouped according to continents; specifically, it was lower in Europe and Oceania (Supplemental material: Figures S7-S16). Meta-regressions findings for the studies that used DSM and/or ICD criteria for ADHD diagnosis (main analyses) in children and adolescents presented the following significant covariates: quality of the study (p-value 0,0349: heterogeneity accounted for [HAF] = 23.54%), country (p-value = 0.0391; HAF = 14.97%) and study design (p-value = 0.0230, HAF = 33.69%), indicating that these variables did significantly impact heterogeneity, while meta-regression findings in relation to non-ADHD children and adolescents were non-significant (Supplemental material: Tables S7 and S8).

To assess influence of diagnostic method, we also meta-analyzed all samples of children and adolescents with and without ADHD diagnosis (29 and 17 studies, respectively) in which ADHD diagnosis was assessed either by DSM/ICD criteria or just through a question about previous ADHD diagnosis. As studies where the diagnosis was made based on the answer to only one question about previous ADHD diagnosis include treatment-seeking populations, they presented inflated rates of treatment for children and adolescents with the diagnosis [0.516 (95% CI: 0.435-0.596) vs. 0.191 (95% CI: 0.115-0.299), Supplemental material: Figure S17], and deflated rates of treatment for children and adolescents without a diagnosis [0.001 (95% CI: 0.000-0.049) vs. 0.009 (95% CI: 0.005-0.017), Supplemental material: Figure S18].

Finally, the pooled pharmacological treatment rate was 0.315 (95% CI: 0.255-0.382), in our analyses with all 29 included studies with samples of children and adolescents diagnosed with ADHD (n = 24,106), as shown in Supplemental material, Figure S19. Data from all 17 studies of children and adolescents without an ADHD diagnosis (n = 48,681) indicated a pooled rate of medication use of 0.007 (95% CI: 0.004-0.013), as reported in Supplemental material, Figure S20.

**Extrapolation of the findings based on available population data for three countries in different continents (the US, the Netherlands and Australia)**

 For the purpose of our subsequent analyses, we conservatively assumed that at least 70% of the children and adolescents with a proper ADHD diagnose might benefit from a trial with ADHD medication (see discussion for reasons to establish this threshold).

Combining our findings for the US, the Netherlands and Australia (Supplemental materials, figures S10 and S15) with the estimated youth population between 5 and 19 years of age in these countries according to the United Nations74, and the estimated prevalence of ADHD using DSM criteria in this age range in these countries,75-77 we estimated the rates of treatment for children and adolescents affected by ADHD and use of medication for ADHD by those without the disorder in these three countries from different continents.

 In the US, data indicates that: a) an estimated 1.97 million youths diagnosed with ADHD are treated with medication (33.3% of total ADHD cases); b) 2.17 million individuals might still benefit from ADHD pharmacological treatment but do not receive it (36.7%: 70% eligible for medication minus the 33.3% already treated); and c) 677,425 children and adolescents without a formal ADHD diagnosis might be using medication for the disorder (total population between 5-19 years of age in the US [62,378,000] minus those affected by ADHD [9.5%] multiplied by the prevalence of medication for ADHD use in those without a formal diagnosis for the disorder [1.2%]). Thus, for each child and adolescent without ADHD using medication for the disorder, there are more than 3 children with ADHD who might benefit from pharmacological interventions and are not receiving it in the US.

 In Australia, while 45,000 children/adolescents with ADHD (12.8%) are estimated to be treated with medication, 202,000 children/adolescents may be diagnosed and are still not pharmacologically treated despite eligible, and only 18,000 children/adolescents without formal diagnosis of ADHD (0.4%) may be using ADHD medication, representing an 11-fold difference between under pharmacological treatment and overtreatment/misuse rates.

 In the Netherlands, while 17,000 children/adolescents with ADHD (22.2%) are estimated to be treated with medication, 37,000 may be diagnosed and are still not pharmacologically treated despite eligible, and 22,000 youths without formal diagnosis of ADHD (0.8%) may be using ADHD medication, representing less than 2-fold difference between under and overtreatment/misuse.

**DISCUSSION**

To our knowledge, this is the first systematic review and meta-analysis investigating the prevalence of ADHD medication use in both individuals diagnosed with ADHD and in those without the disorder. Our main analyses suggest that 19.1% (95% CI: 11.5-29.9) of the school-age children and adolescents affected by ADHD are treated with medication for the disorder, and 0.9% (95% CI: 0.5-1.7) of individuals without the diagnosis use medication for ADHD. As expected, substantial heterogeneity was found in our analyses.

