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## The causal effect of education and cognitive performance on risk for suicide attempt: a combined instrumental variable and co-relative approach in a Swedish national cohort

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## Abstract

**Background:** The aim of this study was to clarify the possible causal associations between education phenotypes and non-fatal suicide attempts. In particular, we evaluated the roles of academic achievement (school grades), cognitive performance (IQ), and educational attainment (education level).

**Methods:** Based on longitudinal Swedish registry data, we included 2,335,763 individuals (48.7% female) with available school grades, 1,448,438 men with IQ measures, and 4,352,989 individuals (48.4% female) with available data on education level. We combined two different approaches to aid in causal inference: 1) instrumental variables analysis, using month of birth as an instrument related to education but not suicide attempt, to control for measured and unmeasured confounders, and 2) co-relative analysis, comparing pairs of different genetic relatedness (cousins, half, and full siblings) to control for genetic and environmental influences.

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Conflicts of Interest

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**Results:** High education was associated with reduced risk of suicide attempt. Instrumental variable analysis indicated evidence of a likely causal association between higher school grades and lower risk of suicide attempts (HR=0.71). Co-relative analyses supported the causality between the three predictors and suicide attempt risk (*school grades*, HR=0.80, *IQ*, HR=0.83, *education level*, HR=0.76). Finally, we examined the specificity of education phenotypes and found that both cognitive (IQ) and non-cognitive (school grades, education level) processes were involved in suicide attempt risk.

**Limitations:** IQ was only available in men, limiting the generalizability of this analysis in women.

**Conclusions:** Efforts to support causal associations in psychiatric research are needed to offer better intervention. Programs improving education during adolescence would decrease suicide attempt risk.

#### Keywords

School grades; IQ; Education level; Suicide; Causality

## Introduction

Suicide is a leading cause of death in the US and suicidal behaviors have important emotional, interpersonal, and economic impacts. According to the Centers for Disease Control and Prevention (2022), suicide death increased 30% between 2000 and 2018 and then declined in 2019-2020. Despite this decline, it is estimated that in 2020, about 50,000 people died by suicide and 1.2 million people attempted suicide in the US (Centers for Disease Control and Prevention, 2022). Suicidal behaviors represent a substantial economic burden, with an estimated \$93.5 billion in annual costs (Shepard et al., 2016). In addition, inestimable emotional costs can be ascribed through the impact of suicidal behaviors at personal, familial, and societal levels (Ports et al., 2017). In view of these burdens, increasing efforts have emerged to prevent suicidal behaviors and improve treatment care. However, the efficacy of currently available prevention and intervention actions remains limited (Cha et al., 2018; Turecki and Brent, 2016). First, efforts to improve prevention could be hampered by the fact that large samples are needed to properly study the related risk factors due to the low prevalence of suicidal behaviors in the general population (Van Orden et al., 2010). Second, while the etiologies of non-fatal suicide attempts and suicide deaths are not entirely overlapping (Edwards et al., 2021), prevention efforts are not necessarily tailored for distinct outcomes. Third, to design effective prevention and intervention, we need to shift from the identification of factors that may merely be indicators of increased probability of suicidal behaviors to the identification of causal factors that can directly explain these outcomes (Van Orden et al., 2010).

Several risk factors have been described in association with suicidal behaviors (Sher, 2006; Turecki and Brent, 2016). One of the most important factors described in the literature is education, a complex indicator of social, intellectual, and professional achievement, including the level of school grades (academic achievement), the ability to learn from experiences, adapt, and solve problems (cognitive performance), and the level of education

reached in young adulthood (educational attainment) (Malanchini et al., 2020; Plomin and von Stumm, 2018). These indicators are correlated and influenced by genes and familial environment. Twin studies have reported heritability estimates of around 60% for academic achievement (Pokropek and Sikora, 2015), 60% for cognitive performance (Malanchini et al., 2020) and 55% for educational attainment (Marks, 2017; Rowe and Jacobson, 1999). In addition, a strong influence of family environment have been described (Engelhardt et al., 2019), particularly for cognitive performance (Rowe and Jacobson, 1999).

