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The combined effects of young relative age and ADHD on negative long-term outcomes

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Conflicts of Interest

J Kuntsi has given talks at educational events sponsored by Medice; all funds are received by King's College London and used for studies of ADHD. H Larsson has served as a speaker for Medice, Evolan Pharma and Shire/Takeda and has received research grants from Shire/Takeda; all outside the submitted work. The other authors have no potential conflicts of interest to declare.

Keywords

Relative age; attention-deficit/hyperactivity disorder; ADHD; long-term outcomes

ABSTRACT

OBJECTIVE: Young relative age – being young-in-class – and attention-deficit/hyperactivity disorder (ADHD) are both potential risk factors for adverse long-term outcomes. Young relative age also increases the risk of ADHD diagnosis. Using data from Swedish national registers, we investigate the independent and joint long-term effects of young relative age and ADHD on educational achievement, substance use disorder (SUD), criminality and depression.

METHOD: We identified a national cohort of individuals with young relative age (born November-December) and a comparison group with old relative age (born January-February). Of the total sample of 297,840 individuals, 6,528 individuals had a diagnosis of ADHD in childhood. The four outcomes were measured at ages 15-23. We examined main effects, additive and interactive effects of young relative age and ADHD on the long-term outcomes.

RESULTS: In the individuals without ADHD, young relative age was associated with increased risks of depression (odds ratio [OR] = 1.14 [1.09-1.20]), SUD (OR = 1.14 [1.09-1.20]) and low educational achievement (OR = 1.17 [1.14-1.20]), but not criminality (OR = 1.00 [0.98-1.03]). In the individuals with ADHD, young relative age was associated with increased risks of SUD (OR = 1.23 [1.01-1.50]) and low educational achievement (OR = 1.12 [1.00-1.26]; CI included 1) but not depression or criminality (ORs 0.88 [0.73-1.07] and 0.89 [0.79-1.01], respectively). An interaction emerged between young relative age and ADHD for depression (OR = 0.78 [0.64-0.95]).

CONCLUSION: We observed relative age effects that add to the evidence supporting a more flexible approach to school starting age and emphasize the importance of careful age-match comparisons during assessment of childhood ADHD symptoms.

INTRODUCTION

Being among the youngest children in a school class places a child at a disadvantage in relation to a range of outcomes, including academic and sport achievement [1-8]. This phenomenon, known as the relative age effect, also emerges for attention-deficit/hyperactivity disorder (ADHD): several large-scale studies report higher rates of diagnosis and pharmacological treatment for the disorder among children who were relatively younger than their peers [9]. These findings are not explained by season of birth, as cross-country and cross-state comparisons indicate that the differences in outcomes relate to school year cut-offs rather than birth month *per se* [10-12].

A recent systematic review of the relative age effect on ADHD identified 20 studies, of which 16 reported a significantly higher proportion of relatively younger children being diagnosed with or treated for ADHD [9]. A meta-analysis involving 17 of the 20 studies further indicated a significant risk ratio of 1.27 for receipt of ADHD medication [9]. These studies include very large cohort and register studies, across many countries and continents with varying ages of school entry and prescription rates. The Nordic register-based studies from Sweden, Finland, Norway and Iceland all indicated significant relative age effects on ADHD [4,11,13,14], but an exception is the Danish dataset that reported almost no relative age effect on medication use for ADHD [15]. The most likely explanation for the lack of a relative age effect in Denmark is the more flexible approach to school starting age, with a high proportion of relatively young children held back by one year. Overall, the findings on the relative age effect on ADHD raise the possibility that the disorder may be over-diagnosed among the youngest and therefore developmentally least mature children in class (or alternatively the disorder may be under-diagnosed among the oldest in class).

The data from nationwide Swedish registers indicated that the children born in November and December, the youngest in class, had a greater likelihood of being diagnosed with ADHD (odds ratios 1.2 to 1.5) or being prescribed medication for ADHD (odds ratios 1.4 to 1.8), when comparing to those born in January and February [13]. Yet no corresponding differences emerged for parent- or self-reported ADHD symptoms in two complementary population-based cohorts of 9-year-old and adult twins [13]. A further study in the US reported only a weak relative age effect for parent ratings on ADHD symptoms, but a strong effect for teacher ratings [12]. These findings, combined, are consistent with the possibility that teacher perceptions of immaturity relative to peers may contribute to over-diagnosis of ADHD among the youngest in class.