Even though ADHD guidelines worldwide recommend medication as part of the treatment of the disorder, they present differences regarding their recommendations on pharmacological treatment. While some guidelines, mostly from America, recommend pharmacotherapy as the first-line treatment,20–24 some European guidelines tend to recommend non-pharmacological treatments prior to medications, or for moderate/severe cases of ADHD. 25,26 Although the evidence for efficacy of non-pharmacological treatment in ADHD and for the percentage of patients who respond to them are controversial,78 available randomized clinical studies using sequential approaches (e.g., medication or placebo after no response to non-pharmacological interventions) suggest that 18-23% of the patients might respond to an initial trial of parent training79 or behavioral interventions without a need for medication.80 In the same direction, the definition of what constitutes a moderate/severe ADHD case is not clear in the literature. However, some epidemiological studies describe the percentage of ADHD cases categorized according to its severity.61,81 In these studies, 70-76% of all ADHD cases defined by DSM criteria are classified as moderate or severe. Thus, a conservative appraisal of this literature indicates that around 70% of the patients with ADHD might benefit from a trial with pharmacological treatment (no dispute among different guidelines). Thus, we conservatively assumed this figure (70%) as the one reflecting the proportion of the children and adolescents with properly diagnosed ADHD who might unequivocally benefit from a trial with ADHD medication.

It is important to highlight that we could not exclude from our analysis several groups that might be using stimulants adequately but are otherwise included in the group of non-affected individuals treated with ADHD medication, such as: a) previously diagnosed patients who responded to treatment and did not present anymore full ADHD diagnostic criteria when assessed in the studies; 47 b) subthreshold cases of ADHD who might have impairment and treatment indication;82 and c) individuals with other diagnoses that are also indications for stimulant use (e.g., narcolepsy or resistant depression).83 Nonetheless, our findings support the presence of over/inadequate treatment in different countries, raising concerns on stimulant overuse/ misuse, as recently suggested by others.84

The high heterogeneity observed in this meta-analysis, anticipated in our protocol,30 indicates that our findings should be considered with caution. However, rather than the heterogeneity per se, it is more informative to focus on the reasons for heterogeneity. Our sensitivity meta-regression analyses identified that quality of the study, country and study design were significant covariates with important impact on heterogeneity for samples with children and adolescents with ADHD. In fact, these findings are congruent with the literature in several ways. Previous investigations suggest that ADHD medication use is predicted by sociodemographic variables and different practice parameters for ADHD prescriptions among countries. Galera et al. observed that being male, with a mother with low education levels or being immigrant increases the hazard risk ~2 fold for ADHD medication use.85 Wallach-Kildemoes et al. described the impact of different prescribing practices on rates of patients with ADHD treated in Denmark.86 In our analysis including all samples (n = 29) of children and adolescents with ADHD independently of the diagnostic procedure (DSM/ICD criteria and diagnosis only reported by caregivers), as expected, the diagnostic method was a very influential covariate on our estimates. It is important to highlight that even larger meta-analyses on ADHD prevalence, with more than one hundred studies, observed similar high levels of heterogeneity.2,87,88 Moreover, as in our study, methodological variables, as study design and diagnostic method, were found as the most important covariates explaining heterogeneity in those epidemiological studies.

Rather than a reductionist vision focusing only on either ADHD pharmacological overtreatment/misuse or under-treatment, we suggest that “*the two sides of the coin”* should be considered. The data presented in this study shows clearly that both ADHD pharmacological overtreatment/misuse and ADHD pharmacological undertreatment occurs concomitantly across the different countries with available data. However, it is important to appreciate that undertreatment and overtreatment are not uncommon in medicine. In fact, this dichotomy dates back to the initial use of antibiotics throughout nowadays.89 More specifically, in psychiatry, studies on depression already demonstrated the diversity of clinical practices, with mixtures of both overtreatment of patients that do not fulfill diagnostic criteria and undertreatment of moderate and severe cases of the disorder,90 apparently a worrisome paradox with multiple associated factors.91

Our study should be considered in light of its limitations. First, it is important to note that even though the data collected constitute the most comprehensive evidence available in the literature and response/completion rates observed are acceptable, it does not constitute a world representative sample. Moreover, differences in patterns of medication use exist even within countries.85,92 Second, the funnel plots of our main analyses present a scattered pattern. However, the Eggers’ tests were non-significant, and non-statistical methods were also extensively implemented against publication bias, an approach even more important in meta-analysis with a small number of studies.93 Third, a relatively limited number of studies was included in our analyses. In addition, they presented substantial heterogeneity. Both issues reduce our external validity. However, heterogeneity was expected from the beginning, and it was also found in the three previous epidemiological ADHD meta-analyses that relied on worldwide samples,2,87,88 even when the number of studies was over one hundred. Fourth, most of the selected studies were from developed countries, with USA samples being dominant. This finding most certainly inflates the treatment rates due to the exclusion of a large proportion of the world population with significant financial, cultural, and health access barriers to ADHD treatment. Fifth, we excluded studies on populations under five years from the main analyses, since treatment with medication in that age range is controversial and guidelines consensually do not recommend medication as first-line treatments. Sixth, several of the included studies performed medication assessment through only questioning the patient/caregiver on ADHD medication use, without using confirmatory methods. However, the medication assessment method was not a significant variable in meta-regression analyses. In addition, some studies assessed only lifetime ADHD or did not provide sufficient data to inform on the approach used in the assessment (e.g., lifetime, current, past year diagnosis), making the evaluation of temporality between the presence of the disorder and use of medication a challenge. However, this issue was far less pronounced in studies included in our main analyses. Seventh, most non-ADHD samples did not allow differentiation between overtreatment and misuse. However, the prevalence of nonmedical use of medication is a reality mostly among adult and older adolescent populations. Finally, our data include the evidence on the pharmacological treatment of ADHD, and it does not address a potential more global under-treatment of ADHD, including non-pharmacological interventions.