Numerous studies have supported the role of education – academic achievement (Sorberg Wallin et al., 2020), cognitive performance (Kosik et al., 2017), and educational attainment (Balint et al., 2016) – in risk for suicidal behaviors. National studies with adequate sample sizes from the US and several European and Asian countries support low education as a risk factor for suicidal behaviors (Gunnell et al., 2011; Hansson Bittar et al., 2020; Kimura et al., 2016; Nyberg et al., 2020; Oien-Odegaard et al., 2021; Park et al., 2018; Phillips and Hempstead, 2017; Pompili et al., 2013; Shah and Bhandarkar, 2009; Sorberg Wallin et al., 2020), suggesting the strong role of education beyond cultural differences. However, information is lacking regarding the causality of this association i.e., does education participate in risk for suicide attempt among other factors, or is education directly related to increased suicide attempt risk? Specifically, despite substantial heritability estimates for both education and suicidal behaviors (Edwards et al., 2021; Marks, 2017), no study has disentangled a potential causal association from familial confounding factors. One recent exception offered an investigation of the causal relation between educational attainment, cognitive performance, and suicide attempts by using Mendelian randomization in a large European sample. The authors found that educational attainment, but not cognitive performance, may causally influence the risk of suicide attempts after controlling for genetic influences (Rosoff et al., 2020). This study supports the notion that education level may be targeted for prevention of suicide attempts. Yet, much remains unknown regarding the specific role of familial factors (both genetic and shared environment), other potential confounders, and the causal association with academic achievement.

In the current study, we aimed to expand on the report by Rosoff et al. (2020) by further evaluating the association between education and risk for non-fatal suicide attempt, considering three related measures: academic achievement (school grades at age 16), cognitive performance (IQ at age 19), and educational attainment (years of education at age 25). We used two complementary methods validated to support causal inference in epidemiological research (Ohlsson and Kendler, 2020): a) Instrumental variable analysis, involving the identification of an instrument, i.e., a variable that influences the risk factor (education) but has no direct effect on the outcome (suicide attempt), to control for measured and unmeasured confounders; and b) Co-relative analysis, estimating the association between risk factors and outcome by comparing relative pairs of different genetic relatedness to control for genetic and familial environmental confounding. These methods complement one another, in that instrumental variable analysis accounts for a wide range of confounders, while co-relatives' analysis specifically accounts for genetic factors and familial environment, which are known to have a strong influence on both education and suicide attempts.

We pursued three research goals: (1) examining the overall associations between education and suicide attempt; (2) determining the degree to which the associations between education and suicide attempt are causal by using instrumental variable and co-relatives analyses; and (3) estimating the specific role of cognitive performance (IQ) versus education-related variables (academic achievement, educational attainment), given previous support for a causal role of educational attainment but not IQ (Rosoff et al., 2020).

## Methods

#### Participants

Participants were part of a Swedish population-based cohort and followed longitudinally for a mean of 26.3 (SD=13.4) years. They were selected from Swedish registries with national coverage linking each person's unique personal identification number (replaced with a serial number by Statistics Sweden to preserve confidentiality). The sample included three subgroups of individuals according to the availability of our phenotypes in the registries: (1) 2,335,763 individuals (born 1972-1995, 48.7% female) for the analysis on academic achievement (school grades), (2) 1,448,438 men (born 1951-1980) for the analysis on cognitive performance (IQ), and (3) 4,352,989 individuals (born 1950-1993, 48.4% female) for the analysis on educational attainment (education level). We evaluated the first suicide attempt that occurred after the measure of academic achievement (16 years old), cognitive performance (19 years old, only men), or educational attainment (25 years old). We secured ethical approval for this study from the Regional Ethical Review Board of Lund University (No. 2008/409, 2012/795, and later amendments 2016/679).

