**​Association between relative age at school and persistence of attention-deficit hyperactivity disorder in prospective studies: an individual participant data meta-analysis**

SIMBA study group\*

\* Collaborators are listed at the end of the Article

**Corresponding author:**

Dr Corentin J. Gosling

DysCo laboratory, Paris-Nanterre University

92001 Nanterre, France

E-mail: cgosling@parisnanterre.fr

**RESEARCH IN CONTEXT**

**Evidence before this study**Some studies have shown a relative age effect on the diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD), i.e., the youngest children in a school class are more likely to receive a diagnosis of ADHD. We did a PubMed/MEDLINE search, with no language restrictions, from database inception until February 1st, 2020 (while planning the current study) and updated it on April 1st, 2022, to identify systematic reviews with/without meta-analysis on the relative age effect in ADHD. We used the following search terms and syntax: "(“ADHD” or “attention-deficit/hyperactivity disorder” or “attention deficit” or “hyperkinetic syndrome” or “hyperkinetic disorder”) AND (“relative age” OR “relative immaturity” OR “birth” OR young\*)". We found two systematic reviews without meta-analysis and one systematic review with meta-analysis confirming that children and adolescents who are relatively younger compared with their classmates have a higher likelihood of being diagnosed with ADHD. Additionally, these reviews showed that the relative age effect is less frequent in older school-grade children than younger ones. The relative age effect may raise doubts about the diagnosis of ADHD in children with a young relative age, who would be labelled with ADHD and be unnecessarily exposed to possible side effects of medications for ADHD solely because of their temporary immaturity. However, it is unknown to what extent ADHD diagnosed in children with a young relative age persists later on.

**Added value of this study**We gathered individual patient data (IPD) from 57 prospective cohorts that followed 6,504 children with ADHD for a period ranging from 4 to 33 years. This resulted in the largest available dataset to assess the association between relative age and the persistence of ADHD at older ages. We found that a younger relative age did not decrease the persistence of ADHD in later years. Compared to previous studies exploring whether younger relative age is associated with increased risk of being diagnosed with ADHD, the present meta-analysis demonstrates that relative age does not lead to particularly unstable ADHD diagnoses over time. Future studies are needed to determine whether this reflects the persistence of an appropriate or inappropriate diagnostic label.

**Implications of all the available evidence**To explain our finding, two alternative interpretations could be proposed. First, the relative age effect may not increase the number of children identified with ADHD among those with a younger relative age; rather it may decrease the number of children identified with ADHD among those with an older relative age. Second, potential carry-over effects, such as teachers, parents, or other informants maintaining an endorsement of impairing ADHD symptoms once a diagnosis of ADHD is assigned, may also lead to a persistence of an inappropriate diagnostic label. Given the implications on the diagnostic process for ADHD, it is important for future studies to disentangle these two interpretations.

 **SUMMARY**

**Background:** The youngest children in a school class are more likely to be diagnosed with ADHD, but this relative age effect is less frequent in older than in younger school-grade children. However, no study has explored the association between relative age and the persistence of ADHD diagnosis at older ages. The aim of this meta-analysis was to quantify the association between the relative age and persistence of ADHD at later ages. **Methods:** We gathered individual-participant data (IPD) from prospective cohorts that included children identified with ADHD before the age of 10 years. ADHD was defined by either a clinical diagnosis or symptoms exceeding clinical cut-offs. Our outcome was ADHD status at a diagnostic reassessment, conducted at least 4 years after the initial assessment and after the age of 10 years. No information on sex/gender or ethnicity was collected. We did a two-stage random-effects IPD meta-analysis to assess the association of relative age with the persistence of ADHD at follow-up. **Findings:** We gathered IPD from 57 prospective studies, conducted in 19 countries. These studies followed, for a period ranging from 4 to 33 years, 6504 children with ADHD. We found that younger relative age was not statistically significantly associated with ADHD persistence at follow-up (OR = 1.02, 95% CI = [0.99, 1.06], p = 0.19). Additional analyses revealed similar results in cohorts with a robust relative age effect at baseline. Sensitivity analyses, including those restricted to cohorts involving children with a clinical diagnosis of ADHD or with a follow-up duration of over 10 years, confirmed the robustness of our findings.**Interpretation:** Contrary to our hypothesis,the present study demonstrates that younger relative age is not significantly associated with decreased ADHD persistence at later ages. Alternative explanations for this result, limitations of the study, and implications of the findings are discussed.

The present study received no funding.

**INTRODUCTION**

Attention-deficit/hyperactivity disorder (ADHD) is characterised by impairing and pervasive inattention and/or hyperactivity and impulsivity, that are inconsistent with developmental levels. With an estimated prevalence around 5-7% in school-age children internationally, ADHD is the most common neurodevelopmental condition in childhood.1,2 Rates of ADHD tend to decrease in adulthood, with an estimated prevalence of around 2.5%.3 The management of individuals with ADHD includes pharmacological (stimulant and non-stimulant medications) and non-pharmacological options.4

In many countries, school entry is only possible when children have reached a minimum age by a certain cut-off date. This procedure results in age disparities among children in the same class, which can be as large as a full year. Cross-sectional and longitudinal studies have shown that the youngest children in a school class are more likely to be diagnosed with ADHD. This variation in the likelihood of receiving a diagnosis depending on child age within a class was called the ‘relative age effect’.5-7 In school systems where the school entry cut-off date is at the end of August (as in the UK and many states in the US), children born in the fall are among the oldest in their school class, and they are the least likely to be diagnosed with ADHD.8 This effect cannot be attributed to seasonal influences on neurodevelopment, because when the school entry cut-off date is at the end of December (as in most European countries), children born in the fall are among the youngest in their school class and the most likely to be diagnosed with ADHD.9

A key moderator of this relative age effect on ADHD diagnosis is children’s absolute age. In classes of older children, the relative age effect on ADHD diagnosis is less evident.7,10 A common explanation for this relative age effect is that developmental immaturity is associated with higher levels of inattention, hyperactivity, and impulsivity that can be judged as age-inappropriate when compared to the class norm, rather than being considered in relation to the chronological age of each child. The relative age effect would be moderated by absolute age because developmental difference caused by an age gap of up to twelve months attenuates with increasing age.5

Overall, the relative age effect may raise concerns about misdiagnosing children with ADHD because of their temporary immaturity, and thus possibly exposing them to unnecessary labelling and medications. However, to our knowledge, no study has yet explored the persistence over time of the ADHD diagnosis in children with young relative age. Our hypothesis was that younger relative age would be associated with a lower likelihood of ADHD persistence over time. Indeed, if some children are diagnosed with ADHD due to their relative immaturity, a diagnostic reassessment of these children at a later age (i.e., when the influence of the relative age has reduced) should be more likely to no longer support the initial diagnosis.11 Here, we conducted a systematic review with individual participant data meta-analysis (IPD-MA) of prospective cohort studies to assess the association between relative age and persistence of ADHD at older ages.

**METHODS**

This IPD-MA, based on a pre-published protocol (PROSPERO CRD42020212650),11 was conducted and reported according to relevant guidelines.12,13 The PRISMA checklist is reported in the Appendix (p.1).

**Search strategy and selection criteria***Search and study selection.* We searched MEDLINE, Embase, CINAHL, PsycINFO, and PubPsych, with terms related to two constructs -‘cohort’ and ‘ADHD’- up to April 1st, 2022 (see Appendix, p.6). No date, publication type, or language restrictions were applied.

Screening of the titles and abstracts was performed independently by two author pairs, CJG, SCa and CP. Study selection was performed by CJG and SCa, and disagreements were resolved by SC. References of included studies and Google Scholar were searched to identify non-published references.

We included prospective studies in which at least 10 children categorised as having ADHD were re-assessed for ADHD at least 4 years after the initial assessment.
Studies were eligible if they included children with: 1) a diagnosis of ADHD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) (from III to 5th); 2) or a diagnosis of hyperkinetic syndrome per the International Classification of Diseases (ICD) 9 or 10; 3) or ADHD symptoms exceeding clinical cut-offs established using either a clinical interview or a questionnaire with adequate psychometric properties (see Appendix, p.7 for a list of included tools). We required the initial diagnosis to have occurred before the age of 10 years (and after the children had started pre-school). When multiple informants provided a measure of ADHD symptoms, we used the recommended averaging approach to categorise ADHD.14 When multiple assessments of ADHD had been performed at baseline, we used multiple independent samples for the same cohort when building the meta-analytic model (see Statistical Analyses).