Despite these limitations, our meta-analysis provides evidence for a substantial under-treatment of children and adolescents affected by ADHD in different countries. This is a relevant public health issue worldwide, since ADHD undertreatment is associated with known negative outcomes in education, health care, and productivity systems. At the same time, we found evidence of overtreatment/misuse in individuals without a formal ADHD diagnosis. This practice might expose individuals to undesirable side effects of medications, increased risk of medication misuse, and unmeasured costs for the health care system. Our findings indicate that, more than disputes between supporters and detractors of medication treatment for ADHD, additional evidence-based medical and parental education on ADHD is needed worldwide, as part of public health policies.

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**REFERENCES**

1. *Diagnostic and statistical manual of mental disorders: DSM-5*. (American Psychiatric Association, 2013).

2. Polanczyk, G., de Lima, M. S., Horta, B. L., Biederman, J. & Rohde, L. A. The Worldwide Prevalence of ADHD: A Systematic Review and Metaregression Analysis. *American Journal of Psychiatry* **164**, 942–948 (2007).

3. Simon, V., Czobor, P., Bálint, S., Mészáros, Á. & Bitter, I. Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. *British Journal of Psychiatry* **194**, 204–211 (2009).

4. Upadhyay, N., Chen, H., Mgbere, O., Bhatara, V. S. & Aparasu, R. R. The Impact of Pharmacotherapy on Substance Use in Adolescents With Attention-Deficit/Hyperactivity Disorder: Variations Across Subtypes. *Substance Use & Misuse* **52**, 1266–1274 (2017).

5. Chang, Z. *et al.* Association Between Medication Use for Attention-Deficit/Hyperactivity Disorder and Risk of Motor Vehicle Crashes. *JAMA Psychiatry* **74**, 597–603 (2017).

6. Ruiz-Goikoetxea, M. *et al.* Risk of unintentional injuries in children and adolescents with ADHD and the impact of ADHD medications: A systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews* **84**, 63–71 (2018).

7. Dalsgaard, S., Leckman, J. F., Mortensen, P. B., Nielsen, H. S. & Simonsen, M. Effect of drugs on the risk of injuries in children with attention deficit hyperactivity disorder: a prospective cohort study. *The Lancet Psychiatry* **2**, 702–709 (2015).

8. Chang, Z., D’Onofrio, B. M., Quinn, P. D., Lichtenstein, P. & Larsson, H. Medication for Attention-Deficit/Hyperactivity Disorder and Risk for Depression: A Nationwide Longitudinal Cohort Study. *Biol Psychiatry* **80**, 916–922 (2016).

9. Lichtenstein, P. *et al.* Medication for Attention Deficit–Hyperactivity Disorder and Criminality. *N Engl J Med* **367**, 2006–2014 (2012).

10. Septier, M., Stordeur, C., Zhang, J., Delorme, R. & Cortese, S. Association between suicidal spectrum behaviors and Attention-Deficit/Hyperactivity Disorder: A systematic review and meta-analysis. *Neurosci Biobehav Rev* **103**, 109–118 (2019).

11. Dalsgaard, S., Østergaard, S. D., Leckman, J. F., Mortensen, P. B. & Pedersen, M. G. Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study. *The Lancet* **385**, 2190–2196 (2015).

12. Doshi, J. A. *et al.* Economic Impact of Childhood and Adult Attention-Deficit/Hyperactivity Disorder in the United States. *Journal of the American Academy of Child & Adolescent Psychiatry* **51**, 990-1002.e2 (2012).

13. Saul, R. ADHD does not exist. *Time magazine* (2014).

14. Breggin, P. ADHD is a misdiagnosis. *New York Times* (2011).

15. Taylor, E. Uses and misuses of treatments for ADHD. The second Birgit Olsson lecture. *Nordic Journal of Psychiatry* **68**, 236–242 (2014).

16. Zuvekas, S. H. & Vitiello, B. Stimulant medication use in children: a 12-year perspective. *Am J Psychiatry* **169**, 160–166 (2012).

17. Renoux, C., Shin, J.-Y., Dell’Aniello, S., Fergusson, E. & Suissa, S. Prescribing trends of attention-deficit hyperactivity disorder (ADHD) medications in UK primary care, 1995-2015. *Br J Clin Pharmacol* **82**, 858–868 (2016).