#### **Outcome and Predictors**

The main outcome was the first non-fatal suicide attempt identified via medical records. We followed previous recommendations regarding the importance of distinguishing non-fatal suicide attempts and deaths by suicide (Edwards et al., 2021) and aligned with the definition of suicide attempt as a non-fatal outcome proposed by the NIMH (n.d.). Time to first suicide attempt was evaluated as a function of school grades at age 16, IQ in men at age 19, and education level at age 25 in three separate approaches. These variables were selected via National School Register, Military Conscription Register, and Statistics Sweden's longitudinal database LISA (Longitudinal integrated database for health insurance and labour market studies).

**School grades.**—School grades were obtained from the 9th school year (corresponding at approximately 16 years old), which is the final year of mandatory education in Sweden. The grades reflected the overall performance of students, their knowledge on specific subject tests, and were decisive for admission to upper secondary schools. The grading system changed in Sweden during the follow-up period. We therefore performed a sensitivity analysis to evaluate the associations between school grades and suicide attempts according to the different grading systems (see supplement).

**IQ.**—The evaluation of IQ was part of a test battery required by the Swedish Military at conscription time (18-19 years old in men). The assessment was based on 4 series

of tests (40 questions each): (1) combined ability of problem-solving, induction capacity, and numerical ability, (2) verbal comprehension, (3) spatial ability, and (4) technical and physical abilities. The global IQ score, derived from a summation of the four subtests, was standardized to give a Gaussian distributed score between 1 and 9.

**Education level.**—Educational level was measured as the number of years of education the individual had attained at 25 years old. We chose to end our observation at 25 years old, as most individuals had reached their highest education level at this age (supplementary Figure 1).

More details regarding data processing are reported in supplement. All three predictors were standardized by birth year and sex, hazard ratios (HRs) are reported by SD of education.

## Statistical analyses

We evaluated the association between academic achievement (school grades), cognitive performance (IQ), or educational attainment (education level) and risk for suicide attempt, and used instrumental variable analysis and co-relative design to improve causal inference.

First, we used Cox proportional hazards models to investigate time to first suicide attempt as a function of school grades, IQ, and education level, from the age of this measurement (16, 19, 25 years old, respectively) to the end of follow-up (suicide attempt registration, death, emigration, or December 31, 2018). In the first step, we estimated the crude association between suicide attempt and the three predictors (i.e., not adjusted for potential confounders) and used this for comparison with further analyses. The proportionality assumption was checked in all models by including an interaction term between time and the predictor variable of interest. In the second step, we estimated the association between the three predictors and suicide attempts by controlling for parental education.

Second, in order to strengthen causal interpretation, we used two complementary approaches. We performed an instrumental variable analysis using month of birth as an instrument (Kendler et al., 2018; Solli, 2017). For this approach, we first evaluated the relationship between month of birth and the three predictors with linear regressions. In the absence of a meaningful association in this step, further analyses are not warranted. In a second step, we assessed the association between month of birth and suicide attempt, as the relation between the instrument and the outcome should *not* be meaningful to meet the assumptions of instrumental variable analysis. Finally, we evaluated the relationship between month of birth and suicide attempt by using the predicted values from step 1 as the exposure variable in a Cox regression model. As the unmeasured and measured confounders are assumed to be equally distributed among the estimated values from step 1, the resulting HRs are considered to be controlled for confounding factors (principle of randomization). Causality is supported if, when using the predicted values from step 1 (controlling for confounders), we observe a significant association between the predicted values and suicide attempt.