**Data collection, transfer, and extraction**Anticipating that a significant proportion of primary study authors would not be able to share their sensitive data, we developed a script in R to automatically analyse the data and generate anonymised outputs for our IPD-MA. Primary study authors were invited to either share the raw data through secured data transfer, or apply the R script locally and then share the anonymized results. Authors were provided with extensive guidance on the script during videoconference meetings. Several study-level variables were also independently extracted by two authors (CG and SCa). Importantly, the relative age variable was obtained by recoding the month of birth in relation to the school-entry cut-off date. Children whose birth month was just after the school-entry cut-off date were coded 1, children whose birth month was the second month after the school-entry cut-off date were coded 2, and so on. This coding was applied for all cohorts regardless of their school-entry cut-off dates, ensuring that the oldest children in the class were assigned a relative age of 1 while youngest children in the class were assigned a relative age of 12. For each cohort, the school-entry cut-off date was first obtained from administrative/scientific sources, and then confirmed by the authors of the primary studies. Critically, in some geographic areas, there was some flexibility in the application of the school entry cut-off date, such as when school-entry depended on the results of some developmental tests. In these situations, because the month of birth was no longer necessarily related to relative age, we excluded the data of the cohorts from the main analyses, but we retained them in a secondary analysis. For details on the data extraction, see the Appendix (p.8).

**Risk of bias**The risk of bias of the included studies was assessed independently by two authors (CG and SCa) using an adapted version of the Newcastle Ottawa Scale for cohort studies.16

**Outcome**The primary and only outcome was the persistence of the ADHD diagnosis at follow-up (i.e., whether the initial diagnosis before the age of 10 was confirmed at a later follow-up diagnostic assessment). The follow-up diagnostic reassessment needed to have occurred after the age of 10 (based on evidence that the relative age effect tends to decline after this age) and at least four years after the initial diagnostic assessment*.*15

**Statistical analysis**We did all statistical analyses in the R environment.17 To analyse the data of primary studies, we fitted, for each study, a logistic regression model assessing the association of relative age with persistence of ADHD at follow-up. When cohorts used a complex survey design, we conducted survey-weighted logistic regression using the R survey package.19-21 In all our analyses, an OR value greater than 1 indicates that younger relative age is associated with an increased likelihood of having a persistent diagnosis of ADHD at follow-up.

All meta-analytic pooled estimates were obtained using a random-effects meta-analysis with a restricted maximum likelihood estimator, using the ‘meta’ package.18 When necessary, we added a random effect at the sample-level to account for the dependency between effect sizes derived from cohorts with several independent subsamples. Heterogeneity was estimated using the Q and I² statistics.

We first did a post-hoc data quality check.As most of our studies were composed of samples of participants with ADHD, we were unable to systematically ascertain whether the participants displayed a relative age effect at baseline. Therefore, we explored whether we could detect the relative age effect on ADHD diagnosis at baseline in a subsample of nine large community cohort studies that allowed us to test this hypothesis.
To further ensure that the absence of relative age effect on ADHD persistence was not related to the potential inclusion of participants who were not in their age-appropriate school grade, we excluded participants who were born within two months before or after the school-entry cut-off date[1] (because children born close to the school-entry cut-off are specifically likely to have been enrolled to school one year earlier or later).22 Note that for this analysis, which was not planned initially, we were only able to include 22 of the 41 studies from our main analysis for feasibility reasons but - as shown in the results section - this subsample generates a pooled effect size similar to that of our main analyses when all participants are included.
We also limited our analyses to participants 1) with a follow-up longer than 10 years, 2) with a baseline diagnosis made before the age of eight and re-assessed at follow-up after the age of 16, and 3) assessed with the same measure at baseline and follow-up.
Moreover we: 1) replicated our analyses by categorising the month of birth, and retaining in the analysis only participants with the youngest and oldest relative age (for this analysis, we selected children born in the 4 months that preceded or followed the school entry cut-off date; as mentioned previously, we were also able to include 24 of the 41 studies from our main analysis), 2) conducted a Jackknife leave-one-out meta-analysis, 3) excluded samples with a large Cook’s distance, and 4) replicated our analyses conducting a robust regression model (aiming to limit the effect of violation of assumptions of the generalised linear model).
In the nine cohort studies that allowed us to explore the relative age effect on ADHD diagnosis at baseline, we conducted a meta-regression exploring if the relative age effect on ADHD persistence varied depending on 1) the statistical significance (p-value above or below 0·05) and 2) the strength of the relative age effect at baseline (OR value above or below 1·05).

We also conducted meta-regressions exploring whether effect sizes varied depending on 1) the tools used to assess ADHD (research interviews, symptoms count, or broad-based scales), 2) the sampling type, 3) participants’ ADHD presentation at baseline (combined, predominantly inattentive or predominantly hyperactive/impulsive), 4) participant’s IQ (below vs. above the median value of 100), and 5) school entry system (flexible versus non-flexible).
Deviations from the protocol (all minor) are listed in the Appendix (p.8).

**Role of the funding source**There was no funding source for this study. For each cohort, CJG and all the cohort team members had access to the raw data..

**RESULTS**

Results (including raw data, R code supporting data analysis, and detailed results) are publicly available: <https://simba-adhd.com/HTMLresults.html>.
From an initial pool of 33,119 potentially relevant references, we identified 130 eligible unique studies (Figure 1). We gathered data from 57 studies (44%), 56 published data23-78 and one personal communication (Abd Elkmasoud, 2022), encompassing 6,504 participants categorised as having ADHD (Appendix, p.9). The list of eligible and excluded studies (after full-text reading), are available in the Appendix (p.9 and 20, respectively). 25 (44%) studies were conducted in North or South America (22 [39%] in the USA), 22 (39%) in Europe, 5 (9%) in Africa, 3 (5%) in Asia, and 2 (4%) in Oceania (Appendix, p.35). The number of participants per study ranged from 10 to 813. The mean length of follow-up ranged from 4 to 33 years (median=7 years, IQR=4 years). The persistence of ADHD at follow-up ranged from 0% to 100% (median=45%, IQR=40%). A total of 16 studies were excluded from the primary analysis because they were conducted in regions/countries with a flexible school entry system that did not allow us to confidently link the birthdate to the relative age. Among the 41 studies included in our primary analysis, 20 categorised ADHD using a formal diagnostic procedure, 13 based on symptom count using interviews or questionnaires, and eight based on scores above the threshold of broad-based scales assessing ADHD symptoms. No participant-level information on sex/gender or ethnicity was collected.

We pooled the results of nine community cohort studies including each more than 1000 participants (with and without ADHD) at baseline (n=88,753 participants in total). As predicted, younger relative age was statistically significantly associated with increased odds of being diagnosed with ADHD at baseline (OR = 1·04, 95% CI = [1·02, 1·06], p < 0·0001); Appendix p.36). All eight community cohorts generated a positive effect size (OR ≥ 1); three generated a relative age effect larger than OR=1·05, and six led to a statistically significant effect. Therefore, this analysis confirmed that younger relative age is associated with increased likelihood of being diagnosed with ADHD at baseline.

In the primary analysis, pooling the results of 41 cohorts of children with ADHD, there was no substantial association between relative age and persistence of ADHD: younger relative was associated – contrary to what we had hypothesised – with a very small and non-statistically significant increase in persistence of ADHD (OR = 1·02, 95% CI = [0·99, 1·06], p = 0·19, Figure 2; Appendix p.37). We observed statistically significant heterogeneity in our model (Q = 75·82, p = 0·0011, I² = 45%), which we explored further in our sensitivity and meta-regression analyses.

In sensitivity analyses (Figure 3, Appendix, p.38), we started by replicating our primary analysis but excluding participants born in the two months before or after the school entry cut-off date. We still found no statistically significant association of relative age with ADHD persistence. Then, restricting our analyses, in turn, to participants: (a) with a follow-up duration of more than 10 years, (b) with a baseline diagnosis before the age of 8 and the follow-up diagnosis after the age of 16 or (c) with the same ADHD measure at baseline and follow-up did not materially change the results.

In robustness checks (Figure 3, Appendix, p.41), we found that using robust regression or excluding samples (n=2) with a large Cook’s distance did not materially change the results. Similarly, the largest and smallest pooled effect sizes obtained in a Jackknife analysis were extremely close to those obtained in our primary model. Last, dichotomizing relative age by restricting to participants with the youngest *versus* oldest relative age also led to similar results (OR = 1·33, 95% CI = [1·00; 1·76], p = 0·049).

Results of our meta-regressions are presented in Appendix, p.44. Most importantly, meta-regressions conducted in the nine population-based cohorts revealed that the association between relative age and ADHD persistence was not moderated by the statistical significance of the relative age effect at baseline (i.e., *p-value* < 0·05 *versus* >= 0·05; QM = 1·81, p = 0·18) or the strength of the relative age effect at baseline (OR > 1·05 *versus* <= 1·05; QM = 0·99, p = 0·32). Additionally, we found no statistically significant moderating effect of the tool used for the diagnosis of ADHD, when focusing the analyses on studies using diagnostic interviews, symptoms count, or broad-based scales (QM = 2·85, p = 0·42). Results of other meta-regression analyses did not reveal any important moderator.

**DISCUSSION**

We tested the association between relative age and ADHD persistence at later ages using an IPD-MA of prospective cohort studies. Contrary to our hypothesis, results showed that younger relative age was not associated with a statistically significant decrease in the persistence of the ADHD diagnosis over time. All our additional analyses confirmed the robustness of this finding. Importantly, all participants in the included studies underwent a similar diagnostic process (a baseline and a follow-up assessment for ADHD using validated measures), and a large variability in the persistence of ADHD was observed. Therefore, the absence of association between relative age and persistence of ADHD cannot be attributed to a lack of variability in our outcome variable caused, for example, by the use of inappropriate measures.

