Association between relative age at school and persistence of ADHD in prospective studies: an individual participant data meta-analysis

*Synergy for the Influence of the Month of Birth in ADHD (SIMBA) study group**

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Summary

Background The youngest children in a school class are more likely than the oldest 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. We aimed to quantify the association between relative age and persistence of ADHD at older ages.

Methods For this meta-analysis, we searched MEDLINE, Embase, CINAHL, PsycINFO, and PubPsych up to April 1, 2022, with terms related to "cohort" and "ADHD" with no date, publication type, or language restrictions. We gathered individual participant data from prospective cohorts that included at least ten children identified with ADHD before age 10 years. ADHD was defined by either a clinical diagnosis or symptoms exceeding clinical cutoffs. Relative age was recorded as the month of birth in relation to the school-entry cutoff date. Study authors were invited to share raw data or to apply a script to analyse data locally and generate anonymised results. Our outcome was ADHD status at a diagnostic reassessment, conducted at least 4 years after the initial assessment and after age 10 years. No information on sex, gender, or ethnicity was collected. We did a two-stage random-effects individual participant data meta-analysis to assess the association of relative age with persistence of ADHD at follow-up. This study was registered with PROSPERO, CRD42020212650.

Findings Of 33 119 studies generated by our search, we identified 130 eligible unique studies and were able to gather individual participant data from 57 prospective studies following up 6504 children with ADHD. After exclusion of 16 studies in regions with a flexible school entry system that did not allow confident linkage of birthdate to relative age, the primary analysis included 41 studies in 15 countries following up 4708 children for a period of 4 to 33 years. We found that younger relative age was not statistically significantly associated with ADHD persistence at follow-up (odds ratio 1·02, 95% CI 0·99–1·06; p=0·19). We observed statistically significant heterogeneity in our model (Q=75·82, p=0·0011, I^2=45%). Participant-level sensitivity analyses showed similar results in cohorts with a robust relative age effect at baseline and when restricting to cohorts involving children with a clinical diagnosis of ADHD or with a follow-up duration of more than 10 years.

Interpretation The diagnosis of ADHD in younger children in a class is no more likely to be disconfirmed over time than that of older children in the class. One interpretation is that the relative age effect decreases the likelihood of children of older relative age receiving a diagnosis of ADHD, and another is that assigning a diagnostic label of ADHD leads to unexplored carryover effects of the initial diagnosis that persist over time. Future studies should be conducted to explore these interpretations further.

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Introduction

ADHD is characterised by impairing and pervasive inattention, and hyperactivity and impulsivity that are inconsistent with developmental levels. With an estimated prevalence of 5–7% in school-age children internationally, ADHD is the most common neurodevelopmental condition in childhood.[1,2] Prevalence of ADHD tends to decrease in adulthood, when it is estimated to be 2·5%.[3] 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 cutoff date. This procedure results in age disparities of up to a full year among children in the same class. Cross-sectional and longitudinal studies have shown that the youngest children in a school class are more likely than their older classmates to be diagnosed with ADHD.[5] This variation in the likelihood of receiving a diagnosis depending on child age within a class is called the relative age effect.[6,7] In school systems where the school-entry cutoff date is at the end of August (as in the UK and many states in the USA), children born

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Research in context

Evidence before this study

Some studies have shown an effect of relative age on the diagnosis of ADHD—ie, that the youngest children in a school class are more likely to receive a diagnosis of ADHD than the oldest. We did a PubMed/MEDLINE search, with no language restrictions, from database inception until Feb 1, 2020 (while planning the current study), and updated on April 1, 2022, to identify systematic reviews with and 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 and one with meta-analysis, which confirmed that children and adolescents who are younger than 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 in younger ones. The relative age effect could raise doubts about the validity of the diagnosis of ADHD in children of young relative age, who could be labelled with ADHD and 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 participant data from 57 prospective cohorts that followed up 6504 children with ADHD for a period ranging from 4 to 33 years, resulting 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 of children diagnosed with ADHD did not decrease the persistence of ADHD in later years.