18. Safer, D. J. & Krager, J. M. A Survey of Medication Treatment for Hyperactive/Inattentive Students. *JAMA* **260**, 2256–2258 (1988).

19. Cortese, S. *et al.* Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: a systematic review and network meta-analysis. *Lancet Psychiatry* **5**, 727–738 (2018).

20. *Canadian Attention Deficit Hyperactivity Disorder Resource Alliance (CADDRA): Canadian ADHD Practice Guidelines*. (CADDRA).

21. Pliszka, S. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder. *Journal of the American Academy of Child & Adolescent Psychiatry* **46**, 894–921 (2007).

22. Bolea-Alamañac, B. *et al.* Evidence-based guidelines for the pharmacological management of attention deficit hyperactivity disorder: Update on recommendations from the British Association for Psychopharmacology. *J Psychopharmacol* **28**, 179–203 (2014).

23. Wolraich et al. Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics* **144**, e20192528 (2019).

24. Cortese S. Pharmacologic Treatment of Attention Deficit-Hyperactivity Disorder. *N Engl J Med* **383** (11):1050-1056 (2020) doi: 10.1056/NEJMra1917069. PMID: 32905677.

25. Taylor, E. *et al.* European clinical guidelines for hyperkinetic disorder – first upgrade. *European Child & Adolescent Psychiatry* **13**, i7–i30 (2004).

26. NICE Guideline NG 87 - Attention deficit hyperactivity disorder: diagnosis and management. (2018).

27. Raman, S. R. *et al.* Trends in attention-deficit hyperactivity disorder medication use: a retrospective observational study using population-based databases. *The Lancet Psychiatry* **5**, 824–835 (2018).

28. Moher, D. *et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* **4**, 1 (2015).

29. Stroup, D. F. *et al.* Meta-analysis of Observational Studies in Epidemiology A Proposal for Reporting. *JAMA* **283**, 2008–2012 (2000).

30. Moreira-Maia, C. R. *et al.* Are ADHD medications under or over prescribed worldwide?: Protocol for a systematic review and meta-analysis. *Medicine (Baltimore)* **97**, e10923–e10923 (2018).

31. Wells, G. *et al.* The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses.

32. Wang, N. *How to Conduct a Meta-Analysis of Proportions in R: A Comprehensive Tutorial*. (2018). doi:10.13140/RG.2.2.27199.00161

33. Tobi, H., van den Berg, P.B. & de Jong-van den Berg, L.T. Small proportions: what to report for confidence intervals? *Pharmacoepidemiol Drug Saf.* **14**, 239‐247 (2005).

34. DerSimonian, R. & Laird, N. Meta-analysis in clinical trials. *Controlled Clinical Trials* **7**, 177–188 (1986).

35. Higgins, J. P. T., Thompson, S. G., Deeks, J. J. & Altman, D. G. Measuring inconsistency in meta-analyses. *BMJ* **327**, 557–560 (2003).

36. Egger, M., Smith, G. D., Schneider, M. & Minder, C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* **315**, 629 (1997).

37. Miller, R. G. The Jackknife--A Review. *Biometrika* **61**, 1–15 (1974).

38. St. Amour, M. D., O’Leary, D. D., Cairney, J. & Wade, T. J. What is the effect of ADHD stimulant medication on heart rate and blood pressure in a community sample of children? *Canadian Journal of Public Health* **109**, 395–400 (2018).

39. Angold, A., Erkanli, A., Egger, H. L. & Costello, E. J. Stimulant Treatment for Children: A Community Perspective. *Journal of the American Academy of Child & Adolescent Psychiatry* **39**, 975–984 (2000).

40. Barbaresi, W. J. *et al.* How Common Is Attention-Deficit/Hyperactivity Disorder?: Incidence in a Population-Based Birth Cohort in Rochester, Minn. *JAMA Pediatrics* **156**, 217–224 (2002).

41. Bauermeister, J. J. *et al.* Stimulant and Psychosocial Treatment of ADHD in Latino/Hispanic Children. *Journal of the American Academy of Child & Adolescent Psychiatry* **42**, 851–855 (2003).

42. Bird, H. R. *et al.* A Study of Disruptive Behavior Disorders in Puerto Rican Youth: II. Baseline Prevalence, Comorbidity, and Correlates in Two Sites. *Journal of the American Academy of Child & Adolescent Psychiatry* **45**, 1042–1053 (2006).

43. Bussing, R. *et al.* Use and Persistence of Pharmacotherapy for Elementary School Students with Attention-Deficit/Hyperactivity Disorder. *Journal of Child and Adolescent Psychopharmacology* **15**, 78–87 (2005).

44. Cohen, Y. G., Segev, R. W., Shlafman, N., Novack, V. & Ifergane, G. Methylphenidate use among medical students at Ben-Gurion University of the Negev. *J Neurosci Rural Pract* **6**, 320–325 (2015).