Two possible interpretations could explain our main finding. A first is that, contrary to what is commonly assumed, younger relative age might not increase the likelihood of receiving a diagnosis of ADHD. Instead, it is possible that the relative age effect decreases the likelihood of children with older relative age receiving a diagnosis of ADHD. This interpretation would explain both the well-established association between younger relative age and increased ADHD prevalence, and the absence of association between relative age and the persistence of ADHD found in our study. In terms of prevalence, the relative maturity conferred by having an older relative age could result in some ADHD symptoms being missed or overlooked. The higher rate of ADHD among children with younger relative age would thus be accounted for by under-identification of ADHD in children with older relative age. In relation to ADHD persistence, if older relative age reduces the probability of receiving a diagnosis of ADHD, then the children most affected by relative age were not included in our studies (because participants with no ADHD diagnosis at baseline were excluded from our core analyses). Therefore, if this interpretation is correct, it is not surprising that we failed to observe a substantial association between relative age and persistence of ADHD. Future research should explore whether, among children without ADHD, an older relative age is associated with a higher probability of having emerging ADHD symptoms several years later. In sum, whilst this interpretation supports the validity of ADHD diagnoses in children with younger relative ages, it warns against a possible under-diagnosis of ADHD in children with older relative ages.

An alternative interpretation is that assigning a diagnostic label of ADHD leads to unexplored carry-over effects of the initial diagnosis that outweighs the influence of the relative age. It is possible that, once a diagnostic label of ADHD is assigned, parents, teachers and other persons act differently with the child, and/or modify their expectations because they are influenced by the initial diagnosis. Indeed, it has been shown that labelling young children with ADHD can increase the odds of persistent ADHD symptoms, classroom learning problems, and specialist service use.79 This interpretation reinforces the concern about the influence of relative age on ADHD, as it suggests that this effect may have a long-term impact. The present findings cannot disentangle these two interpretations but highlight the importance of assessing the exact mechanisms underlying the effect of relative age on ADHD, in order to improve the diagnostic process for ADHD.

Our study results should be considered in light of some limitations. First, we were unable to access the exact date when each child in our sample started school, as well as the presence of any school repetition during their education, which would be necessary to determine more accurately whether month of birth was associated with relative age. However, our additional analyses showed that removing the participants born close to the school-entry cut-off date, who are at higher risk of entering school in advance or being held back,80 did not change our results. Second, because of the design of most of the included studies (i.e., cohorts of children diagnosed with ADHD), we could not systematically test if a relative age effect was present at baseline across all included studies. However, the meta-regressions conducted in large community cohort studies with a statistically significant relative age effect at baseline, or with a moderate/large relative age effect at baseline, yielded very similar results to those in our main analysis. Third, despite our efforts, we were able to gather IPD only from about 40% of the identified studies. Although this proportion is not uncommon in IPD-MA, this may affect the generalisation of our findings.81 However, and importantly, rather than aiming at obtaining data from each individual study identified as eligible, IPD meta-analyses should gather a representative sample to test the main effects and the role of possible moderators, which we were able to do. Fourth, we did not have sufficient data to conduct meta-regressions exploring the moderating effect of pharmacological treatments for ADHD on our association of interest. Future analyses of individual studies including accurate measurements of the frequency and duration of pharmacological treatments are required. Fifth, we did not collect any information on sex/gender or ethnicity. This decision had been made because we anticipated that these variables would be considered sensitive information, as they can constitute identifying variables in small samples, and would thus prevent some cohorts from participating.

Overall, after gathering individual-participant data from more than 50 prospective cohorts, the present finding reveal that the diagnosis of ADHD in the younger children in a class is not more likely to be disconfirmed, over time, compared to the diagnosis of ADHD in the older children in the class. Because the mechanisms underlying the relative age effect on childhood ADHD are unknown, it is important that future studies explore whether this reflects the persistence of an appropriate or an inappropriate diagnostic label.

**SIMBA study group**

SIMBA study group is composed of Corentin J Gosling (Paris, France), Serge Caparos (Paris, France), Charlotte Pinabiaux (Paris, France), Guido Schwarzer (Freiburg, Germany), Gerta Rücker (Freiburg, Germany), Sharifah S Agha (Cardiff, United Kingdom), Hekmat Alrouh (Amsterdam, the Netherlands), Antony Ambler (London, United Kingdom), Peter Anderson (Melbourne, Australia), Ainara Andiarena (San Sebastián, Spain), L Eugene Arnold (Columbus, USA), Louise Arseneault (London, United Kingdom), Philip Asherson (London, United Kingdom), Leslie Babinski (Durham, USA), Vittoria Barbati (San Raffaele, Italy), Russel Barkley (Charleston, USA), Aluisio J D Barros (Pelotas, Brazil), Fernando Barros (Pelotas, Brazil), John E Bates (Bloomington, USA), Laura J Bell (Berkeley, USA), Carmen Berenguer (Valencia, Spain), Elsje van Bergen (Amsterdam, the Netherlands), Joseph Biederman† (Boston, USA), Boris Birmaher (Pittsburgh, USA), Tormod Bøe (Bergen, Norway), Dorret I Boomsma (Amsterdam, the Netherlands), Valerie C Brandt (Southampton, United Kingdom), Rodrigo A Bressan (São Paulo, Brazil), Karin Brocki (Uppsala, Sweden), Thomas R Broughton (Cardiff, United Kingdom), Sara J Bufferd (Louisville, USA), Regina Bussing (Gainesville, USA), Meng Cao (Newark, USA), Ariane Cartigny (Paris, France), Ana Miranda Casas (Valencia, Spain), Avshalom Caspi (Durham, USA), F Xavier Castellanos (New York, USA), Arthur Caye (Porto Alegre, Brazil), Luise Cederkvist (Copenhagen, Denmark), Stephan Collishaw (Cardiff, United Kingdom), William E Copeland (Burlington, USA), Sylvana M Cote (Montréal, Québec), William L Coventry (Armidale, Australia), Nanette M.M. Mol Debes (Herlev, Denmark), Hayley Denyer (London, United Kingdom), Kenneth A Dodge (Durham, USA), Hicran Dogru (New York, USA), Daryl Efron (Melbourne, Australia), Jami Eller (Urbana, USA), Marwa Abd Elmaksoud (Alexandria, Egypt), Eyup Sabri Ercan (Izmir, Turkey), Stephen V Faraone (Syracuse, USA), Michelle Fenesy (San Diego, USA), Mariana F Fernández (Granada, Spain), Ana Fernández-Somoano (Oviedo, Spain), Robert Findling (Virginia, USA), Eric Fombonne (Portland, USA), Ingrid N Fossum (Innlandet, Norway), Carmen Freire (Granada, Spain), Naomi P Friedman (Boulder, USA), Mary A Fristad (Columbus, Ohio), Cedric Galera (Bordeaux, France), Miguel Garcia-Argibay (Örebro, Sweden), Cynthia S Garvan (Florida, USA), Llúcia González (València, Spain), Annabeth P Groenman (Amsterdam, the Netherlands), Mònica Guxens (Barcelona, Spain), Jeffrey M Halperin (New York, USA), Randah R Hamadeh (Manama, Bahrain), Catharina A Hartman (Groningen, the Netherlands), Shirley Y Hill (Pittsburgh, USA), Stephen P Hinshaw (Berkeley, USA), Alison Hipwell (Pittsburgh, USA), Laura Hokkanen (Helsinki, Finland), Nathalie Holz (Nijmegen, the Netherlands), Carmen Íñiguez (València, Spain), Haitham A Jahrami (Manama, Bahrain), Pauline W Jansen (Rotterdam, The Netherlands), Lilja K Jónsdóttir (Uppsala, Sweden), Jordi Julvez (Reus, Spain), Anna Kaiser (Mannheim, Germany), Kate Keenan (Chicago, USA), Daniel N Klein (Stony Brook, USA), Rachel G Klein (New York, USA), Jonna Kuntsi (London, United Kingdom), Joshua Langfus (Chapel Hill, USA), Kate Langley (Cardiff, United Kingdom), Jennifer E Lansford (Durham, USA), Sally A Larsen (Armidale, Australia), Henrik Larsson (Örebro, Sweden), Evelyn Law (Singapore), Steve S Lee (Los Angeles, CA), Nerea Lertxundi (San Sebastián, Spain), Xiaobo Li (Newark, USA), Yueling Li (San Deigo, USA), Paul Lichtenstein (Stockholm, Sweden), Jianghong Liu (Philadelphia, USA), Astri J Lundervold (Bergen, Norway), Sebastian Lundström (Gothenburg, Sweden), David J Marks (New York, USA), Joanna Martin (Cardiff, United Kingdom), Gabrielle Masi (Pisa, Italy), Alicia Matijasevich (São Paulo, Brasil), Maria Melchior (Paris, France), Terrie E Moffitt (Durham, USA), Maximilian Monninger (Mannheim, Germany), Claire L Morrison (Boulder, USA), Melissa Mulraney (Melbourne, Australia), Pietro Muratori (Pisa, Italy), Phuc T Nguyen (Berkeley, USA), Jan M Nicholson (Melbourne, Australia), Merete Glenne Øie (Innlandet, Norway), Sarah O'Neill (New York, USA), Cliodhna O’Connor (Dublin, Ireland), Massimiliano Orri (Montreal, Canada), Pedro M Pan (São Paulo, Brazil), Leona Pascoe (Melbourne, Australia), Gregory S Pettit (Auburn, USA), Jolie Price (Bethesda, USA), Marisa Rebagliato (Madrid, Spain), Isolina Riaño-Galán (Madrid, Spain), Luis A Rohde (Porto Alegre, Brazil), Glenn I Roisman (Minneapolis, USA), Maria Rosa (Montreal, Canada), Jerrold F Rosenbaum (Boston, USA), Giovanni A Salum (Porto Alegre, Brazil), Sara Sammallahti (Helsinki, Finland), Ina S Santos (Pelotas, Brazil), Nella S Schiavone (Helsinki, Finland), Lorrie Schmid (Durham, USA), Emma Sciberras (Geelong, Australia), Philip Shaw (Bethesda, USA), Tim J Silk (Melbourne, Australia), Jeffry A Simpson (Minneapolis, USA), Erik W Skogli (Innlandet, Norway), Stephanie Stepp (Pittsburgh, USA), Katrine Strandberg-Larsen (Copenhagen, Denmark), Gustavo Sudre (Bethesda, USA), Jordi Sunyer (Barcelona, Spain), Mini Tandon (St.Louis, USA), Anita Thapar (Cardiff, United Kingdom), Phoebe Thomson (New York, USA), Lisa B Thorell (Stockholm, Sweden), Hannah Tinchant (Paris, France), Maties Torrent (Menorca, Spain), Luciana Tovo (Pelotas, Brazil), Gail Tripp (Okinawa, Japan), Obioha Ukoumunne (Exeter, United Kingdom), Stephanie HM Van Goozen (Cardiff, United Kingdom), Melissa Vos (Groningen, the Netherlands), Solène Wallez (Paris, France), Yufeng Wang (Peking, China), Franz G Westermaier (Wuppertal, Germany), Diana J Whalen (St. Louis, USA), Yuliya Yoncheva (New York, USA), Eric A Youngstrom (Chapel Hill, USA), Kapil Sayal (Nottingham, United Kingdom), Marco Solmi (Ottawa, Canada), Richard Delorme (Paris, France), and Samuele Cortese (Southampton, United Kingdom).