The wider context for the relative age effect on ADHD relates to three observations. First, ADHD lies at the extreme of a continuum of symptoms of inattention and hyperactivity-impulsivity [16]. Second, ADHD symptoms (e.g. 'being on the go', 'blurting out answers', 'difficulty waiting one's turn') are common among young children and decrease, overall, with age [17]. Third, ADHD diagnosis relies on a relative comparison to other children of the same age: the child must show symptoms of inattention or hyperactivity-impulsivity to a significantly greater degree than is typical for their age, to obtain the diagnosis. As such, a child showing ADHD symptoms to a moderate degree, but below the diagnostic cut-off, may appear to cross the threshold to diagnosis if inaccurately compared to children who are somewhat older. In this scenario, while the large majority of children in the group defined by both an ADHD diagnosis and young relative age would still be expected to have 'true' ADHD (i.e. diagnosis not dependent on young relative age), a small proportion of them would be expected to have less severe ADHD due to having crossed the threshold to diagnosis partly due to their relative immaturity.

By studying negative longer-term outcomes associated with ADHD we can investigate if young relative age affects the risk for the outcomes in individuals with ADHD. Previous analyses on the Swedish register data have linked ADHD to increased criminality, substance use, depression and low educational achievement [18-21]. In this study, using the Swedish register data, we aim to examine the long-term effects of young relative age, independently and jointly with ADHD, on these adverse outcomes. First, we test if there is an independent (main) effect of young relative age – in addition to the effect of ADHD – on each of these outcomes. Second, we examine if young relative age worsens or improves the outcome for the individuals with ADHD. If young relative age increases the risk for the negative outcome beyond the effect attributed to ADHD (additive effects of young relative age and ADHD), this would indicate that relative immaturity contributes to the risk for the outcome among individuals with ADHD. For outcomes that do not show such an increased risk with relative immaturity in individuals with ADHD, we can examine if the effect of young relative age on the outcome is, instead, significantly reduced among those with ADHD, compared to those without ADHD. Such an interaction between young relative age and ADHD, indicating a protective effect of young relative age on individuals with ADHD, would be consistent with the hypothesised reduced severity of ADHD among the young-in-class.

METHODS

Data sources

Data were derived through linkage of nationwide population-based registers in Sweden; unique personal identification numbers enabled accurate linkage [22]. The National Patient Register has coverage for psychiatric in-patient care and information on out-patient visits to specialist physicians since 2001, with diagnoses based on the International Classification of Diseases (ICD). The Prescribed Drug Register includes information on all prescribed medical drugs since July 2005. The Criminal Conviction Register provides criminal conviction records from Swedish lower courts since 1973, regardless of the medico-legal disposition of the convicted offender. Since the age of criminal responsibility in Sweden is 15 years [23], law-breaking behaviors before age 15 years are not registered. The National School Register holds information on individual school performance from all municipal and independent schools from 1988.

Study population

The cut-off date for school entrance in Sweden is the 1st of January. All individuals who were born in January-February or November-December during 1990 to 1997 in Sweden were included in the study (N=323,472). Individuals who had died (n=1948) or emigrated before age 15 (n=16,642) and individuals with first ADHD diagnosis or prescription before age 6 (n=109) or after age 15 (n=6933) were excluded from the study sample, which resulted in a final sample of 297,840 individuals. The four outcomes were measured at ages 15-23. Specifically, all individuals were followed from their 15th birthday to their birthday in 2013, and were between 16 to 23 years old by the end of follow-up. Demographic characteristics of the study participants are reported in Table 1.

Measures

ADHD diagnosis. Individuals with ADHD were identified from two sources: (1) at least 1 record of inpatient or outpatient diagnosis of ADHD from the National Patient Register (ICD-9 code 314; ICD-10 code F90); (2) one or more dispensed prescriptions of ADHD medications amphetamine, dexamphetamine, methylphenidate, atomoxetine or lisdexamfetamine from the Prescribed Drug Register (Anatomical Therapeutic Chemical [ATC] codes N06BA01, N06BA02, N06BA04, N06BA09, and N06BA12, respectively).