In a complementary analysis that enables causal inference, we used a co-relative design to examine if the crude association between the predictors and suicide attempt reflects

confounding by familial risk factors by comparing pairs of different genetic relativeness, i.e., cousins, half-siblings, and full-siblings. Relative pairs that were discordant in education/ cognitive variables are informative to these analyses. We used stratified Cox proportional hazards models, with a separate stratum for each relative pair. In this model, the HR is adjusted for a range of unmeasured genetic and familial environmental factors shared within the relative pair. Full-siblings, half-siblings, and cousins share, respectively, on average 50%, 25% and 12.5% of their genes identical by descent. We combined all four samples (i.e., population, full-siblings, half-siblings, and cousins) into one dataset in which we performed two analyses. In the first, we allowed all parameters for each sample to be independent (i.e., four separate analyses). In the second, we modeled the association between the predictors and suicide attempts with two parameters: one main effect and one as a linear function of the genetic resemblance, i.e., 0 for the population, 0.125 for the cousin, 0.25 for the half sibling, and 0.50 for the sibling dataset. The HRs for the second parameter gave an indication of the size of the familial confounding. If the second model fits the data well (as indexed by the AIC), we obtain an improved estimation of the association among all relatives and an *extrapolated* value for monozygotic (MZ) twins (who share 100% of their genes). A causal interpretation is supported if, after controlling for genetic factors and familial environment, we observe significant associations (i.e., HRs that differ from 1) between education/cognitive variables and suicide attempt.

Finally, we estimated the role of cognitive performance versus education-related variables by relying on co-relatives analysis and selecting pairs that are discordant for education and cognitive variables: (1) Model 1a, controlling for IQ: pairs are concordant for IQ but discordant for school grades, (2) Model 1b, controlling for school grades: pairs are concordant for school grades but discordant for IQ, (3) Model 2a, controlling for IQ: pairs are concordant for IQ but discordant for education level, (4) Model 2b, controlling for education level: pairs are concordant for education level but discordant for IQ. As for the second research question, we computed both observed (allowing all parameters to be independent) and predicted (modelling a linear function of the genetic resemblance) models and compared their fit by using the AIC.

## Results

Below, we describe the three samples used in this study and then present analyses according to our three research aims: (1) the associations between education and suicide attempt (univariate Cox models); (2) the causality of the associations between education and suicide attempt (instrumental variable and univariate co-relatives analyses); and (3) the specific role of cognitive performance versus education-related variables (Cox models and multivariate co-relative analysis).

#### **Descriptive analyses**

**School grades.**—We identified 2,335,763 individuals with available school grades at age 16, of whom 3.5% (n=81,158) attempted suicide during the follow-up period. The mean age of the first suicide attempt in this subsample was 24.7 (SD=6.5).

**IQ.**—A total of 1,448,438 men had IQ scores available at age 19, with 3.6% (n=52,048) attempting suicide during the follow-up period (mean age=37.3, SD=11.4).

**Education level.**—We identified 4,352,989 individuals with available data on education level at age 25, of whom 2.5% (n=108,223) were registered for suicide attempt during the follow-up period (mean age=39.0, SD=10.3).

The correlations between the three predictors were moderate, supporting the usefulness of distinguishing their specific roles in suicide attempt risk (school grades and IQ, *r*=0.62, *p*<0.001, education level and IQ, *r*=0.50, *p*<0.001, school grades and education level, *r*=0.60, *p*<0.001).

#### The associations between education and suicide attempt

**Univariate Cox proportional hazards models**—We evaluated the crude associations between the three predictors and first suicide attempt. Results, per SD of the predictor variable, showed that lower risk of suicide attempt was associated with higher school grades (HR=0.60, 95% CI=0.60;0.61), IQ (HR=0.67, 95% CI=0.66;0.67), and education level (HR=0.62, 95% CI=0.62;0.63). These associations remained when controlling for parental education (see supplement). We also conducted a sensitivity analysis with type of school grade assessment, wherein results indicated that the association between school grades and suicide attempt was significant for both types of assessment (see supplement). This first analysis supports high education as a protective factor for suicide attempt but does not inform about causality.

#### The causality of the associations between education and suicide attempt

**Instrumental variable analyses**—We report results from the instrumental variable analysis in Table 1. While there was an association between month of birth and school grades, the magnitude of these associations was not meaningful for IQ and education level (see Supplementary Figure 2). Our instrumental variable analysis thus utilized only for school grades.