45. Gudmundsdottir, B. G., Weyandt, L. & Ernudottir, G. B. Prescription Stimulant Misuse and ADHD Symptomatology Among College Students in Iceland. *J Atten Disord* 1087054716684379 (2016). doi:10.1177/1087054716684379

46. Hailpern, S. M. *et al.* Blood Pressure, Heart Rate, and CNS Stimulant Medication Use in Children with and without ADHD: Analysis of NHANES Data. *Front Pediatr* **2**, 100–100 (2014).

47. Jensen, P. S. *et al.* Are Stimulants Overprescribed? Treatment of ADHD in Four U.S. Communities. *Journal of the American Academy of Child & Adolescent Psychiatry* **38**, 797–804 (1999).

48. Luby, J. L., Stalets, M. M. & Belden, A. C. Psychotropic Prescriptions in a Sample Including Both Healthy and Mood and Disruptive Disordered Preschoolers: Relationships to Diagnosis, Impairment, Prescriber Type, and Assessment Methods. *Journal of Child and Adolescent Psychopharmacology* **17**, 205–216 (2007).

49. Merikangas, K. R., He, J., Rapoport, J., Vitiello, B. & Olfson, M. Medication Use in US Youth With Mental DisordersMedication Use in US Youth With Mental Disorders. *JAMA Pediatrics* **167**, 141–148 (2013).

50. Montiel, C., Peña, J. A., Montiel-Barbero, I. & Polanczyk, G. Prevalence Rates of Attention Deficit/Hyperactivity Disorder in a School Sample of Venezuelan Children. *Child Psychiatry and Human Development* **39**, 311–322 (2008).

51. Mortier, P. *et al.* *The epidemiology of ADHD in first-year university students*. **57**, (2015).

52. Sawyer, M. G., Rey, J. M., Graetz, B. W., Clark, J. J. & Baghurst, P. A. Use of medication by young people with attention-deficit/hyperactivity disorder. *Med. J. Aust.* **177**, 21–25 (2002).

53. Sawyer, M. G. *et al.* The Prevalence of Stimulant and Antidepressant Use by Australian Children and Adolescents with Attention-Deficit/Hyperactivity Disorder and Major Depressive Disorder: A National Survey. *Journal of Child and Adolescent Psychopharmacology* **27**, 177–184 (2017).

54. Sciberras, E. *et al.* Health-related impairments in young children with ADHD: a community-based study: Health-related impairments in young children with ADHD. *Child: Care, Health and Development* **42**, 709–717 (2016).

55. Szatmari, P., Offord, D. R. & Boyle, M. H. Correlates, associated impairments and patterns of service utilization of children with attention deficit disorder: findings from the Ontario Child Health Study. *J Child Psychol Psychiatry* **30**, 205–217 (1989).

56. Tremmery, S. *et al.* The use of health care services and psychotropic medication in a community sample of 9-year-old schoolchildren with ADHD. *European Child & Adolescent Psychiatry* **16**, 327–336 (2007).

57. Froehlich, T. E. *et al.* Prevalence, Recognition, and Treatment of Attention-Deficit/Hyperactivity Disorder in a National Sample of US Children. *Archives of Pediatrics & Adolescent Medicine* **161**, 857 (2007).

58. de Graaf, R. *et al.* The prevalence and effects of adult attention-deficit/hyperactivity disorder (ADHD) on the performance of workers: results from the WHO World Mental Health Survey Initiative. *Occupational and Environmental Medicine* **65**, 835–842 (2008).

59. Sayal, K., Ford, T. & Goodman, R. Trends in Recognition of and Service Use for Attention-Deficit Hyperactivity Disorder in Britain, 1999–2004. *Psychiatric Services* **61**, 803–810 (2010).

60. Visser, S. N., Lesesne, C. A. & Perou, R. National Estimates and Factors Associated With Medication Treatment for Childhood Attention-Deficit/Hyperactivity Disorder. *Pediatrics* **119**, S99–S106 (2007).

61. Danielson, M. L. *et al.* A National Profile of Attention-Deficit Hyperactivity Disorder Diagnosis and Treatment Among US Children Aged 2 to 5 Years: *Journal of Developmental & Behavioral Pediatrics* **38**, 455–464 (2017).

62. Toomey, S. L., Chan, E., Ratner, J. A. & Schuster, M. A. The Patient-Centered Medical Home, Practice Patterns, and Functional Outcomes for Children with Attention Deficit/Hyperactivity Disorder. *Academic Pediatrics* **11**, 500–507 (2011).

63. Walls, M., Allen, C. G., Cabral, H., Kazis, L. E. & Bair-Merritt, M. Receipt of Medication and Behavioral Therapy Among a National Sample of School-Age Children Diagnosed With Attention-Deficit/Hyperactivity Disorder. *Academic Pediatrics* **18**, 256–265 (2018).

64. Concannon, P. & Tang, Y. Management of attention deficit hyperactivity disorder: A parental perspective. *Journal of Paediatrics and Child Health* **41**, 625–630 (2005).