Implications of all the available evidence

Compared with previous studies exploring whether younger relative age is associated with increased risk of being diagnosed with ADHD, the present meta-analysis shows that relative age does not lead to particularly unstable ADHD diagnoses over time. Two alternative interpretations could be proposed. First, the relative age effect might not increase the number of children identified with ADHD among those with a younger relative age; rather, it might decrease the number of children identified with ADHD among those with an older relative age. Second, potential carryover effects, such as teachers, parents, or other informants maintaining an endorsement of impairing ADHD symptoms once a diagnosis of ADHD is assigned, could lead to 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.

in the autumn 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 in systems where the school-entry cutoff date is at the end of December (as in most European countries), children born in the autumn 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 the absolute age of children. 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 is moderated by absolute age because the developmental difference caused by an age gap of up to 12 months attenuates with increasing age.[5]

Overall, the relative age effect could 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 ADHD diagnosis in children of young relative age. Our hypothesis was that younger relative age would be associated with a lower likelihood of ADHD persistence over time. If some children are diagnosed with ADHD due to their relative immaturity, a diagnostic reassessment of these children at a later age (ie, when the influence of the relative age has reduced) should be more likely to no longer support the initial diagnosis.[11] We conducted a systematic review with an individual participant data meta-analysis of prospective cohort studies with the aim of assessing the association between relative age and persistence of ADHD at older ages.

Methods

Search strategy and selection criteria

This individual participant data meta-analysis, based on a prepublished protocol (PROSPERO CRD42020212650),[11] was conducted and reported according to relevant guidelines.[12,13] The PRISMA checklist is reported in the appendix (p 1).

See Online for appendix

We searched MEDLINE, Embase, CINAHL, PsycINFO, and PubPsych with terms related to two constructs—"cohort" and "ADHD"—up to April 1, 2022. A full list of search terms is in the appendix (p 6). No date, publication

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type, or language restrictions were applied. Screening of the titles and abstracts was performed independently by CJG, SCa, and CP. Study selection was performed by CJG and SCa, and disagreements were resolved by SCor. References of included studies and Google Scholar were searched to identify additional references.

We included prospective studies in which at least ten children who were categorised as having ADHD were reassessed for ADHD at least 4 years after the initial assessment. Studies were eligible if they included children with a diagnosis of ADHD according to DSM versions III to 5, a diagnosis of hyperkinetic syndrome according to ICD versions 9 or 10, or ADHD symptoms exceeding clinical cutoffs established using either a clinical interview or a questionnaire with adequate psychometric properties (a list of included tools is in the appendix p 7). We required the initial diagnosis to have occurred before children were age 10 years, and that children were at least of age to start preschool. 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.

Data analysis

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 analyse the data automatically and generate anonymised outputs for our meta-analysis. Primary study authors were invited either to share the raw data through secured data transfer or to apply the R script locally and then share the anonymised results. Authors were provided with extensive guidance on the script during videoconference meetings. Several study-level variables were also independently extracted by two authors (CJG and SCa). Importantly, the relative age variable was obtained by recoding the month of birth in relation to the school-entry cutoff date. Children whose birth month was in the first month after the school-entry cutoff date were coded 1, those whose birth month was in the second month after the school-entry cutoff date were coded 2, and so on for each subsequent month. This coding was applied for all cohorts regardless of their school-entry cutoff dates, ensuring that the oldest children in the class were assigned a relative age of 1 and the youngest children in the class were assigned a relative age of 12. For each cohort, the school-entry cutoff date was first obtained from administrative or scientific sources and then confirmed by the authors of the primary studies. Crucially, in some geographical areas, there was some flexibility in the application of the school-entry cutoff 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 retained them in a secondary analysis. Details on the data extraction are in the appendix (p 8).

The risk of bias of the included studies was assessed independently by two authors (CJG and SCa) using an adapted version of the Newcastle Ottawa Scale for cohort studies.[15]

The primary and only outcome was the persistence of ADHD diagnosis at follow-up, which was defined by the initial diagnosis before age 10 years being confirmed at a later follow-up diagnostic assessment. The follow-up diagnostic reassessment needed to have occurred after age 10 years (based on evidence that the relative age effect tends to decline after this age) and at least 4 years after the initial diagnostic assessment.[16]

We did all statistical analyses in the R environment (version 4.1.1). 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.[17,18] In all our analyses, an odds ratio (OR) 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.[19] 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 I^2 statistics.

We then did a post-hoc data quality check. As most of our studies were composed of samples of participants with ADHD, we were unable to ascertain systematically 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.