Criminality. We measured criminality in the Criminal Conviction Register and defined it as a conviction of any crime during or after the age of 15 years. Our measure of criminality was coded as a binary variable (i.e., 1 = has been convicted, 0 = has not been convicted).

SUD. SUD was indexed as a diagnosis of any SUD from the National Patient Register (ICD-10 codes F10-F19) during or after 15 years of age. SUD was coded as a binary variable (1 = any diagnosis of SUD, 0 = no diagnosis of SUD).

Depression. Depression was indexed as a diagnosis of any depression from the National Patient Register (ICD-10 codes F32-F33) during or after 15 years of age. Depression was also coded as a binary variable.

Low educational achievement. Low educational achievement was operationalized as not eligible for upper secondary school (binary variable). The Swedish primary and lower secondary education is compulsory by law and usually 9 years in length. Leaving certificates received upon graduation in the 9th year determines whether a student is eligible to advance to upper secondary school. The eligibility requires the student to pass all "core subjects" (Swedish, English and mathematics) and 5 or 9 additional subjects for vocational education or preparatory programs, respectively.

Statistical analyses

Risks of long-term outcomes (any crime, SUD, depression and low educational achievement) were determined stratified by relative age (young/old) and ADHD status. A series of multivariate logistic regression models were fitted, controlling for sex and birth year (with each year as a category), to estimate the joint effect of ADHD and the relative age categorization on long-term outcomes. Results are presented as adjusted odds ratios (ORs) with 95% confidence intervals. An interaction term between ADHD and the relative age categorization was used to test whether the associations between birth month and the outcomes were moderated by ADHD status, which compares the effects (ORs) of relative age on the outcomes in ADHD vs non-ADHD individuals. All analyses were conducted in SAS 9.4 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

The prevalence of ADHD was higher in children with young relative age (2.8%) compared to those with old relative age (1.7%, $p<0.001$; Table 2).

Both relative age groups of children with ADHD (old 23.7% and young 21.7%) showed higher rates of criminality compared to the groups of children without ADHD (old 8.8%, $p<0.001$ and young 8.9%, $p<0.001$; Figure 1). A similar pattern of results was observed for SUD (6.3% and 7.8% vs. 2.3% and 2.6%, both $p<0.001$), depression (7.4% and 6.8% vs. 2.3% and 2.7%, both $p<0.001$), and low educational achievement (36.1 and 39.2% vs. 10.0% and 11.5%, both $p<0.001$).

ADHD was associated with higher risks of all long-term outcomes (OR=3.52 [3.20-3.87] for criminality; OR=3.73 [3.18-4.38] for SUD; OR=5.22 [4.49-6.06] for depression; OR=4.87 [4.45-5.32] for low educational achievement; Table 3). Young relative age was associated with increased risks of SUD (OR=1.14 [1.09-1.20]) and low educational achievement (OR=1.17 [1.14-1.20]), but not with criminality (OR=1.00 [0.98-1.03]), compared with old relative age. For depression, a statistically significant interaction emerged between young relative age and ADHD (OR for interaction 0.78 [0.64-0.95], Table 3), indicating that the relative risk of depression associated with young relative age was lower in the ADHD group (OR=0.88 [0.73-1.07]) than in the non-ADHD group (OR=1.14 [1.09-1.20]).

In individuals with ADHD, young relative age was associated with an additional risk of SUD (OR=1.23 [1.01-1.50]; Table 4) and low educational achievement (OR=1.12 [1.00-1.26]; CI included 1), compared to old relative age. Young relative age, compared to old relative age, was associated with lower risks for criminality (OR=0.89 [0.79-1.01]) and depression (OR=0.88 [0.73-1.07]) in individuals with ADHD, but the confidence intervals both included 1.

DISCUSSION

Using a very large Swedish register-based dataset we show that, in individuals without ADHD, being young-in-class increases the risk for subsequent low level of education, depression and SUD, but not for criminality, at ages 15-23 years. We further observed additive effects of young relative age and ADHD that identify individuals at greatest risk for the negative outcomes: young relative age increased the risk, beyond the large effect attributed to ADHD, for SUD and low educational achievement (although the latter CI included 1). Young relative age did not increase the risk for depression or criminality among the individuals with ADHD, with a significant interaction between relative age and ADHD status emerging for depression: the effect of young relative age on later depression was reduced among the individuals with ADHD, compared to those without ADHD.