65. Szobot, C. M. *et al.* Is attention-deficit/hyperactivity disorder associated with illicit substance use disorders in male adolescents? A community-based case-control study. *Addiction* **102**, 1122–1130 (2007).

66. Schmitz, M. *et al.* Smoking during pregnancy and attention-deficit/hyperactivity disorder, predominantly inattentive type: a case-control study. *J Am Acad Child Adolesc Psychiatry* **45**, 1338–1345 (2006).

67. Reich, W., Huang, H. & Todd, R. D. ADHD Medication Use in a Population-Based Sample of Twins. *Journal of the American Academy of Child & Adolescent Psychiatry* **45**, 801–807 (2006).

68. Epstein-Ngo, Q. M. *et al.* Diversion of ADHD Stimulants and Victimization Among Adolescents. *Journal of Pediatric Psychology* **41**, 786–798 (2016).

69. Knopf, H., Hölling, H., Huss, M. & Schlack, R. Prevalence, determinants and spectrum of attention-deficit hyperactivity disorder (ADHD) medication of children and adolescents in Germany: results of the German Health Interview and Examination Survey (KiGGS). *BMJ Open* **2**, e000477 (2012).

70. Efron D, Mulraney M, Sciberras E, Hiscock H, Hearps S, Coghill D. Patterns of long-term ADHD medication use in Australian children. *Arch Dis Child*. 2020;105(6):593-597.

71. Fairman RT, Vu M, Haardörfer R, Windle M, Berg CJ. Prescription stimulant use among young adult college students: Who uses, why, and what are the consequences? [published online ahead of print, 2020 Jan 16]. *J Am Coll Health*. 2020;1-8.

72. Russell AE, Ford T, Russell G. Barriers and predictors of medication use for childhood ADHD: findings from a UK population-representative cohort. Soc *Psychiatry Psychiatr Epidemiol*. 2019;54(12):1555-1564.

73. Danielson ML, Bitsko RH, Ghandour RM, Holbrook JR, Kogan MD, Blumberg SJ. Prevalence of Parent-Reported ADHD Diagnosis and Associated Treatment Among U.S. Children and Adolescents, 2016*. J Clin Child Adolesc Psychol.* 2018;47(2):199-212.

74. United Nations, Department of Economic and Social Affairs, Population Division. *World Population Prospects: The 2017 Revision, Key Findings and Advance Tables. ESA/P/WP/248.* (2017).

75. Lawrence, D*. et al.* The mental health of children and adolescents: report on the second Australian Child and Adolescent Survey of Mental Health and Wellbeing. (Department of Health, 2015).

76. Zablotsky, B. *et al.* Prevalence and Trends of Developmental Disabilities among Children in the United States: 2009–2017. *Pediatrics* **144**, e20190811 (2019).

77. Gezondheidsraad. ADHD: medicatie en maatschappij. (2014).

78. Caye, A., Swanson, J. M., Coghill, D. & Rohde, L. A. Treatment strategies for ADHD: an evidence-based guide to select optimal treatment. *Molecular Psychiatry* **24**, 390–408 (2019).

79. Greenhill, L. *et al.* Efficacy and Safety of Immediate-Release Methylphenidate Treatment for Preschoolers With ADHD. *Journal of the American Academy of Child & Adolescent Psychiatry* **45**, 1284–1293 (2006).

80. Coles, E. K. et al. Randomized Trial of First-Line Behavioral Intervention to Reduce Need for Medication in Children with ADHD. Journal of Clinical Child & Adolescent Psychology 1–15 (2019). doi:10.1080/15374416.2019.1630835.

81. Kessler, R. C., Chiu, W. T., Demler, O. & Walters, E. E. Prevalence, Severity, and Comorbidity of 12-Month DSM-IV Disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry* **62**, 617 (2005).

82. Kirova, A.-M. *et al.* Are subsyndromal manifestations of attention deficit hyperactivity disorder morbid in children? A systematic qualitative review of the literature with meta-analysis. *Psychiatry Research* **274**, 75–90 (2019).

83. Greenhill, L. L. *et al.* Practice parameter for the use of stimulant medications in the treatment of children, adolescents, and adults. *J Am Acad Child Adolesc Psychiatry* **41**, 26S-49S (2002).

84. Faraone, S. V. *et al.* Systematic Review: Nonmedical Use of Prescription Stimulants: Risk Factors, Outcomes, and Risk Reduction Strategies. *Journal of the American Academy of Child & Adolescent Psychiatry* (2019) doi:10.1016/j.jaac.2019.06.012.

85. Galéra C. *et al*. Clinical and social factors associated with attention-deficit hyperactivity disorder medication use: population-based longitudinal study. *Br J Psychiatry,* **205**, 291-297 (2014).

86. Wallach-Kildemoes H. *et al*. Social adversity and regional differences in prescribing of ADHD medication for school-age children. *J Dev Behav Pediatr* **36**, 330-341 (2015).

87. Willcutt, E. G. The prevalence of DSM-IV attention-deficit/hyperactivity disorder: a meta-analytic review. *Neurotherapeutics* **9**, 490–499 (2012).