**Data sharing**All the raw data used that generated these results are publicly available (<https://simba-adhd.com/HTMLresults.html>).

**Funding**This study received no funding from any funding agency.

**Contributors**

CJG, SCa, CP, RD, SC conceptualised the study.

All authors contributed to data collection, data curation or data analysis of at least one study.

CJG, GS, GR and SC performed formal meta-analysis.

CJG and SC drafted the manuscript.

For each cohort, CJG and all the cohort team members had access to the raw data.

All authors reviewed and edited the manuscript.

**Conflicts of interest**

GSc declares payment or honoraria for manuscript writing from Springer and personal fees from Roche Pharma AG, Grenzach-Wyhlen, Germany as an external statistical consultant. GR declares payment or honoraria for manuscript writing from Springer and for editorial work from Wiley. LEA declares Grants or contracts from Supernus Pharmaceuticals, Roche/Genentech Phanaceuticals, Otsuka Pharmaceuticals, Axial, YAMO, and Maplight, Consulting fees from Pfizer, Parmaceuticals, Yamo, and CHADD, Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from APA Support for attending meetings and/or travel from CHADD, Participation on a Data Safety Monitoring Board or Advisory Board Otsuka and Roche/Genentech, NIMH and UCLA. PAs declares Royalties or licenses from Patoss, consulting fees from Janssen Cilag, and Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Janssen Cilag and Takeda. RBa declares Royalties or licenses from Guilford Publications, American Psychological Association, PESI.com, ContinuingEdCourses.net and, Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Astra Zeneca, Takeda, Medical College of Wisconsis and Ochsner Medical Center. JB declares grants or contracts from AACAP, Feinstein Institute for Medical Research, Genentech, Headspace Inc., NIDA, Pfizer Pharmaceuticals, Roche TCRC Inc., Sunovion Pharmaceuticals Inc., Takeda/Shire Pharmaceuticals Inc., Tris, NIH, FDA, Royalties or licenses from Biomarin, Bracket Global, Cogstate, Ingenix, Medavent Prophase, Shire/Takeda, Sunovion, and Theravance, royalties from a copyrighted rating scale used for ADHD diagnoses; these royalties were paid to the Department of Psychiatry at MGH, Consulting fees from Cowen Healthcare Investments, Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from UC Davis MGH Psychiatry Academy; Medlearning Inc.; NYU; AACAP; American Psychiatric Nurses Association; BIAL - Portela & C. S.A. (Portugal); Medscape Education Tris; Institute of Integrated Sciences and patents planned, issued or pending (US Patent (#14/027,676) for a non-stimulant treatment for ADHD US Patent (#10,245,271 B2) a on a treatment of impaired cognitive flexibility patent pending (#61/233,686) on a method to prevent stimulant abuse). BB declares and Grants or contracts NIMH, and royalties or licenses from UpToDate. RAB declares consulting fees, payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events and support for attending meetings and/or travel from Janssen. ACay declares consulting fees from Knight Therapeutics. WLC declares grants from the ARC (DP120102414 and DP150102441). HDo declares Grants or contracts from the Scientific and Technological Research Council Of Turkey. RF declares Grants or contracts from Abbvie, Arbor, Lundbeck, Neurim, NIH, PaxMedica, PCORI, Pfizer, Sunovion, Supernus Pharmaceuticals, Takeda, Viatris, consulting fees from Acadia, Adamas, Afecta, Ajna, Akili, Alkermes, Am Acad Child Adol Psychiatry, Axsome, Bioexcel, Idorsia, Intracellular Therapies, Iqvia, Medavante Prophase, MJH Life Sciences, NIH, Novartis, Otsuka, Oxford University Press, PaxMedica, Physicians’ Postgraduate Press, QBiomed, Radius, Receptor Life Sciences, Signant Health, Supernus Pharmaceuticals, Syneos, Tris, and royalties from American Psychiatric Press, Sage. MAF declares research support from Janssen, travel and editorial support from the Society of Clinical Child and Adolescent Psychology, and royalties from American Psychiatric Publishing, Guilford Press, and JK Seminars. JMH declares support from NIMH (grants #R01 MH046448, R01 MH060698, # R01 MH068286). AEH declares grants from NIH. KK declares support from NIMH (#R01 MH046448, R01 MH060698, # R01 MH068286). JK has given talks at educational events sponsored by Medice; all funds are received by King’s College London and used for studies of attention-deficit/hyperactivity disorder (ADHD). JLa declares grants from NIH (NIH R01 MH123443). KL declares support from Wellcome Trust and MRC, and declares Participation on a Data Safety Monitoring Board or Advisory Board from Medice Scientific advisory board. HL declares grants from Shire/Takeda, and Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Shire/takeda, Medici and Evolan. XL declares grants from NIMH (R03 MH109791, R15 MH117368). GM declares support from Italian Ministry of Health, Angelini, Laborest, Humana, Consulting fees from Angelini, and payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Lundbeck and Angelini. PM declares support from IRCCS Fondazione Stella Maris. SO declares grants from NIMH (R34MH122219). PMP declares Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Sandoz, Daiichi Sankyo, Eurofarma, Abbot, Libbs, Instituto Israelita de Pesquisa e Ensino Albert Einstein, Instituto D'Or de Pesquisa e Ensino. LAR declares Grants or contracts from Medice, Novartis/Sandoz, Pzifer/Upjohn, Shire/Takeda, royalties or licences from Oxford Press ArtMed, consulting fees from Abbott, Aché, Bial, Medice, Novartis/Sandoz, Pzifer/Upjohn Shire/Takeda, Abdi Ibrahim, payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Abbott, Aché, Bial, Medice Novartis/Sandoz, Pzifer/Upjohn Shire/Takeda, Abdi Ibrahim, participation on a Data Safety Monitoring Board or Advisory Board from Abbott, Aché, Bial, Medice Novartis/Sandoz, Pzifer/Upjohn Shire/Takeda, Abdi Ibrahim, and Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid from IACAPAP. ES declares royalties or licenses from Elsevier and honoraria from Springer. MTa declares grants or contracts from NICHD, and royalties from Author House. AT declares Grants or contracts from Wellcome Trust (clinical patient sample) and Wolfson Foundation, Royalties or licenses from Wiley, payment or honoraria for lectures, presentations, speakers bureaus, or educational events, support for attending meetings and/or travel all of which go to Cardiff University. ADHD Foundation Exec Board (unpaid), Leadership or fiduciary role in other board, society, committee or advocacy group, from Ministerial Advisory Group for Neurodevelopmental disorders (Welsh Govt) (unpaid). EAY declares Grants or contracts from NIMH, Royalties from American Psychological Association and Guilford Press, Consulting fees from Signant Health , Payment for expert testimony from Public Defender, State of Ohio, Participation on a Data Safety Monitoring Board or Advisory Board from NIMH, and leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid from Helping Give Away Psychological Science. MS declares Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Angelini, Lundbeck and Otsuka, and Participation on a Data Safety Monitoring Board or Advisory Board from Otsuka and Abbvie. SCor declares Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from ACAMH, BAP, and CADDRA.All other authors have no conflict of interest.