Young relative age was a universal risk factor for subsequent SUD for both individuals with and without ADHD (ORs of 1.23 and 1.14, respectively). This shows how being younger than most classmates places a child at a disadvantage long-term, behaviourally and socially, such that the risk for SUD at ages 15-23 years is increased, even independent of the larger (nearly 4-fold) effect linked to ADHD. For future prevention, these results emphasize that the individual child who is most vulnerable for SUD is the child who has both ADHD and is younger than peers in the same class. The results further improve our understanding of ADHD by showing that, in individuals with ADHD, relative immaturity contributes to the risk for later SUD. A similar pattern emerged for low educational achievement, with ORs of 1.12 and 1.17 for those with and without ADHD, respectively. The long-term impact of young relative age on educational achievement is overall in line with previous studies [1-8], although further replication is required in relation to the result for the ADHD group where the CI included 1.

A different pattern emerged for depression and criminality, where young relative age did not increase the risk for these outcomes for the ADHD group (ORs of 0.88 and 0.89). While young relative age also did not increase the risk for later criminality for the individuals without ADHD (OR 1.00), for depression we observed a significant effect (OR 1.14) and a significant interaction between relative age and ADHD status (OR 0.78): the effect of young relative age on depression was significantly reduced among the individuals with ADHD, compared to those without ADHD. This relative reduction in the risk for depression for the young-in-class individuals with ADHD is consistent with potentially less severe ADHD among those who were young-in-class, in line with the overdiagnosis account of the relative age effect on ADHD. However, the evidence for this account is overall limited in our data. Future studies can explore further the possibility of less severe ADHD among those who were young-in-class using other methods, such as genetic analyses or assessing improvement in ADHD symptoms over time.

Considering the size of the individual significant main effects, it is clear that the effects of young relative age on the outcomes are modest in comparison to the much larger effects associated with ADHD diagnosis (ORs of 1.14-1.17 vs 3.52-5.22) [18-21]. While acknowledging the large impact associated with ADHD diagnosis, we must also note an unavoidable limitation of our analyses in that it was not possible to separate, in the young relative age ADHD group, the 'true' ADHD cases from those that reflect possible misclassification due to young relative age. This means we may have under-estimated the size of the effects, even though the very large sample size enabled us to pick up significant differences between the young-in-class and old-in-class ADHD groups. A separate limitation is that the identification of ADHD cases relied on register-based diagnosis of ADHD and dispensation of ADHD medication. Although there is no severity or symptom data in the registers, the findings rely on ADHD patients who are potentially more severely affected than individuals with ADHD who do not receive or seek healthcare support. A further limitation is that our follow-up data were restricted to data collected from 2005 to 2013. Further replication with more recent data is warranted, especially after the implementation of DSM-5 which lifted the age limit of symptom onset from age 7 to 12 in the diagnosis of ADHD.

In these Swedish register data, the prevalence of ADHD diagnosis was 2.8% among the youngest in class (November-December births) and 1.7% among the oldest in class (January-February births) [13]. If perceptions of immaturity relative to peers contribute to over-diagnosis of ADHD among the youngest-in-class, we would expect to find some evidence that the nature of ADHD and, subsequently, the association of ADHD with negative long-term outcomes may differ for those who were young-in-class. The significant interaction we observed for depression between relative age and ADHD status is in line with this possibility: the association between ADHD diagnosis and subsequent depression was reduced among the young-in-class. For criminality, the results were in the same direction, but the interaction was not statistically significant. These findings further indicate that immaturity is unlikely to be part of the underlying mechanism that leads to ADHD increasing the risk for the negative outcomes of depression and criminality, given that young relative age was not a risk factor for these outcomes among those with ADHD. In contrast, relative immaturity increased the risk for SUD and low educational achievement in individuals with ADHD (positive main effects of young relative age on the outcomes), although the latter CI included 1.