The linear association between month of birth and school grades showed that each monthly increment of birth reduced academic achievement by a mean of 2.1% (e.g., those born in September have school grades on average 2.1% lower than those born in August). The raw association between month of birth and risk of suicide attempt (HR=1.004, 95% CI=1.002;1.007) was extremely small but reached significance because of our very large sample size. When the school grades variable was added to the model, the effect size of the association between month of birth and suicide attempt decreased and slightly shifted (HR=0.997, 95% CI=0.995;0.999). These results support the use of month of birth as a good instrument to predict suicide attempt risk as: 1) there is no solid theoretical assumption to explain the association between month of birth and suicide attempt and 2) the current sample size is powerful, which can result in effect sizes that, while statistically significant, are not meaningful (supplementary Figure 3 for the prevalence of suicide attempt by month of birth. Accordingly, we used the predicted values from the association between month of birth and school grades in an instrumental variable analysis to predict risk of suicide attempt.

Compared to the crude association reported above, results indicated a weaker association between school grades and suicide attempt (HR=0.71, 95% CI=0.64;0.78), supporting the existence of both confounding factors and, after controlling for confounders, a causal effect between academic achievement and suicide attempt risk.

**Univariate co-relative analyses**—Results from the co-relative analyses are presented in Table 2. For the three predictors (school grades, IQ, education level), findings showed decreased associations with suicide attempt when the degree of genetic relatedness and shared environment increased. Results showed that the observed model fitted the data better than the predicted model (AIC values; Table 2), suggesting that the assumptions of the co-relative model (relative to genetic and shared environmental effects) are not fully met. Nevertheless, residual associations were found when controlling for 100% of the genes and shared environment (predicted models extrapolated for MZ twins: *school grades*, HR=0.80, 95% CI=0.78;0.82, *IQ*, HR=0.83, 95% CI=0.81;0.86, and *education level*, HR=0.76, 95% CI=0.74;0.77), supporting the existence of some familial confounding and a causal effect.

These findings support potential causal associations between education (school grades, IQ, education level) and suicide attempt using two statistical approaches. To evaluate the differential importance of each predictor, we next conducted multivariate co-relative analyses.

#### The role of cognitive performance versus education-related variables

Here, we evaluated the role of IQ by controlling for school grades on the one hand and education level on the other hand.

**School grades and IQ.**—The first model was designed to evaluate the effect of school grades versus IQ in the prediction of risk for suicide attempt. The sample included 403,818 men (born 1972-1980), among which 12,162 reported suicide attempts (3.0%).

**Cox proportional hazards models:** In univariate analyses, results showed that higher values of both predictors were related to reduced risk of suicide attempt (*school grades*, HR=0.56, 95% CI=0.55;0.57 and *IQ*, HR=0.64, 95% CI=0.63;0.65). In multivariate analysis, the strong role of school grades was only modestly attenuated (HR=0.59, 95% CI=0.57;0.60) while the role of IQ decreased substantially (HR=0.91, 95% CI=0.89;0.94) but still remained significant.

**Multivariate co-relative analysis:** Co-relative analysis reinforced these results, and the predicted model provided a superior fit than the observed one (Table 3, model 1), so we focus here on the predicted results. When controlling for IQ (pairs concordant for IQ but discordant for school grades), the model provided further support for a strong and potentially causal association between school grades and suicide attempt. Moreover, the decreased association between IQ and suicide attempt reported in the multivariate model was also observed in the co-relative analysis controlling for school grades (pairs concordant for school grades but discordant for IQ). First, results indicated that, when controlling for school grades, the association between IQ and suicide attempt is no longer explained by the effect of shared genetic factors and familial environment (as indicated by similar effect sizes

between pairs of different genetic relatedness; Table 3). Second, 95% CI for full-sibling and MZ twin pairs overlapped with 1, indicating little support for a residual causal effect of IQ when controlling for school grades.

**Education level and IQ.**—The second model was designed to evaluate the effect of education level versus IQ in the prediction of risk for suicide attempt. The sample included 1,412,653 men (born 1951-1980), among which 42,597 had attempted suicide (3.0%).