**Acknowledgements**

ADSAT cohort: This research was supported by two Australian Research Council Discovery Project Grants: DP 120102414 (2012-2014) and DP 150102441 (2015-2018). Access to the sample was facilitated by Twins Research Australia, a national resource supported by a Centre of Research Excellence Grant (ID: 1079102), from the National Health and Medical Research Council.

ADSU cohort: Grant RO1MH57399, NIH, USA

ALSPAC cohort: The Avon Longitudinal Study of Parents and Children (ALSPAC) is a prospective pregnancy cohort based in the United Kingdom. Pregnant women resident in Avon, UK with expected dates of delivery between 1st April 1991 and 31st December 1992 were invited to take part in the study. An initial number of 14,541 women returned questionnaire or attended a clinic subsequently. Of these pregnancies there were 13,988 children who were alive at 1 year of age. The study website contains details of all the available through a fully searchable data dictionary and variable search tool (http://www.bristol.ac.uk/alspac/researchers/our-data/). Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Consent for biological samples has been collected in accordance with the Human Tissue Act (2004). Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time.

The UK Medical Research Council and Wellcome (Grant ref: 217065/Z/19/Z) and the University of Bristol provide core support for ALSPAC. A comprehensive list of grants funding is available on the ALSPAC website (http://www.bristol.ac.uk/alspac/external/documents/grant-acknowledgements.pdf).

BGALS cohort: This research was supported by funding from National Institute of Mental Health Grant R01 45064 (to Stephen P. Hinshaw), USA.

BHRC cohort: This work is supported by the National Institute of Developmental Psychiatry for Children and Adolescents, a science and technology institute funded by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq; National Council for Scientific and Technological Development; grant number 573974/2008-0). This study was also financed by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—Brasil (CAPES)—Finance Code 001 and by National Institute of Mental Health (NIMH), grant number RO1 MH120482-01, subaward nº 576811.The Brazilian High Risk Cohort Study was supported with grants from the National Institute of Development Psychiatric for Children and Adolescent (INPD). Grant: Fapesp 2014/50917-0 - CNPq 465550/2014-2 and the National Center for Research and Innovation in Mental Health (CISM) - Grant Fapesp 2021/12901-9 and Banco Industrial do Brasil S/A.

CAP cohort: The Children’s Attention Project was funded by the National Health and Medical Research Council of Australia (NHMRC) Project grants 1008522 and 1065895, and a grant from the Collier Foundation.

CATSS cohort: We acknowledge The Swedish Twin Registry for access to data. The Swedish Twin Registry is managed by Karolinska Institutet and receives funding through the Swedish Research Council under the grant no 2017-00641

CDP cohort: The Child Development Project has been funded by grants MH56961, MH57024, and MH57095 from the National Institute of Mental Health, HD30572 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and DA016903 from the National Institute on Drug Abuse.

CJCCS cohort: Funding supported by the National Institutes of Health in the US: R01-ES-018858, K02-ES-019878, K01-ES015877, and P30-ES013508.

CLASS cohort: Funding from: UK Medical Research Council (G1000632), Wellcome Trust (079711), Action Medical Research and The Baily Thomas Foundation.

NTR cohort: Genotype/phenotype database for behavior genetic and genetic epidemiological studies (ZonMw Middelgroot 911-09-032); “Why some children thrive” (OCW\_Gravity program –NWO-024.001.003), The impact of parental genes on offspring health: nurture via nature (NWO-Hestia : VidW.1154.19.013); Netherlands Twin Registry Repository: researching the interplay between genome and environment (NWO-Groot 480-15-001/674); Genetics of Mental Illness (ERC Advanced, 230374)

DNBC cohort: The Danish National Birth Cohort was established with a significant grant from the Danish National Research Foundation. Additional support was obtained from the Danish Regional Committees, the Pharmacy Foundation, the Egmont Foundation, the March of Dimes Birth Defects Foundation, the Health Foundation and other minor grants. The DNBC Biobank has been supported by the Novo Nordisk Foundation and the Lundbeck Foundation. Follow-up of mothers and children have been supported by the Danish Medical Research Council (SSVF 0646, 271-08-0839/06-066023, O602-01042B, 0602-02738B), the Lundbeck Foundation (195/04, R100-A9193), The Innovation Fund Denmark 0603-00294B (09-067124), the Nordea Foundation (02-2013-2014), Aarhus Ideas (AU R9-A959-13-S804), University of Copenhagen Strategic Grant (IFSV 2012), and the Danish Council for Independent Research (DFF – 4183-00594 and DFF - 4183-00152).

ERICA: This project was funded by a grant from the Swedish Council for Health, Working Life and Welfare (Forte), 2020-00630

Fenesy cohort: National Institutes of Health (grant number R03AA020186 to Steve S. Lee)

GENR cohort: The general design of the Generation R Study is supported by the Erasmus Medical Center-Rotterdam, the Erasmus University Rotterdam, the Netherlands Organization for Health Research and Development, the Netherlands Organization for Scientific Research, and the Ministry of Health, Welfare and Sport, the Municipal Health Service Rotterdam area, and the Stichting Trombosedienst and Artsenlaboratorium Rijnmond.

GSMS cohort: The Great Smoky Mountains Study has been funded by various NIH Insitutes over the past 25 years.

IMAGE-UK/SEFOS cohort: This project was supported by generous grants from Action Medical Research and the Peter Sowerby Charitable Foundation (grant reference GN1777). Initial sample recruitment of the ADHD sample was supported by NIMH Grant R01MH062873 to SV Faraone; the recruitment of the control sample and initial cognitive assessments of ADHD and control groups were supported by UK Medical Research Council grant G0300189 to J Kuntsi.

INMA cohort: This study was funded by grants from Instituto de Salud Carlos III (Red INMA G03/176; CB06/02/0041; PI041436; PI04/2018; PI081151 incl. FEDER funds; PI09/02311 incl. FEDER funds; PI12/01890 incl. FEDER funds; CP13/00054 incl. FEDER funds; PI13/02429 incl. FEDER funds; PI15/00118 incl. FEDER funds; CP16/00128 incl. FEDER funds; PI16/00118 incl. FEDER funds; PI16/00261 incl. FEDER funds; PI17/01340 incl. FEDER funds; PI18/00547 incl. FEDER funds; PI18/00909 incl. FEDER funds), CIBERESP, Fundación Cajastur, Universidad de Oviedo, Generalitat de Catalunya-CIRIT 1999SGR 00241, Generalitat de Catalunya-AGAUR (2009 SGR 501, 2014 SGR 822), Fundació La marató de TV3 (090430), Spanish Ministry of Economy and Competitiveness (SAF2012-32991 incl. FEDER funds), Agence Nationale de Securite Sanitaire de l’Alimentation de l’Environnement et du Travail (1262C0010; EST-2016 RF-21), EU Commission (261357, 308333, 603794 and 634453). Margarita Salas Grant MS21-125 and co-funded by European Union- Next Generation EU. We acknowledge support from the grant CEX2018-000806-S funded by MCIN/AEI/10.13039/501100011033, and support from the Generalitat de Catalunya through the CERCA Program.

LAMS Cohort: The Longitudinal Assessment of Manic Symptoms (LAMS) study was supported by NIH grants R01MH073967, R01MH073801, R01MH73953, and R01MH073816. The LAMS Group includes Eric A. Youngstrom, Sarah M. Horwitz, Mary A. Fristad, L. Eugene Arnold, Boris Birmaher, and Robert L. Findling, as well as principal investigators for performance sites and coinvestigators on the Steering and Publication Committee for the LAMS Consortium.

LINEUP cohort: Innlandet Hospital Trust: grant numbers 150663, 150610, 150624, 150616, 150186. South-Eastern Norway Regional Health Authority: grant number: 150663. The Norwegian Centre of Expertise for Neurodevelopmental Disorders and Hypersomnias, Department of Rare Disorders and Disabilities, Oslo University Hospital grant number 150616, 150182.

LSUY cohort: Funded by grants R01MH046448 and R01MH060698 (PI: J. M. Halperin), NIH, USA

Masi cohort: This research is supported by a grant from the IRCCS Fondazione Stella Maris (Ricerca Corrente, and by the ‘5\*1000’ voluntary contributions, Italian Ministry of Health).

