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The causal effect of resilience on risk for drug abuse: a Swedish national instrumental variable, co-relative and propensity-score analysis

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Abstract

Background. We sought to quantify and investigate the causal nature of the association between resilience at age 18 and future drug abuse (DA).

Method. In a national sample of Swedish men (n = 1 392 800), followed for a mean of 30.3 years, resilience was assessed during military conscription and DA defined from medical, criminal and pharmacy registers. For causal inference, we utilized three methods: (i) instrumental variable analyses with the month of birth as the instrument; (ii) co-relative analyses using the general population, cousins, siblings and monozygotic twins; and (iii) propensity scoring on a subsample (n = 48 548) with strong resilience predictors. Cox proportional hazards models were utilized to examine survival time till DA diagnosis.

Results. Low resilience was most robustly predicted from internalizing symptoms. Lower levels of standardized resilience strongly predicted the risk for DA (HR = 2.31, 95% CIs 2.28–2.33). In instrumental, co-relative, and propensity score analyses, the association between resilience and DA was estimated at HR = 3.06 (2.44–3.85), 1.34 (1.28–1.39), and 1.40 (1.28–1.53), respectively. Sensitivity analyses suggested that our instrument was weak and, despite our large sample, likely under-estimated confounding.

Conclusions. Low resilience strongly predicts DA risk. Three different causal analysis methods, with divergent assumptions, concurred in estimating that an appreciable proportion of this association was causal, probably around 40%, with the remainder arising from confounding variables many of which are likely familial. Consistent with prior interventions focused on substance use prevention, our results suggest that prevention programs that increase resilience in adolescence should meaningfully reduce the long-term risk for DA.

While low levels of resilience (Rutter, 1985; Werner, 1993) are associated with increased risk for drug abuse (DA) (Meschke & Patterson, 2003; Rudzinski, McDonough, Gartner, & Strike, 2017), the degree to which this association results from causal processes or from confounding variables is less clear. A better understanding of the nature of the relationship between resilience and DA is of practical import. If resilience is causally related to DA risk, then interventions targeted to improve resilience should meaningfully reduce future rates of DA.

A number of prevention programs have demonstrated in experimental research designs that improving youth resilience reduces substance use (Botvin, Baker, Dusenbury, Botvin, & Diaz, 1995; Brown, Catalano, Fleming, Haggerty, & Abbott, 2005; Dodge et al., 2015). They do so by using various strategies, including strengthening the individual assets (e.g. self-efficacy, communication and coping skills, and emotional regulation) and social supports (e.g. positive relationships with parents) needed to overcome adversity. However, most such studies had short follow-up periods rarely extending into adulthood, and few examined the more clinically meaningful outcome of DA.

In Sweden, utilizing both structured personal interviews and a systematic record review, psychologists rated resilience on all men screened for military service, nearly the entire male population. In this study, we examine the potential causal effect of this measure on risk for DA in 1 392 800 Swedish males followed for mean of 30.3 years. A range of causal methods is increasingly used across research settings (Ohlsson & Kendler, 2019). Since each

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method has its own strengths and weaknesses, we use triangulation and rely on results from three different approaches to examine the support for causal inference. The first is an instrumental variable (IV) analysis based on evidence that month-of-birth predicts resilience and meets the statistical requirements for a valid instrument while the second is a co-relative design that controls for potential family confounders, including genetic factors. The third method is propensity score matching, which due to increased data requirements could only be applied to a subset of our sample with a rich set of predictors of resilience.

This paper has two major goals: (i) quantify the magnitude of the resilience-DA association in Swedish males, and (ii) determine the degree to which it is likely causal.

Methods

We analyzed information on individuals from Swedish population-based registers with national coverage. These registers were linked using each person's unique identification number replaced by a serial number to preserve confidentiality. We secured ethical approval from the Regional Ethical Review Board of Lund University.