<u>Cox proportional hazards models</u>: Univariate analyses supported the association between suicide attempt and both low education level (HR=0.64, 95% CI=0.64;0.65) and IQ (HR=0.68, 95% CI=0.67;0.68). A similar level of attenuation was seen for both predictors in the multivariate model (*education level*, HR=0.75, 95% CI=0.74;0.75 and *IQ*, HR=0.77, 95% CI=0.76;0.78).

**Multivariate co-relative analysis:** The predicted model provided a superior fit for this corelative analysis (Table 3; model 2). Results showed that the causal roles of both education level and IQ were attenuated compared to results from the univariate co-relative models (Table 2) but remained associated with risk of suicide attempt even in pairs of increased genetic relatedness. The residual extrapolated association in pairs of MZ twins was stronger for IQ than for education level. When controlling for IQ, part of the association between education level and suicide attempt was explained by familial factors (i.e., HR estimates were closer to 1 as an increasing degree of genetic relatedness was accounted for across pairs), with the modest residual association between education level and suicide attempt risk being interpreted as causal. However, when controlling for education level, the association between IQ and suicide attempt no longer showed evidence of familial confounding and is consistent with a causal role of IQ.

Beyond the overall role of education, these multivariate analyses underscore the importance of both cognitive (IQ) and non-cognitive (strong evidence for school grades, little evidence for education level) processes in risk for suicide attempt.

## Discussion

Numerous studies have shown the association between education and risk for suicidal behaviors, with higher education being considered a protective factor. Nevertheless, to our knowledge, only one study has supported the causality of this association (Rosoff et al., 2020). In the present study, we used complementary statistical methods to attempt to replicate and expand the findings reported by Rosoff and colleagues (2020).

First, using a co-relative design, we replicated the causal association between educational attainment and risk for suicide attempt (Rosoff et al., 2020). Here, we capitalized on the strong role of familial confounding factors to infer the causality between education level and suicide attempt risk (Kendler et al., 2014). These findings supported the role of genetic factors and familial environment, as observed by decreased HRs with increased degrees of genetic relatedness. This is in line with studies showing the heritability of both education level (Marks, 2017; Rowe and Jacobson, 1999) and suicide attempt (Edwards

et al., 2021) and underscores that their association is also partially explained by familial factors. Additionally, when accounting for genetic and familial environmental confounders, our results supported educational attainment as a potential causal mechanism mitigating the risk of suicide attempt. This reinforces the potential benefits of continued education in reducing suicide risk.

Second, while Rosoff et al. (2020) reported a non-causal role of cognitive performance, we did identify evidence of a causal association between high IQ at the beginning of adulthood (19 years old) and lower risk for subsequent suicide attempt. This result is, moreover, supported when controlling for education level. Indeed, the multivariate co-relative analysis showed that the effect of genetic and familial factors in the association between IQ and suicide attempt disappeared when controlling for education level, as indicated by similar effect sizes in pairs of increased genetic relatedness. However, the residual causal role of IQ as a potential protective factor for suicide attempt remained significant. It is worth mentioning that our measure of cognitive performance is different than that used by Rosoff et al. (2020): (1) IQ was measured at 19 years old as part of a two-day test before military conscription while Rosoff et al. (2020) extracted genetic variations (single nucleotide polymorphisms) for cognitive performance from genomewide association studies using older cohorts, (2) IQ was only available for men in the present study; (3) the measure used in this study was fairly homogeneous whereas the cognitive performance measure in the study of Rosoff et al. (2020) included various cognitive abilities. Overall, this observation brings some insight into the mechanisms that may explain the association between education and suicide attempt risk. Prior research has hypothesized a role for coping skills in risk of suicide attempts (Horwitz et al., 2018). Problem-solving, as evaluated in this study, is a key component of coping abilities and may explain the relationship between higher cognitive abilities and lower risk for suicide attempts (Spirito et al., 1996). Cognitive interventions have been recommended to improve problem-solving and coping abilities in patients with a history of suicide attempts (Ghahramanlou-Holloway et al., 2012; Gysin-Maillart et al., 2020). By providing support of a causal association, this study strengthens the need for cognitive interventions to decrease suicide-related morbidity, even before the occurrence of the first suicide attempt.