MPHC cohort: This research was supported by grants from the National Institute of Mental Health (NIMH) to Byron Egeland, L. Alan Sroufe, and W. Andrew Collins (R01-MH40864) and to Jeffry A. Simpson (R01- MH49599); a National Institute for Child Health and Human Development grant to W. Andrew Collins, Byron Egeland, and L. Alan Sroufe (R01-HD054850); a National Institute on Aging (NIA) grant to Jeffry A. Simpson (R01-AG039453).

NEUROIMAGE cohort: Funding support for the IMAGE project was provided by National Institutes of Health (NIH) grants R01MH62873 and R01MH081803 (to Stephen V. Faraone). The follow-up and extension studies of the NeuroIMAGE project were supported by a Netherlands Organization for Scientific Research (NWO) Large Investment Grant 1750102007010 and NWO Brain & Cognition an Integrative Approach grant (433-09-242) (to Jan K. Buitelaar), and grants from Radboud University Nijmegen Medical Center, University Medical Center Groningen and Accare, VU University Amsterdam, and by the ECNP Network ADHD across the Lifespan.

NYS cohort: Grant R01DA016979, NIH, USA; Grant R01MH018579, NIH, USA; The Scientific and Technological Research Council Of Turkey (TUBİTAK) grant # 1059B192101153

PELOTAS cohort: The 2004 Pelotas Birth Cohort was conducted by Postgraduate Program in Epidemiology at Universidade Federal de Pelotas, with the collaboration of the Brazilian Public Health Association (ABRASCO). Supported by the Wellcome Trust from 2009 to 2013, the World Health Organization, National Support Program for Centers of Excellence (PRONEX), Brazilian National Research Council (CNPq), Brazilian Ministry of Health, and Children’s Pastorate. The 1993 Pelotas Birth Cohort was conducted by the Postgraduate Program in Epidemiology at Universidade Federal de Pelotas with the collaboration of the Brazilian Public Health Association (ABRASCO). From 2004 to 2013, the Wellcome Trust supported the 1993 birth cohort study. The European Union, National Support Program for Centers of Excellence (PRONEX), the Brazilian National Research Council (CNPq), and the Brazilian Ministry of Health supported previous phases of the study. The 22-year follow-up was supported by the Science and Technology Department/Brazilian Ministry of Health, with resources transferred through the Brazilian National Council for Scientific and Technological Development (CNPq), grant 400943/2013-1

PDS cohort: Funded by grants R01 5R01MH090786; K23 MH118426

PGS cohort: The Pittsburgh Girls Study was supported by the National Institute of Health (MH056630, Loeber)

QCPP cohort: The project was supported by the National Institute of Mental Health (R01 MH68286; PI: J. M. Halperin)

QLSCD cohort: The Québec Longitudinal Study of Child Development was supported by funding from the ministère de la Santé et des Services sociaux, le ministère de la Famille, le ministère de l’Éducation et de l’Enseignement supérieur, the Lucie and André Chagnon Foundation, the Institut de recherche Robert-Sauvé en santé et en sécurité du travail, the Research Centre of the Sainte-Justine University Hospital, the ministère du Travail, de l’Emploi et de la Solidarité sociale and the Institut de la statistique du Québec. Additional funding was received by the Fonds de Recherche du Québec - Santé (FRQS), the Fonds de Recherche du Québec - Société et Culture (FRQSC), the Social Science and Humanities Research Council of Canada (SSHRC), the Canadian Institutes of Health Research (CIHR). Data collection is conducted by the Institut de la statistique du Québec (ISQ).

SAGE cohort: Was supported by funding from the Wellcome Trust (grant no. 079711), Medical Research Council Centre (grant no. MR/L010305/1), Health and Care Research Wales (grant no. 514032)

SBTS cohort: This study was supported by the National Institute of Mental Health (R01 MH069942; PI: Klein)

TEMPO cohort: The TEMPO cohort received funding from the French National Research Agency (ANR) including the Flash COVID-19 funding scheme; the French Institute for Public Health Research-IReSP (TGIR Cohortes); the French Inter-departmental Mission for the Fight against Drugs and Drug Addiction (MILDeCA); the French Institute of Cancer (INCa); and the Pfizer Foundation.

Uppsala cohort: The EFFECT study - A longitudinal study of Dit

Funding support for the IMAGE project was provided by National Institutes of Health (NIH) grants R01MH62873 and R01MH081803 (to Stephen V. Faraone). The second follow-up study of the NeuroIMAGE project was supported by a Netherlands Organization for Scientific Research (NWO) Large Investment Grant 1750102007010 and NWO Brain & Cognition an Integrative Approach grant (433-09-242) (to Jan K. Buitelaar), and financial support from Radboud University Nijmegen Medical Center, University Medical Center Groningen and Accare, and VU University Amsterdam.

VAL-IMAGE: The follow-up and extension studies of the Val- IMAGE project was supported by Generalitat Valenciana Grant AICO/2018/198

ViBES cohort: Australia’s National Health & Medical Research Council (Project grants 237117, 491209, 1066555; Centre for Research Excellence in Newborn Medicine 1153176; Senior Research Fellowship 1081288; Leadership Fellowship 1176077) and the Victorian Government’s Operational Infrastructure Support Program. Centre for Research Excellence in Newborn Medicine 1153176 and the Victorian Government’s Operational Infrastructure Support Program

**REFERENCES**

1. Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. Am J Psychiatry. 2007;164(6):942-948. doi:10.1176/ajp.2007.164.6.942

2. Thomas R, Sanders S, Doust J, Beller E, Glasziou P. Prevalence of attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. Pediatrics. 2015;135(4):e994-e1001. doi:10.1542/peds.2014-3482

3.Song P, Zha M, Yang Q, Zhang Y, Li X, Rudan I. The prevalence of adult attention-deficit hyperactivity disorder: A global systematic review and meta-analysis. J Glob Health. 2021;11:04009. Published 2021 Feb 11. doi:10.7189/jogh.11.04009

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

5. Whitely M, Raven M, Timimi S, et al. Attention deficit hyperactivity disorder late birthdate effect common in both high and low prescribing international jurisdictions: a systematic review. J Child Psychol Psychiatry. 2019;60(4):380-391. doi:10.1111/jcpp.12991

6. Holland J, Sayal K. Relative age and ADHD symptoms, diagnosis and medication: a systematic review. Eur Child Adolesc Psychiatry. 2019 Nov;28(11):1417-1429. doi: 10.1007/s00787-018-1229-6.

7.Caye A, Petresco S, de Barros AJD, et al. Relative Age and Attention-Deficit/Hyperactivity Disorder: Data From Three Epidemiological Cohorts and a Meta-analysis. J Am Acad Child Adolesc Psychiatry. 2020;59(8):990-997. doi:10.1016/j.jaac.2019.07.939

8. Layton TJ, Barnett ML, Hicks TR, Jena AB. Attention Deficit-Hyperactivity Disorder and Month of School Enrollment. N Engl J Med. 2018;379(22):2122-2130. doi:10.1056/NEJMoa1806828

9.Morrow RL, Garland EJ, Wright JM, Maclure M, Taylor S, Dormuth CR. Influence of relative age on diagnosis and treatment of attention-deficit/hyperactivity disorder in children. CMAJ. 2012;184(7):755-762. doi:10.1503/cmaj.111619

10.Halldner L, Tillander A, Lundholm C, et al. Relative immaturity and ADHD: findings from nationwide registers, parent- and self-reports. J Child Psychol Psychiatry. 2014;55(8):897-904. doi:10.1111/jcpp.12229

11.Gosling CJ, Pinabiaux C, Caparos S, Delorme R, Cortese S. Influence of the month of birth on persistence of ADHD in prospective studies: protocol for an individual patient data meta-analysis. BMJ Open. 2020;10(11):e040952. doi:10.1136/bmjopen-2020-040952

12. Stewart LA, Clarke M, Rovers M, Riley RD, Simmonds M, Stewart G, Tierney JF; PRISMA-IPD Development Group. Preferred Reporting Items for Systematic Review and Meta-Analyses of individual participant data: the PRISMA-IPD Statement. JAMA. 2015;313(16):1657-1665.

13. Tierney JF, Stewart LA, Clarke M. Chapter 26: Individual participant data. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from www.training.cochrane.org/handbook.

14. Martel MM, Schimmack U, Nikolas M, Nigg JT. Integration of symptom ratings from multiple informants in ADHD diagnosis: a psychometric model with clinical utility. Psychol Assess. 2015;27(3):1060-1071. doi:10.1037/pas0000088

15.Sayal, K., Chudal, R., Hinkka-Yli-Salomäki, S., Joelsson, P., & Sourander, A. Relative age within the school year and diagnosis of attention-deficit hyperactivity disorder: a nationwide population-based study. The lancet. Psychiatry; 2017, 4(11), 868–875. [https://doi.org/10.1016/S2215-0366(17)30394-2](https://doi.org/10.1016/S2215-0366%2817%2930394-2)

16.Stang A. (). Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. European journal of epidemiology. 2010; 25(9), 603–605. https://doi.org/10.1007/s10654-010-9491-z

17.R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

18. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial, Evidence-Based Mental Health. 2019;22: 153-160.