While the solid, consistently reported observation of relative age effect on ADHD deserves increased scientific study, this phenomenon must not be misconstrued such that the overall validity of ADHD diagnosis would be questioned. The validity of the ADHD diagnostic construct is shown by a wide range of consistent evidence of, for example, etiological and neurobiological risk factors, a characteristic pattern of developmental changes and outcomes, prediction of treatment response, and associated significant clinical and psychosocial impairments, as reviewed in detail elsewhere [24,25]. The issue that the relative age effect on ADHD raises, instead, is about how to improve accuracy of diagnosis in borderline cases, specifically raising the importance of careful age-match comparisons among younger children. In common with other psychiatric disorders where we lack an objective gold standard and diagnosis relies on reported behavioural symptoms, further evidence-based fine-tuning of the potentially grey area around the exact diagnostic threshold on the symptom continuums will be of benefit. Considering the overall pattern of our and previous results on the relative age effect, a key educational implication is the support for a more flexible approach to school starting age, as already adopted in some countries.

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Table 1. Demographic characteristics of the study participants by relative age and attention-deficit/hyperactivity disorder status

	No ADHD (n, %)		**ADHD (n, %)**	
	Young relative age (born Jan-Feb)	Old relative age (born Nov-Dec)	Young relative age (born Jan-Feb)	Old relative age (born Nov-Dec)
Individual level				
Male	82003 (50.88)	66072 (50.76)	2139 (78.73)	2911 (76.38)
Born abroad	24328 (15.10)	18624 (14.31)	175 (6.44)	200 (5.25)
Family level				
At least one parent born abroad	50950 (31.62)	43659 (33.54)	653 (24.03)	944 (24.77)
Highest parental education:				
Primary and lower secondary education	9481 (5.88)	7957 (6.11)	184 (6.77)	296 (7.77)
Upper secondary education	68000 (42.20)	55765 (42.84)	1521 (55.98)	2173 (57.02)

Post-secondary and postgraduate education	72756 (45.15)	59215 (45.50)	893 (32.87)	1233 (32.35)
Unknown	10918 (6.77)	7220 (5.55)	119 (4.38)	109 (2.86)

Table 2. Prevalence of attention-deficit/hyperactivity disorder in the two relative age groups

	Old relative age (born Jan-Feb)	Young relative age (born Nov-Dec)
No ADHD	161,155 (98.3%)	130,157 (97.2%)
ADHD	2717 (1.7%)	3811 (2.8%)

Note: The difference between the young and old relative age groups is significant (*p*<0.001, chi-square test).

ADHD = attention-deficit/hyperactivity disorder.

Table 3. Associations of attention-deficit/hyperactivity disorder and relative age with long-term outcomes from multivariate logistic regressions (odds ratio with 95% confidence interval)

	Criminality	SUD	Depression	Low educational achievement
ADHD	3.52 (3.20-3.87)	3.73 (3.18-4.38)	5.22 (4.49-6.06)	4.87 (4.45-5.32)
Relative age (young vs old relative age)	1.00 (0.98-1.03)	1.14 (1.09-1.20)	1.14 (1.09-1.20)	1.17 (1.14-1.20)
ADHD x young relative age	0.90 (0.79-1.02)	1.10 (0.90-1.35)	0.78 (0.64-0.95)	0.98 (0.87-1.10)

Note: Odds ratios were adjusted for sex and birth year.

ADHD = attention-deficit/hyperactivity disorder; SUD = substance use disorder.

Table 4. Associations between relative age and long-term outcomes from multivariate logistic regressions in individuals with and without attention-deficit/hyperactivity disorder (odds ratio with 95% confidence interval)