In the main analysis, the outcome variable was DA which was identified in the Swedish medical and mortality registers by ICD codes [ICD8: Drug dependence (304); ICD9: Drug psychoses (292) and Drug dependence (304), Nondependent abuse of drugs (305; excluding 305.0); ICD10: Mental and behavioral disorders due to psychoactive substance use (F10–F19), except those due to alcohol (F10) or tobacco (F17)]; in the Suspicion Register by codes 3070, 5010, 5011 and 5012, that reflect crimes related to DA; in the Crime Register by references to laws covering narcotics (law 1968:64, paragraph 1, point 6) and drug-related driving offences (law 1951:649, paragraph 4, subsection 2 and paragraph 4A, subsection 2); and in the Prescribed Drug Register in individuals (excluding those suffering from cancer) who had retrieved (in average) more than four defined daily doses a day for 12 months from either of Hypnotics and Sedatives [Anatomical Therapeutic Chemical (ATC) Classification System N05C and N05BA] or Opioids (ATC: N02A). DA was treated as dichotomous variable.

The main explanatory variable, resilience, was collected from the Swedish Military Conscription Register, which includes results of the conscription examinations for nearly all 18-year-old men in Sweden. Resilience was designed by the Swedish military to assess the ability to cope with psychologically stressful situations and was scored on a normally distributed 1–9 scale. The score is assigned by psychologists who conduct, with every conscript, a semi-structured interview averaging 25 min. These psychologists are carefully trained so as to standardize assessments across Sweden. The conscript is encouraged to describe his everyday life, covering five areas: school, work experiences, leisure time, home environment, and emotional stability. Background information including school grades, job experiences, and test results are provided to the interviewer in advance. In the analyses, we have standardized resilience for each year [mean = 0, standard deviation (S.D.) = 1]. The Swedish military has shown that this measure strongly predicts the degree of coping and the quality of performance of conscripts under simulated battlefield conditions (Carlstedt, 1999).

In the database, we included all males born in Sweden 1951–1980 who had a resilience score from the Military Conscription Register ($n = 1\,395\,410$), excluding those with a DA registration prior to conscription ($n = 2610$). For individuals born in 1951, more extensive data relevant to risk for DA was collected at conscription through questionnaires (for details see online Appendix Table S1).

In the first analysis, we performed, for individuals born 1951, a linear regression with resilience as an outcome, including variables from the questionnaire as predictors. To assess the relative contribution for each predictor, we specified two models for each predictor. The first contained all predictors, and the second omitted the predictor of interest. By comparing these two models, we could assess the percentage of variance explained by each predictor by computing the Proportional Reduction of Error.

In the second analysis, we used a Cox proportional hazards model to investigate the risk of DA as a function of resilience, from date of conscription until end of follow-up (DA registration, death, emigration, or 12–31–2015). The hazard ratio (HR) represents the increased risk for DA per standard deviation decrease in resilience. We then used an IV approach to control for unmeasured confounding using month of birth as an instrument. We used month of birth because, with rare exceptions, all members of school classes in Sweden are born in the same calendar year. The month of birth is strongly related to academic achievement (Kendler et al., 2018) and we here test whether a similar association would be found with resilience. We used a two-stage-regression model adapted to a Cox-regression framework. The first stage predicts the expected value of resilience based on month of birth in a linear model. The first-stage F-test showed that our instrument fulfilled the assumption that resilience and month of birth were sufficiently strongly associated [$F = 2123.6$ (1/1 392 798), $p < 0.001$].

The predicted values were thereafter used in a Cox Regression model as the exposure variable. To obtain 95% confidence interval (CI), we used nonparametric bootstrap with 1000 replications. Methodological concerns have been raised with the use of month of birth as an instrument because of possible differences between children born at different times of the year. Indeed, our sample shows the parents of children born early in the year have a small but significant decrease in DA ($\chi^2 = 51.5$, df = 11, $p < 0.0001$) and increase in educational level [$F = 9.2$ (1/1 384 976; p: 0.0024)]. As these results might violate important IV assumptions, we conducted sensitivity analyses by adding controls for parental DA and educational status in both the first and second stage of the IV analysis to see their impact on our model results (see online Appendix Table S2).

