**​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\*

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**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.

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

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**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**

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**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.