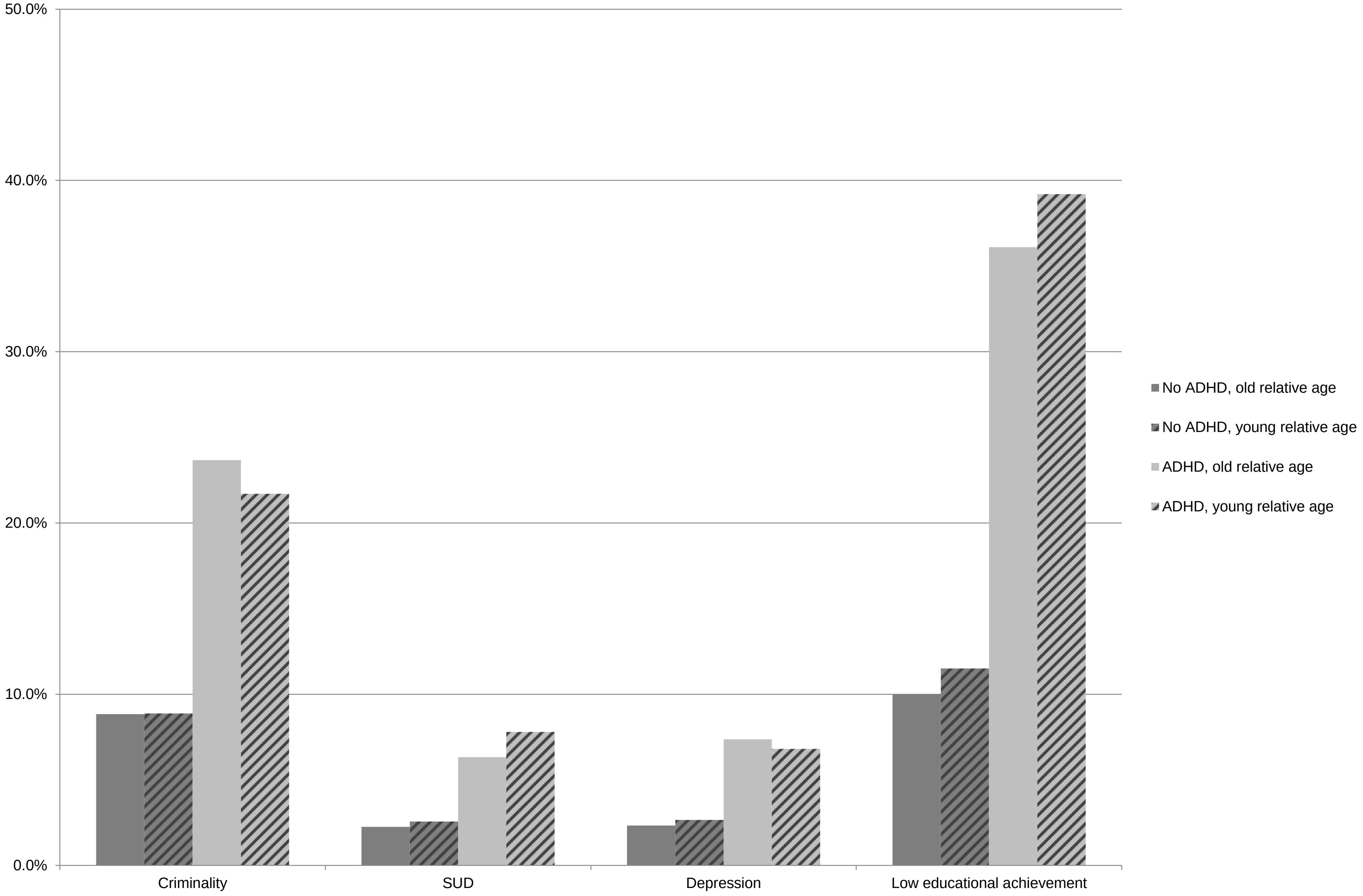
	Relative age	Criminality	SUD	Depression	Low educational achievement
ADHD	Young	0.89 (0.79-1.01)	1.23 (1.01-1.50)	0.88 (0.73-1.07)	1.12 (1.00-1.26)
	Old	1	1	1	1
No ADHD	Young	1.00 (0.98-1.03)	1.14 (1.09-1.20)	1.14 (1.09-1.20)	1.17 (1.14-1.20)
	Old	1	1	1	1

Note: Odds ratios were adjusted for sex and birth year.

ADHD = attention-deficit/hyperactivity disorder; SUD = substance use disorder.

Figure 1. Risks of long-term outcomes in the individuals with and without attention-deficit/hyperactivity disorder , by relative age.

Note: 29,165 individuals had missing information on low educational achievement.


50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
Criminality
SUD
Depression
Low educational achievement
No ADHD, old relative age
No ADHD, young relative age
ADHD, old relative age
ADHD, young relative age