88. Thomas, R., Sanders, S., Doust, J., Beller, E. & Glasziou, P. Prevalence of Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-analysis. *PEDIATRICS* **135**, e994–e1001 (2015).

89. Jones, B. E. & Samore, M. H. Antibiotic Overuse: Clinicians Are the Solution Antibiotic Overuse. *Annals of Internal Medicine* **166**, 844–845 (2017).

90. Yttri, J.-E. & Videbech, P. [Overtreatment and undertreatment of depression]. *Ugeskr. Laeg.* **179**, (2017).

91. de Leon, J. Paradoxes of US Psychopharmacology Practice in 2013: Undertreatment of Severe Mental Illness and Overtreatment of Minor Psychiatric Problems. *Journal of Clinical Psychopharmacology* **34**, 545–548 (2014).

92. Piper, B. J. *et al.* Trends in use of prescription stimulants in the United States and Territories, 2006 to 2016. *PLOS ONE* **13**, e0206100 (2018).

93. Lin L. *et al.* Empirical Comparison of Publication Bias Tests in Meta-Analysis. *J Gen Intern Med,* **33**, 1260–1267 (2018).

**Table 1: Characteristics of studies in children and adolescent included in the meta-analysis.**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *Study* | *Sample description* | *Country* | *Design* | *Diagnosis* | *Age* | *Response/ Completion rates (%)* | *Controls* | *ADHD* | *NOS* |
| *Treatment Negative* | *Treatment Positive* | *Treatment Negative* | *Treatment Positive* | *selection (up to 4)* | *comparability (up to 2)* | *total* |
| Angold et al., 2000 | Great Smoky Mountains Study, 1992-1996 | USA | Retrospective | DSM | 9-16 | 71 | 1179 | 86 | 34 | 58 | 3 | 2 | 5 |
| Barbaresi et al., 2002 | Rochester Epidemiology Project, 1976-1982 | USA | Retrospective, Administrative | DSM | NS | NS | 5045 | 10 | 41 | 264 | 4 | 1 | 5 |
| Bauermeister et al., 2003 | Puerto Rico Service Use Study, 1999-2000 | USA | Retrospective | DSM | 4-17 | 90 | 1513 | 6 | 132 | 11 | 3 | 2 | 5 |
| Bird et al., 2008 | New York (South Bronx) and Boricua Youth Study (Puerto Rico) | USA | Prospective | DSM | 5-13 | 85 | 2263 | 42 | 155 | 20 | 3 | 1 | 4 |
| Bussing et al., 2005 | North Central Florida public school, 1998-1999 | USA | Prospective | DSM | 5-11 | 55 | 61 | 0 | 92 | 67 | 4 | 1 | 5 |
| Concannon et al., 2005 | Northern Sydney, 2000 | Australia | Cross Sectional | Question | 10-12 | 65 | - | - | 128 | 150 | 1 | 0 | 1 |
| Danielson et al., 2018 | National Survey of Children’s Health (NSCH), 2016 | USA | Cross Sectional | Question | 2-17 | 41 | - | - | 1618 | 2640 | 2 | 0 | 2 |
| Efron et al., 2019 | Longitudinal Study of Australian Children (LSAC), 2004-2015 | Australia | Prospective | Question | 14-15 | 71 | - | - | 19 | 72 | 2 | 0 | 2 |
| Epstein-Ngo et al., 2015 | Midwestern United States public schools, 2009-2013 | USA | Cross Sectional | Question | NS | 68 | - | - | 581 | 179 | 1 | 1 | 2 |
| Froehlich et al., 2007 | National Health and Nutrition Examination Survey (NHANES) 2001-2004 | USA | Cross Sectional | DSM | 8-15 | 79 | - | - | 143 | 79 | 4 | 1 | 2 |
| Hailpern et al., 2014 | National Health and Nutrition Survey (NHANES) 1999–2004 | USA | Cross Sectional | Question | 12-18 | NS | 4524 | 0 | 272 | 111 | 3 | 0 | 5 |
| Jensen et al., 1999 | Epidemiology of Child and Adolescent Mental Disorders (MECA) Study (1992) | USA | Cross Sectional | DSM | 9-17 | 85 | 904 | 8 | 53 | 8 | 4 | 1 | 3 |
| Knopf et al., 2012 | German Health and Examination Survey for Children and Adolescents (KiGGS), 2003-2006 | Germany | Cross Sectional | Question | 0-17 | 67 | 12682 | 3 | 512 | 142 | 2 | 1 | 5 |
| Merikangas et al., 2013 | National Comorbidity Survey Adol. Suppl. (NCS-A), 2001-2004 | USA | Cross Sectional | DSM | 13-18 | 83 | 5953 | 93 | 355 | 82 | 3 | 1 | 3 |
| Montiel et al., 2008 | Maracaibo, Venezuela | Venezuela | Cross Sectional | DSM | 4-12 | 88 | 75 | 4 | 148 | 6 | 3 | 1 | 4 |
| Reich et al., 2006 | Missouri twins sample, 1996-2001 | USA | Cross Sectional | DSM | 7-17 | 65 | 273 | 9 | 20 | 21 | 4 | 1 | 4 |
| Russel et al., 2019 | Millennium Cohort Study, 2014-2015 | England | Cross Sectional | Question | 14 | 61 | - | - | 104 | 141 | 2 | 0 | 5 |
| Sayal et al., 2010 | British Child and Adolescent Mental Health Survey (B-CAMHS) 2004 | England | Cross Sectional | DSM/ICD | 5-16 | 76 | - | - | 123 | 53 | 2 | 1 | 2 |
| Sawyer et al., 2002 | Australian National Survey of Mental Health and Well-Being, Feb-May 1998 | Australia | Cross Sectional | DSM | 6-17 | 70 | 3149 | 16 | 345 | 52 | 3 | 1 | 3 |
| Sawyer et al., 2016 | Australian National Child and Adolescent Mental Health Survey. 2013–2014 | Australia | Cross Sectional | DSM | 4-17 | 55 | 5854 | 22 | 374 | 55 | 4 | 1 | 4 |
| Sciberras et al., 2016 | Children’s Attention Project, Melbourne, Australia, 2011-2015 | Australia | Prospective | DSM | 6-8 | 60 | 212 | 0 | 156 | 21 | 4 | 0 | 5 |
| Schmitz et al., 2006 | Public schools in Porto Alegre, 2002-2005 | Brazil | Cross Sectional | DSM | 6-18 | 93 | - | - | 97 | 3 | 4 | 1 | 4 |
| St Amour et al., 2018 | Heart Behavioural and Environmental Assessment Team | Canada | Cross Sectional | Question | 10-14 | 31 | 1863 | 50 | 50 | 49 | 2 | 1 | 5 |
| Szatmari et al., 1989 | The Ontario Child Health Study (OCHS) 1966-1979 | Canada | Cross Sectional | DSM | 4-16 | NS | 2542 | 2 | 149 | 8 | 4 | 0 | 3 |
| Szobot et al., 2007 | Canoas, 2004 | Brazil | Cross Sectional | DSM | 15-20 | 70 | - | - | 41 | 0 | 4 | 0 | 4 |
| Toomey et al., 2011 | National Survey of Children’s Health (NSCH) 2007 | USA | Cross Sectional | Question | 6-17 | 47 | - | - | 1666 | 3463 | 1 | 0 | 4 |
| Tremmery et al., 2007 | Study of Attention Disorders in Maastricht (SAM) 1999-2000 | Netherlands | Prospective | DSM | 9 | 32 | 236 | 2 | 35 | 10 | 3 | 1 | 1 |
| Visser et al., 2007 | National Survey of Children’s Health (NSCH) 2003 | USA | Cross Sectional | Question | 4-17 | 55 | - | - | 2711 | 3786 | 1 | 0 | 4 |
| Walls et al., 2017 | National Survey of the Diagnosis and treatmentof Attention-Deficit/Hyperactivity Disorder and Tourette Syndrome (NS-DATA) 2014 | USA | Cross Sectional | Question | 8-17 | 11 | - | - | 712 | 1689 | 1 | 0 | 1 |