As a post-hoc sensitivity analysis to test whether 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 2 months before or after the school-entry cutoff date (because children born close to the school-entry cutoff date are particularly likely to have been enrolled to school 1 year earlier or later) and repeated the primary analysis.[20] In planned sensitivity analyses, we limited our analyses to participants: (1) with a follow-up longer than 10 years; (2) with a baseline diagnosis made before age 8 years and re-assessed at follow-up after age 16 years; and (3) assessed with the same measure at baseline and follow-up.

As further robustness checks, we replicated our analyses by categorising the month of birth and retaining

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in the analysis only participants with the youngest and oldest relative age. For this post-hoc analysis, we selected children born in the 4 months that preceded or followed the school-entry cutoff date. We also conducted a post-hoc Jackknife leave-one-out meta-analysis, we excluded samples with a large Cook's distance (planned), and we replicated our analyses with a planned robust regression model, aiming to limit the effect of violation of assumptions of the generalised linear model.

In the cohort studies that allowed us to explore the relative age effect on ADHD diagnosis at baseline, we conducted a meta-regression exploring whether the relative age effect on ADHD persistence varied depending on the statistical significance (p value above or below 0·05) and 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, symptom count, or broad-based scales); (2) the sampling type; (3) participants' ADHD presentation at baseline (combined, predominantly inattentive, or predominantly hyperactive or impulsive); (4) participant IQ (below *vs* above the median value of 100); and (5) school entry system (flexible *vs* 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.

Results

From an initial pool of 33 119 potentially relevant studies, we identified 130 unique eligible studies (figure 1), of which we were able to obtain data from 57 studies (44%), including 56 published studies[21–77] and one personal communication (Abd Elkmasoud, Department of Paediatrics, Alexandria University, Egypt, 2022) and encompassing 6504 participants categorised as having ADHD (appendix p 9). The appendix lists the eligible (p 9) and excluded studies after full-text reading (p 20). 25 (44%) of the 57 studies were conducted in North or South America (22 [39%] in the USA), 22 (39%) in Europe, five (9%) in Africa, three (5%) in Asia, and two (4%) in Oceania (appendix p 35). The number of participants per study ranged from ten to 813, and the mean length of follow-up ranged from 4 to 33 years (median 7, IQR 6–9). The persistence of ADHD at follow-up ranged from 0% to 100% (44%, 25%–65%).

16 studies were excluded from the primary analysis because they were conducted in regions or countries with a flexible school entry system that did not allow us to confidently link the birthdate to the relative age. The primary analysis was therefore done in 41 studies in 15 countries following up 4708 children for a period of 4 to 33 years. Among the 41 studies, 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 that each included more than 1000 participants (with and without ADHD) at baseline (N=88 753). As expected, 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 nine 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.