19. Lumley T. (2020) "survey: analysis of complex survey samples". R package version 4.0.

20. Lumley T. Analysis of complex survey samples. Journal of Statistical Software. 2004;9(1): 1-19

21. Lumley T. (2010) Complex Surveys: A Guide to Analysis Using R. John Wiley and Sons.

22.Muehlenweg, A., & Puhani, P. A. Persistence of the school entry age effect in a system of flexible tracking. Journal of Human Resources. 2010; 45(2), 407-438.

23. Riglin L, Collishaw S, Thapar AK, et al. Association of Genetic Risk Variants With Attention-Deficit/Hyperactivity Disorder Trajectories in the General Population. JAMA Psychiatry. 2016;73(12):1285-1292. doi:10.1001/jamapsychiatry.2016.2817

24. Langley K, Fowler TA, Grady DL, et al. Molecular genetic contribution to the developmental course of attention-deficit hyperactivity disorder. Eur Child Adolesc Psychiatry. 2009;18(1):26-32. doi:10.1007/s00787-008-0698-4

25. Biederman, J., Faraone, S. V., Keenan, K., Benjamin, J., Krifcher, B., Moore, C., Sprich-Buckminster, S., Ugaglia, K., Jellinek, M. S., Steingard, R., Spencer, T., Norman, D., Kolodny, R., Kraus, I., Perrin, J., Keller, M. B. & Tsuang, M. T. (1992). Further evidence for family-genetic risk factors in attention deficit hyperactivity disorder. Patterns of comorbidity in probands and relatives in psychiatrically and pediatrically referred samples. Arch Gen Psychiatry 49, 728-38.

26. Biederman, J., Faraone, S. V., Mick, E., Williamson, S., Wilens, T. E., Spencer, T. J., Weber, W., Jetton, J., Kraus, I., Pert, J. & Zallen, B. (1999). Clinical correlates of ADHD in females: findings from a large group of girls ascertained from pediatric and psychiatric referral sources. J Am Acad Child Adolesc Psychiatry 38, 966-75.

27. Li Y, Baker-Ericzen M, Ji N, et al. Do SNPs of DRD4 gene predict adult persistence of ADHD in a Chinese sample?. Psychiatry Res. 2013;205(1-2):143-150. doi:10.1016/j.psychres.2012.08.016

28. Brandt V, Patalay P, Kerner Auch Koerner J. Predicting ADHD symptoms and diagnosis at age 14 from objective activity levels at age 7 in a large UK cohort. Eur Child Adolesc Psychiatry. 2021;30(6):877-884. doi:10.1007/s00787-020-01566-9

29. Mulraney M, Giallo R, Efron D, Brown S, Nicholson JM, Sciberras E. Maternal postnatal mental health and offspring symptoms of ADHD at 8-9 years: pathways via parenting behavior. Eur Child Adolesc Psychiatry. 2019;28(7):923-932. doi:10.1007/s00787-018-1254-5

30. Cheung CH, Rijdijk F, McLoughlin G, Faraone SV, Asherson P, Kuntsi J. Childhood predictors of adolescent and young adult outcome in ADHD. J Psychiatr Res. 2015;62:92-100. doi:10.1016/j.jpsychires.2015.01.011

31. Agnew-Blais JC, Polanczyk GV, Danese A, Wertz J, Moffitt TE, Arseneault L. Are changes in ADHD course reflected in differences in IQ and executive functioning from childhood to young adulthood?. Psychol Med. 2020;50(16):2799-2808. doi:10.1017/S0033291719003015

32. Heiervang, E., Stormark, K. M., Lundervold, A. J., Heimann, M., Goodman, R., Posserud, M., Ullebø, A. K., Plessen, K. J., Bjelland, I., Lie, S. A., & Gillberg, C. (2007). Psychiatric disorders in Norwegian 8- to 10-year-olds. J. Am. Acad. Child Adolesc. Psychiatry, 46(4), 438–447. https://doi.org/10/d8kr3v

33. Cortese S, Imperati D, Zhou J, et al. White matter alterations at 33-year follow-up in adults with childhood attention-deficit/hyperactivity disorder. Biol Psychiatry. 2013;74(8):591-598. doi:10.1016/j.biopsych.2013.02.025

34. Biederman J, Petty C, Hirshfeld-Becker DR, et al. A controlled longitudinal 5-year follow-up study of children at high and low risk for panic disorder and major depression. Psychol Med. 2006;36(8):1141-1152. doi:10.1017/S0033291706007781

35. van Goozen SHM, Langley K, Northover C, et al. Identifying mechanisms that underlie links between COMT genotype and aggression in male adolescents with ADHD J Child Psychol Psychiatry 2016;57(4):472-480. doi: 10.1111/jcpp.12464.

36. Geller B, Tillman R. Prepubertal and early adolescent bipolar I disorder: review of diagnostic validation by Robins and Guze criteria. J Clin Psychiatry. 2005;66 Suppl 7:21-28.

37. Li L, Li Y, McDonald C, Liu J. Parent-Reported Mild Head Injury History in Children: Long-Term Effects on Attention-Deficit Hyperactivity Disorder. Glob Pediatr Health. 2018;5:2333794X18756465. Published 2018 Feb 27. doi:10.1177/2333794X18756465

38. Halperin JM, Rucklidge JJ, Powers RL, Miller CJ, Newcorn JH. Childhood CBCL bipolar profile and adolescent/young adult personality disorders: a 9-year follow-up. J Affect Disord. 2011;130(1-2):155-161. doi:10.1016/j.jad.2010.10.019

39. Bell L, Kellison I, Garvan CW, Bussing R. Relationships between child-reported activity level and task orientation and parental attention-deficit/hyperactivity disorder symptom ratings. J Dev Behav Pediatr. 2010;31(3):233-237. doi:10.1097/DBP.0b013e3181d5a328

40. Hinshaw SP, Owens EB, Sami N, Fargeon S. Prospective follow-up of girls with attention-deficit/hyperactivity disorder into adolescence: Evidence for continuing cross-domain impairment. J Consult Clin Psychol. 2006;74(3):489-499. doi:10.1037/0022-006X.74.3.489

41. Lorber MF, Egeland B. Infancy parenting and externalizing psychopathology from childhood through adulthood: developmental trends. Dev Psychol. 2009;45(4):909-912. doi:10.1037/a0015675

42. Barkley RA, Fischer M. The unique contribution of emotional impulsiveness to impairment in major life activities in hyperactive children as adults. J Am Acad Child Adolesc Psychiatry. 2010;49(5):503-513. doi:10.1097/00004583-201005000-00011

43. Santos IS, Barros AJD, Matijasevich A, Domingues MR, Barros FC, Victora CG. Cohort Profile: The 2004 Pelotas (Brazil) Birth Cohort Study. International Journal of Epidemiology 2011; 40(6):1461–1468

44. Fenesy MC, Teh SE, Lee SS. Negative Parenting Moderates the Prospective Association of ADHD Symptoms and Youth Social Problems. J Abnorm Child Psychol. 2019;47(10):1583-1597. doi:10.1007/s10802-019-00542-5

45. Koisaari T, Michelsson K, Holopainen JM, et al. Traffic and Criminal Behavior of Adults with Attention Deficit-Hyperactivity with a Prospective Follow-Up from Birth to the Age of 40 Years. Traffic Inj Prev. 2015;16(8):824-830. doi:10.1080/15389588.2015.1029068

46. Galéra C, Bouvard MP, Lagarde E, et al. Childhood attention problems and socioeconomic status in adulthood: 18-year follow-up. Br J Psychiatry. 2012;201(1):20-25. doi:10.1192/bjp.bp.111.102491

47. Ercan ES, Kandulu R, Uslu E, et al. Prevalence and diagnostic stability of ADHD and ODD in Turkish children: a 4-year longitudinal study. Child Adolesc Psychiatry Ment Health. 2013;7(1):30. Published 2013 Aug 7. doi:10.1186/1753-2000-7-30

48. López-Vicente M, Sunyer J, Lertxundi N, et al. Maternal circulating Vitamin D3 levels during pregnancy and behaviour across childhood. Sci Rep. 2019;9(1):14792. Published 2019 Oct 15. doi:10.1038/s41598-019-51325-3

49. Masi G, Pisano S, Milone A, Muratori P. Child behavior checklist dysregulation profile in children with disruptive behavior disorders: A longitudinal study. J Affect Disord. 2015;186:249-253. doi:10.1016/j.jad.2015.05.069

50. Sciberras E, Efron D, Schilpzand EJ, et al. The Children's Attention Project: a community-based longitudinal study of children with ADHD and non-ADHD controls. BMC Psychiatry. 2013;13:18. Published 2013 Jan 10. doi:10.1186/1471-244X-13-18