“NS” = not stated (papers do not supply a range or mean age for those samples)**; “**NOS” = Newcastle Ottawa Scale.

**Figure 1: Search and screening flowchart.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Records identified |

|  |
| --- |
|  |

 | Duplicates removed |  |
| (n = 27,192) |  | (n = 1,516) |  |
|

|  |
| --- |
|  |

 |  |  |  |
|  |  |  |  |
| Records screened |

|  |
| --- |
|  |

 | Records excluded |  |
| (n = 25,676) |  | (n = 25,023) |  |
|

|  |
| --- |
|  |

 |  |  |  |
|  |  |  |  |
| Full-text articles assessed for eligibility |

|  |
| --- |
|  |

 | Full-text articles excluded |   |
| (n = 653) |  | (n = 617) |   |
|

|  |
| --- |
|  |

 |  | *254 - No proper ADHD diagnosis* |
|  |  | *126 - Clinical sample* |
|  |  | *114 - Prevalence based on prescriptions*  |   |
|  |  | *72 - Without or inadequate data on medication for ADHD* |
| Studies included in quantitative synthesis |  | *23 - Review or metanalysis* |   |
|  | *13 - Same sample of an included study* |   |
| (n = 36) |  | *10 - Prevalence based on medical visits*  |
|  |  | *5 - News or unrelated articles* |

**Figure 2: Forest plot showing the meta-analysis results of ADHD medication use among children and adolescents diagnosed with ADHD according to the DSM/ICD criteria**



**Figure 3: Forest plot showing the meta-analysis results of the rates of ADHD medication use among children and adolescents without a DSM/ICD diagnosis of ADHD**