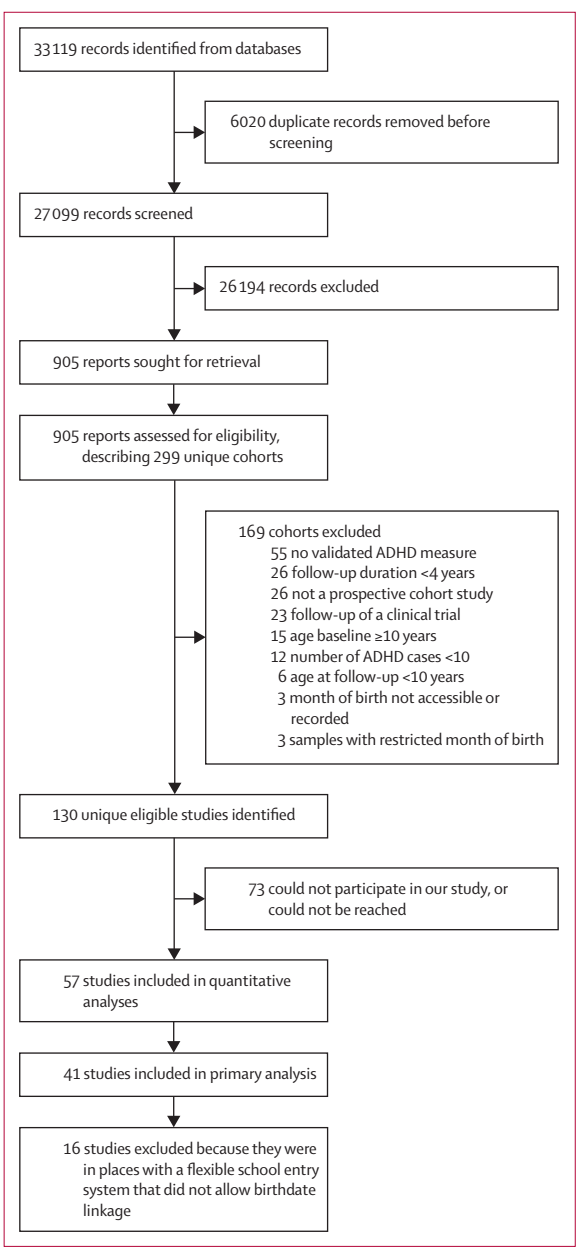

Figure 1: **Study selection**

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In the primary analysis, there was no substantial association between relative age and persistence of ADHD. We found no association between younger relative age and 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, I^2=45%).

In the sensitivity analysis that excluded participants born in the 2 months before or after the school-entry cutoff date, only 21 of the 41 studies from our main analysis were feasible for inclusion. This subsample showed a pooled effect size similar to that of our main analyses and we still found no statistically significant association of relative age with ADHD persistence (figure 3, appendix p 38). When we restricted our analyses to participants with a follow-up of more than 10 years, a baseline diagnosis before age 8 years and follow-up diagnosis after age 16 years, or with the same ADHD measure at baseline and follow-up, this did not materially change the results.

In robustness checks, we found that using robust regression or excluding samples with a large Cook's distance (n=2) did not materially change the results (figure 3, appendix p 41). The largest and smallest pooled effect sizes obtained in a Jackknife analysis were also very close to those obtained in our primary model. Lastly, dichotomising 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), although we were able to include only 24 of the 41 studies in this analysis.

Meta-regressions were done in the nine population-based cohorts that allowed us to explore the relative age effect on ADHD diagnosis at baseline, and they showed that the association between relative age and ADHD persistence was not moderated by the statistical significance of the relative age effect at baseline (ie, p<0·05 *vs* p≥0·05; QM 1·81, p=0·18) or the strength of the relative age effect at baseline (OR>1·05 *vs* OR≤1·05; QM 0·99, p=0·32; appendix p 44). 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, symptom count, or broad-based scales (QM 2·85, p=0·42). Results of other meta-regression analyses did not reveal any important moderator.