51. Sjöwall D, Thorell LB. A critical appraisal of the role of neuropsychological deficits in preschool ADHD. Child Neuropsychol. 2019;25(1):60-80. doi:10.1080/09297049.2018.1447096

52. Groth C, Mol Debes N, Rask CU, Lange T, Skov L. Course of Tourette Syndrome and Comorbidities in a Large Prospective Clinical Study. J Am Acad Child Adolesc Psychiatry. 2017;56(4):304-312. doi:10.1016/j.jaac.2017.01.010

53. Copeland WE, Shanahan L, Costello EJ, Angold A. Childhood and adolescent psychiatric disorders as predictors of young adult disorders. Arch Gen Psychiatry. 2009;66(7):764-772. doi:10.1001/archgenpsychiatry.2009.85

54. Olsen J, Melbye M, Olsen SF, et al. The Danish National Birth Cohort--its background, structure and aim. Scand J Public Health. 2001;29(4):300-307. doi:10.1177/14034948010290040201

55. Brocki KC, Forslund T, Frick M, Bohlin G. Do Individual Differences in Early Affective and Cognitive Self-Regulation Predict Developmental Change in ADHD Symptoms From Preschool to Adolescence?. J Atten Disord. 2017;23(13):1656-1666. Published 2017 Feb 1. doi:10.1177/1087054717693372

56. Roselló B, Berenguer C, Baixauli I, Mira Á, Martinez-Raga J, Miranda A. Empirical examination of executive functioning, ADHD associated behaviors, and functional impairments in adults with persistent ADHD, remittent ADHD, and without ADHD. BMC Psychiatry. 2020;20(1):134. Published 2020 Mar 24. doi:10.1186/s12888-020-02542-y

57. Yates R, Treyvaud K, Doyle LW, et al. Rates and Stability of Mental Health Disorders in Children Born Very Preterm at 7 and 13 Years. Pediatrics. 2020;145(5):e20192699. doi:10.1542/peds.2019-2699

58. Millenet S, Laucht M, Hohm E, et al. Sex-specific trajectories of ADHD symptoms from adolescence to young adulthood. Eur Child Adolesc Psychiatry. 2018;27(8):1067-1075. doi:10.1007/s00787-018-1129-9

59. Fossum IN, Andersen PN, Øie MG, Skogli EW. Development of executive functioning from childhood to young adulthood in autism spectrum disorder and attention-deficit/hyperactivity disorder: A 10-year longitudinal study. Neuropsychology. 2021;35(8):809-821. doi:10.1037/neu0000768

60. Salum GA, Gadelha A, Pan PM, et al. High risk cohort study for psychiatric disorders in childhood: rationale, design, methods and preliminary results. Int J Methods Psychiatr Res. 2015;24(1):58-73. doi:10.1002/mpr.1459

61. Norén Selinus E, Molero Y, Lichtenstein P, et al. Subthreshold and threshold attention deficit hyperactivity disorder symptoms in childhood: psychosocial outcomes in adolescence in boys and girls. Acta Psychiatr Scand. 2016;134(6):533-545. doi:10.1111/acps.12655

62. Larsen SA, Little CW, Grasby K, Byrne B, Olson RK, Coventry WL. The Academic Development Study of Australian Twins (ADSAT): Research aims and design. Twin Res Hum Genet. 2020;23(3):165-173. doi:10.1017/thg.2020.49

63. Plourde V, Boivin M, Forget-Dubois N, et al. Phenotypic and genetic associations between reading comprehension, decoding skills, and ADHD dimensions: evidence from two population-based studies. J Child Psychol Psychiatry. 2015;56(10):1074-1082. doi:10.1111/jcpp.12394

64. Kan KJ, Dolan CV, Nivard MG, et al. Genetic and environmental stability in attention problems across the lifespan: evidence from the Netherlands twin register. J Am Acad Child Adolesc Psychiatry. 2013;52(1):12-25. doi:10.1016/j.jaac.2012.10.009

65. Mian A, Jansen PW, Nguyen AN, Bowling A, Renders CM, Voortman T. Children's Attention-Deficit/Hyperactivity Disorder Symptoms Predict Lower Diet Quality but Not Vice Versa: Results from Bidirectional Analyses in a Population-Based Cohort. J Nutr. 2019;149(4):642-648. doi:10.1093/jn/nxy273

66. Keenan K, Hipwell AE, Chung T, Stepp S, Stouthamer-Loeber M, Loeber R, McTigue K. The Pittsburgh Girls Study: overview and initial findings. J Clin Child Adolesc Psychol. 2010;39(4):506-21. PubMed PMID: 20589562; PMCID: PMC2946599

67. Robinson, T., & Tripp, G. (2013). Neuropsychological functioning in children with ADHD: Symptom persistence is linked to poorer performance on measures of executive and nonexecutive function. Japanese Psychological Research, 55(2), 154-167.

68. Al Ansari A, Hamadeh RR, Jahrami H, Haji EA. Outcomes of children with attention deficit/hyperactivity disorder: global functioning and symptoms persistence. East Mediterr Health J. 2017;23(9):589-593. Published 2017 Nov 19. doi:10.26719/2017.23.9.589

69. Dodge KA, Bates JE, Pettit GS. Mechanisms in the cycle of violence. Science. 1990;250(4988):1678-1683. doi:10.1126/science.2270481

70. Whalen DJ, Dixon-Gordon K, Belden AC, Barch D, Luby JL. Correlates and Consequences of Suicidal Cognitions and Behaviors in Children Ages 3 to 7 Years. J Am Acad Child Adolesc Psychiatry. 2015;54(11):926-37.e2. doi:10.1016/j.jaac.2015.08.009

71. Arnold LE, Demeter C, Mount K, et al. Pediatric bipolar spectrum disorder and ADHD: comparison and comorbidity in the LAMS clinical sample. Bipolar Disord. 2011;13(5-6):509-521. doi:10.1111/j.1399-5618.2011.00948.x

72. Law EC, Sideridis GD, Prock LA, Sheridan MA. Attention-deficit/hyperactivity disorder in young children: predictors of diagnostic stability. Pediatrics. 2014;133(4):659-667. doi:10.1542/peds.2013-3433

73. Karlsberg Bennett J, O'Neill S, Rajendran K, Halperin JM. Do Preschoolers' Neuropsychological Functioning and Hyperactivity/Inattention Predict Social Functioning Trajectories Through Childhood?. J Pediatr Psychol. 2020;45(7):793-802. doi:10.1093/jpepsy/jsaa053

74. Hill SY, Tessner KD, McDermott MD. Psychopathology in offspring from families of alcohol dependent female probands: a prospective study. J Psychiatr Res. 2011;45(3):285-294. doi:10.1016/j.jpsychires.2010.08.005

75. Shaw DS, Lacourse E, Nagin DS. Developmental trajectories of conduct problems and hyperactivity from ages 2 to 10. J Child Psychol Psychiatry. 2005;46(9):931-942. doi:10.1111/j.1469-7610.2004.00390.x

76. Finsaas MC, Bufferd SJ, Dougherty LR, Carlson GA, Klein DN. Preschool psychiatric disorders: homotypic and heterotypic continuity through middle childhood and early adolescence. Psychol Med. 2018;48(13):2159-2168. doi:10.1017/S0033291717003646

77. Groenman AP, Greven CU, van Donkelaar MM, et al. Dopamine and serotonin genetic risk scores predicting substance and nicotine use in attention deficit/hyperactivity disorder. Addict Biol. 2016;21(4):915-923. doi:10.1111/adb.12230

78. Lambert NM, Hartsough CS, Sassone D, Sandoval J. Persistence of hyperactivity symptoms from childhood to adolescence and associated outcomes. Am J Orthopsychiatry. 1987;57(1):22-32. doi:10.1111/j.1939-0025.1987.tb03505.x

79. Sayal, K., Owen, V., White, K., Merrell, C., Tymms, P., & Taylor, E. Impact of early school-based screening and intervention programs for ADHD on children's outcomes and access to services: follow-up of a school-based trial at age 10 years. Archives of pediatrics & adolescent medicine, 2010; 164(5), 462–469. https://doi.org/10.1001/archpediatrics.2010.40

80. Fleming, M., Bandyopadhyay, A., McLay, J. S., Clark, D., King, A., Mackay, D. F., Lyons, R. A., Sayal, K., Brophy, S., & Pell, J. P. Age within schoolyear and attention-deficit hyperactivity disorder in Scotland and Wales. BMC public health, 2022, 22(1), 1070. https://doi.org/10.1186/s12889-022-13453-w

81.Wang, H., Chen, Y., Lin, Y., Abesig, J., Wu, I. X., & Tam, W. The methodological quality of individual participant data meta-analysis on intervention effects: systematic review. BMJ. 2021;373, n736. https://doi.org/10.1136/bmj.n736

**FIGURES**

Figure 1. PRISMA flow diagram.

Figure 2. Forest plot of the primary analysis.

Figure 3. Forest plot of the pooled effect sizes generated during sensitivity and robustness analyses.