In addition, we expanded the results of Rosoff et al. (2020) by looking at school grades as a measure of academic achievement. In the Cox regression models including our three predictors, school grades had the strongest effect size in association with suicide attempt. The protective role of academic achievement in risk for suicidal behaviors is in accordance with previous studies (Gunnell et al., 2011; Kosidou et al., 2014; Sorberg Wallin et al., 2020), while we provide evidence, for the first time, of the likely causal nature of this association. In this study, academic achievement was supported to be causally related to suicide attempt risk by both the instrumental variable analysis, relying on the natural experiment of age differences within individual school classes (month of birth), and the co-relative analysis, controlling for genetic and familial confounders. This combination of inferential methods corroborates the causal role of academic achievement (Kendler and Gardner, 2010; Ohlsson and Kendler, 2020). Moreover, school grades remained associated with a lower risk of suicide attempt when controlling for cognitive performance, suggesting that additional non-cognitive mechanisms play a role in reducing suicide attempt

risk. As we controlled for genetic factors and familial environment in the co-relative design, these mechanisms are not likely to be related to family support or parental expectations during childhood and adolescence. Non-cognitive mechanisms involved in academic achievement might be related to specific environmental factors – e.g., being part of a peer group committed to their education, with potentially fewer exposures to risky behaviors such as drug use – or to specific personality traits such as low impulsivity and high conscientiousness, all of which are negatively related to suicidality in adolescence (Mars et al., 2019a, b). Academic achievement was evaluated early during adolescence and therefore constitutes a promising target for the prevention of suicidal behaviors. Previous studies showed promising results on improving academic achievement in youth (Bradshaw et al., 2009), but their effect on suicidality still needs to be confirmed (Wilcox et al., 2008). Intervention should be directed to youth who have low school grades, to identify their difficulties (detecting potential emotional problems or behaviors that would be related to suicidality), increase their motivation, and improve their grades.

The present study has some limitations that require further investigation. First, although we planned to combine natural experiments to improve our confidence in causal inference, we were not able to find a suitable instrument for the variables of cognitive performance and educational attainment. Co-relative analyses were used with all three predictors but the instrumental variable analysis only informed about academic achievement. Second, the measure of cognitive performance was available only for men, precluding our ability to investigate test for a causal association between cognitive performance and suicide attempt risk in women. As our results are different than those reported by Rosoff et al. (2020), the causal role of cognitive performance in suicidal behaviors warrants follow-up analyses. Finally, the current study captured suicide attempt via medical records, which likely reflect more severe suicide attempt cases (i.e., those requiring medical assistance).

To conclude, the current results shed new light on the risk for suicide attempts by emphasizing the possible causal roles of academic achievement, cognitive performance, and educational attainment. This clarifies the mechanisms underlying these associations, showing the involvement of both cognitive and non-cognitive processes. By supporting causal associations, our findings suggest that programs aiming to improve education during adolescence have the capacity to result in meaningful decreases in suicide risk.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Highlights

- This study clarifies the possible causality between education and suicide attempts
- We evaluated school grades and IQ in adolescence and education level in adulthood
- Lower education was associated with higher risk of later suicide attempt
- Causality was supported after controlling for confounders using natural experiments
- Promoting early education should decrease the long-term risk of suicide attempts