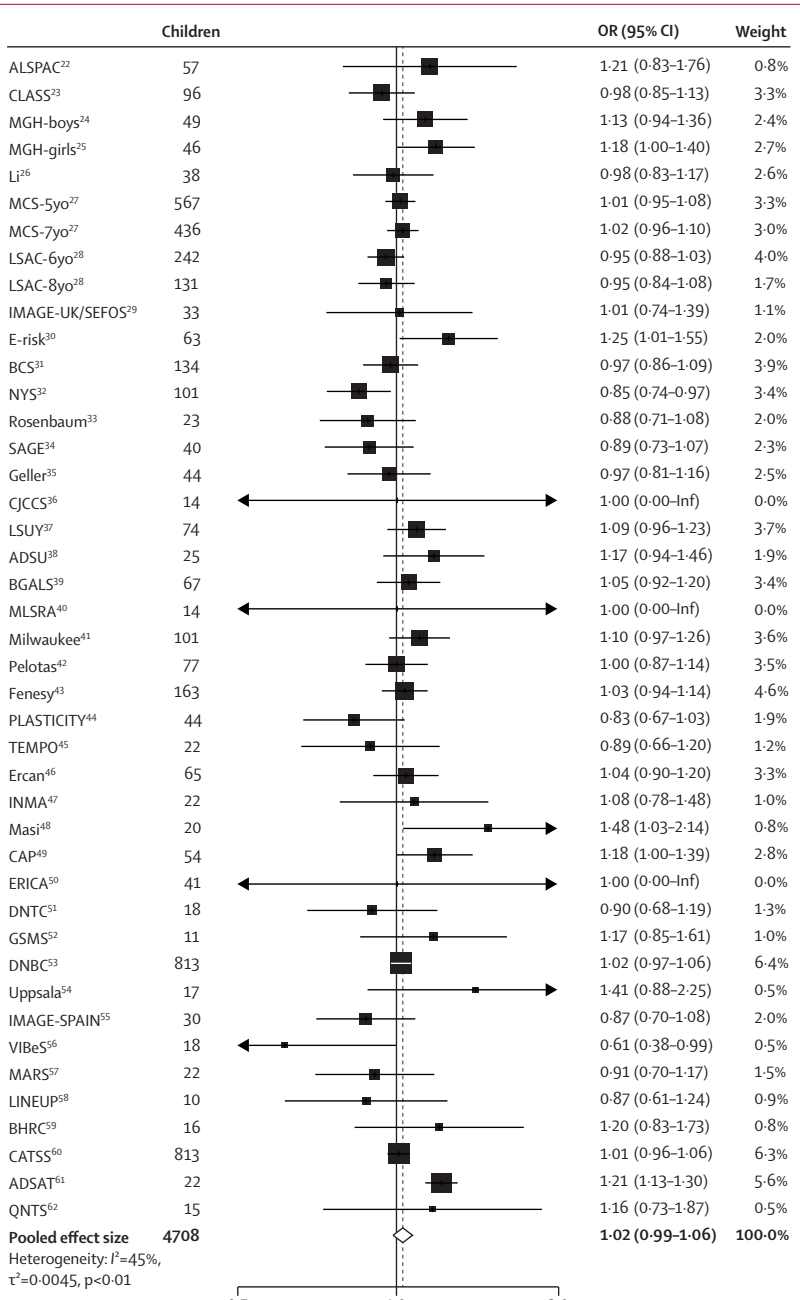

Figure 2: **Forest plot of the association between younger relative age and persistence of ADHD**
OR=odds ratio. ALSPAC=Avon Longitudinal Study of Parents and Children. CLASS=Cardiff Longitudinal ADHD Sample Study. MGH=Massachusetts General Hospital. MCS-5yo=Millennium Cohort Study, sample of children with ADHD identified at 5 years of age. MCS-7yo=Millennium Cohort Study, sample of children with ADHD identified at 7 years of age. LSAC-6yo=Longitudinal Study of Australian Children, sample of children with ADHD identified at 6 years of age. LSAC-8yo=Longitudinal Study of Australian Children, sample of children with ADHD identified at 8 years of age. IMAGE=International Multi-centre ADHD Gene. SEFOS=Sibling EEG Follow-up Study. E-risk=Environmental Risk Study. BCS=Bergen Child Study. NYS=New York Study. SAGE=Study of ADHD, Genes and Environment. Geller=Phenomenology and Course of Pediatric BP-I study. CJCCS=China Jintan Child Cohort Study. LSUY=Longitudinal Study of Urban Youth. ADSU=ADHD Detection and Service Use. BGALS=Berkeley Girls with ADHD Longitudinal Study. MLSRA=Minnesota Longitudinal Study of Risk and Adaptation. PLASTICITY=Perinatal Adverse Events and Special Trends In Cognitive Trajectories. TEMPO=Trajectoires Epidémiologiques en Population. INMA=Infancia y Medio Ambiente (Environment and Childhood). CAP=Children's Attention Project. ERICA=Emotion Regulation in Children with ADHD. DNTC=Danish National Tourette Clinic. GSMS=Great Smoky Mountains Study. DNBC=Danish National Birth Cohort. VIBeS=Victoria Infant Brain Studies. MARS=Mannheim Study of Children at Risk. LINEUP=Lillehammer Neurodevelopmental Follow-Up Study. BHRC=Brazilian High Risk Cohort. CATSS=Child and Adolescent Twin Study in Sweden. ADSAT=Academic Development Study of Australian Twins. QNTS=Quebec Newborn Twin Study.

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Discussion

Contrary to our hypothesis, we found that younger relative age was not associated with a statistically significant decrease in persistence of ADHD diagnosis over time. All our additional analyses confirmed the robustness of this finding from our primary analysis. 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 low variability in our outcome variable caused, for example, by the use of inappropriate measures.

Two possible interpretations could explain our main finding. First, 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 of 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 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 of younger relative age could thus be accounted for by underidentification of ADHD in children of 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 summary, although this interpretation supports the validity of ADHD diagnoses in children of younger relative age, it warns of a possible underdiagnosis of ADHD in children of older relative age.

An alternative interpretation of our main finding is that assigning a diagnostic label of ADHD leads to unexplored carryover effects of the initial diagnosis, which outweigh the influence of relative age. It is possible that, once a diagnostic label of ADHD is assigned, parents, teachers, and others act differently with the child 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.[78] This interpretation reinforces the concern about the influence of relative age on ADHD, as it suggests that this effect might 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.

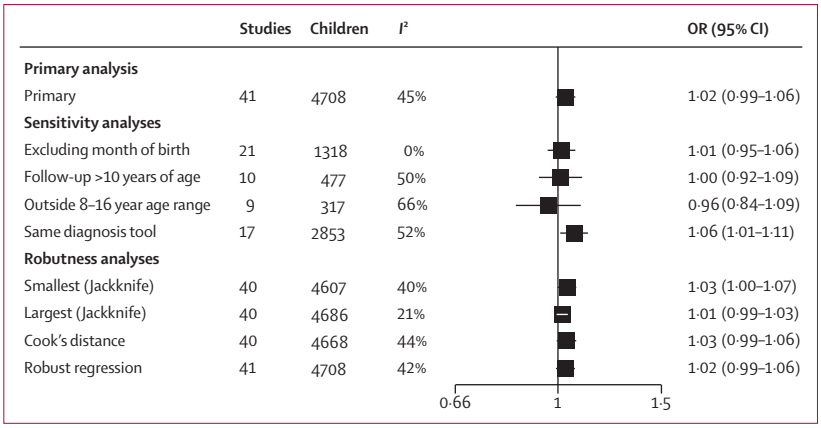

Figure 3: **Forest plot of the pooled effect sizes generated during sensitivity and robustness analyses of the association between younger relative age and persistence of ADHD**

In the sensitivity analysis excluding by month of birth, we excluded participants who were born within 2 months before or after the school-entry cutoff date.

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 or whether they had any school repetition during their education, which would be necessary to determine more accurately whether month of birth was associated with relative age. However, one of our additional analyses addressed this by removing participants born close to the school-entry cutoff date, who are at higher risk of either entering school in advance or being held back.[79] Second, because of the design of most of the included studies (ie, cohorts of children diagnosed with ADHD), we could not systematically test whether a relative age effect was present at baseline across all included studies. To address this, we did meta-regressions in large community cohort studies with a statistically significant relative age effect at baseline, or with a moderate to large relative age effect at baseline. Third, despite our efforts, we were able to gather individual participant data from only about 40% of the identified studies. Although this proportion is not uncommon in individual participant data meta-analyses, this could affect the generalisation of our findings.[80] However, rather than aiming to obtain data from each study, individual participant data 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

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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 was made because we anticipated that these variables would be considered sensitive information, because they can constitute identifying variables in small samples and would thus prevent some cohorts from participating.

Overall, after gathering individual participant data from 57 prospective cohorts, the present findings suggest that the diagnosis of ADHD in the younger children in a class is no more likely to be disconfirmed over time than diagnoses of 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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CJG, SCa, CP, RD, and SCor conceptualised the study. All authors contributed to data collection, data curation, or data analysis of at least one study. CJG, GSc, GR, and SCor performed formal meta-analysis. CJG and SCor 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 and had final responsibility for the decision to submit for publication.

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Data sharing

Results (including raw data, R code supporting data analysis, and detailed results) are publicly available at https://simba-adhd.com/HTMLresults.html.

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includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, and nurses. ALSPAC is a prospective pregnancy cohort based in the UK. Pregnant women resident in Avon, UK with expected dates of delivery between April 1, 1991 and Dec 31, 1992 were invited to take part in the study. An initial 14 541 women returned a questionnaire or attended a clinic subsequently. From these pregnancies, 13 988 children were alive at 1 year of age. When the oldest children were approximately 7 years of age, an attempt was made to bolster the initial sample with eligible cases who had failed to join the study originally. The total eligible sample at age is therefore 15 447 pregnancies, resulting in 15 658 foetuses. Of these, 14 901 children were alive at 1 year of age. The study website contains details of all the data available through a fully searchable data dictionary and variable search tool (https://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 was 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 MRC and Wellcome Trust (217065/Z/19/Z) and the University of Bristol provide core support for ALSPAC. A comprehensive list of grant funding is available on the ALSPAC website (https://www.bristol.ac.uk/alspac/external/documents/grant-acknowledgements.pdf). Berkeley Girls with ADHD Longitudinal Study cohort: this research was supported by funding from NIMH (R01 45064) to SPH. 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