#### Table 1.

## Instrumental variables analysis

	Putative risk factors			
	School Grades	IQ	Education level	
<b>Preliminary step</b> (β, 95% CI)				
Association between putative risk factor and month of birth	-0.021 (-0.022; -0.021)	-0.006 (-0.006; -0.005)	-0.006 (-0.006; -0.005)	
Step 1 (HR, 95% CI)				
Association between month of birth and suicide attempt	1.004 (1.002; 1.007)	-	-	
Association between month of birth and suicide attempt, controlled for the putative risk factor	0.997 (0.995; 0.999)	-	-	
Step 2 (HR, 95% CI)				
Association between putative risk factor and suicide attempt, used the predicted values from step 1	0.71 (0.64; 0.78)	-	-	

#### Table 2.

Univariate co-relative model

	School Grades HR (95% CI)		IQ HR (95% CI)		Education level HR (95% CI)	
	Observed	Predicted	Observed	Predicted	Observed	Predicted
Population	0.60 (0.60; 0.61)	0.61 (0.61; 0.61)	0.67 (0.66; 0.67)	0.67 (0.66; 0.67)	0.62 (0.62; 0.63)	0.62 (0.62; 0.62)
Cousins	0.65 (0.64; 0.65)	0.63 (0.63; 0.63)	0.70 (0.69; 0.71)	0.69 (0.68; 0.69)	0.63 (0.62; 0.62)	0.64 (0.63; 0.64)
Half Siblings	0.69 (0.68; 0.70)	0.65 (0.65; 0.66)	0.72 (0.70; 0.74)	0.71 (0.70; 0.72)	0.62 (0.61; 0.63)	0.65 (0.65; 0.65)
Full Siblings	0.68 (0.67; 0.69)	0.70 (0.69; 0.71)	0.74 (0.74; 0.75)	0.75 (0.73; 0.76)	0.70 (0.69; 0.70)	0.68 (0.68; 0.69)
MZ Twins	-	0.80 (0.78; 0.82)	-	0.83 (0.81; 0.86)	-	0.76 (0.74; 0.77)
AIC	2646159.2	2646252.3	1527238.9	1527239.3	3592342.2	3592379.6

#### Table 3.

Multivariate co-relative model

	Model 1, school grades versus IQ HR (95% CIs)		Model 2, education level versus IQ HR (95% CIs)		
Co-relative pairs	School Grades Concordant for IQ, discordant for school grades	IQ Concordant for school grades, discordant for IQ	Education level Concordant for IQ, discordant for education level	IQ Concordant for education level, discordant for IQ	
	Observed model		Observed model		
Population	0.59 (0.57; 0.60)	0.91 (0.89; 0.94)	0.75 (0.74; 0.75)	0.77 (0.76; 0.78)	
Cousins	0.61 (0.54; 0.69)	0.91 (0.83; 1.00)	0.72 (0.68; 0.76)	0.76 (0.73; 0.79)	
Half Sibling	0.57 (0.40; 0.82)	1.15 (0.88; 1.49)	0.79 (0.72; 0.88)	0.78 (0.72; 0.85)	
Full Sibling	0.62 (0.52; 0.73)	0.91 (0.80; 1.04)	0.81 (0.77; 0.86)	0.79 (0.75; 0.82)	
MZ Twin	-	-	-	-	
AIC	308290.04	308655.92	1182370.1	1185196.9	
	Predicted model		Predicted model		
Population	0.59 (0.57; 0.60)	0.91 (0.89; 0.94)	0.74 (0.73; 0.75)	0.77 (0.76; 0.78)	
Cousins	0.60 (0.58; 0.62)	0.91 (0.88; 0.94)	0.76 (0.75; 0.77)	0.77 (0.76; 0.78)	
Half Sibling	0.61 (0.57; 0.66)	0.91 (0.86; 0.97)	0.77 (0.76; 0.80)	0.78 (0.76; 0.79)	
Full Sibling	0.63 (0.55; 0.73)	0.91 (0.81; 1.02)	0.81 (0.77; 0.85)	0.78 (0.75; 0.81)	
MZ Twin	0.68 (0.51; 0.92)	0.91 (0.72; 1.15)	0.88 (0.79; 0.97)	0.78 (0.73; 0.85)	
AIC	308285.31	308652.48	1182367.0	1185191.6	