Next, we used a propensity score analysis for individuals born 1951. Using the previously described linear regression model with resilience as outcome and variables from the questionnaire as predictors, the predicted values, ranging from −1.9 to 3.7, from this model were used as the 'propensity' for resilience. Thereafter, we used a stratified Cox proportional hazards models, with a separate stratum for each tenth of the predicted resilience (e.g. individuals with the predicted resilience between 0 and 0.1 belong to the same stratum) (Austin, 2011). This means that we are investigating the association between the true value of resilience and DA among individuals with similar values of expected resilience.

Finally, we utilized a co-relative design to examine if the regression results (i.e. the crude association between resilience and DA) reflect confounding by familial risk factors. From the Swedish Multi-Generation and Twin Registers, we identified all MZ twin, full-sibling and cousin pairs. Using stratified Cox proportional hazards models, with a separate stratum for each relative pair, we investigated the risk of DA as a function of resilience.

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The HR is then adjusted for a range of unmeasured genetic and environmental factors shared within the relative pair. MZ twins share 100% of their genes and their rearing environment suggesting that the HR for MZ twins is well controlled for all possible familial confounders. Full-siblings and cousins share, respectively, on average 50 and 12.5% of their genes identical by descent. Finally, we combined all four samples (i.e. population, twin, full-siblings, and cousins) into one dataset in which we performed two analyses. The first allowed all parameters for each sample to be independent (i.e. similar to four separate analyses). In the second, we modelled the association between resilience and DA 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, 0.5 for the sibling and 1 for the MZ twins. The HR for the second parameter gives an indication of the size of the familial confounding. If the second model fitted the data well, as indexed by the Akaike information criterion (AIC), we also obtained an improved estimation of the association among all relatives, but especially MZ twins where the data was sparse.

We estimated the proportion of the resilience-DA association that was potentially causal by calculating the ratio of the relevant beta-coefficients from our Cox models from our IV, propensity and co-relative designs and from the appropriate general population estimate. All statistical analyses were performed using SAS 9.4 (SAS Institute, 2012).

Results

Predictors of resilience

We began by examining predictors of resilience in a unique sample of 48 548 men born in 1951. For those years, the army released a range of self-report measures obtained at the conscription examination [at a mean (s.d.) age of 18.3 (0.5)] for which we selected 13. Table 1 presents, for these variables, results of a univariate and multivariate regression analysis predicting resilience. To assess the relative contributions of each predictor on the same scale, we performed a series of model comparisons (see methods for details). By far the strongest predictor was the internalizing common factor made of the 12 items (see online Appendix Table S1) assessing symptoms of anxiety, depression and somatization. The second strongest was low IQ followed by low parental monitoring and the externalizing common factor.

Association of resilience and DA, month of birth and resilience

In our sample of 1 392 800 subjects born 1951–1980 evaluated for Swedish army service in 1969–99 at a mean age of 18.3 (0.7) and followed up for a mean of 30.3 (s.d. 9.9) years, lower levels of standardized resilience strongly predicted future risk for DA (HR = 2.31, 95% CIs 2.28–2.32). Figure 1 depicts the association between resilience and month of birth. Aside from the months of January and February, a clear monotonic relationship is seen with individuals born later in the year having increasingly lower levels of resilience. Fitting a linear model to this relationship produced a β coefficient of 0.0115 (0.0110–0.0120). That is, for each month of later birth, resilience scores declined by 1.15% of a standard deviation. So, the youngest children in any birth year (born in December) have, on average, resilience scores ∼15% of a s.d. less than the oldest, born in January. Examined on its own, the later month of birth has a very modest positive relationship to DA risk (HR = 1.013, 1.010–1.016). However, when resilience is controlled for, this association substantially declines and is very close to unity: HR = 1.005, 1.003–1.008.

Instrumental variable, propensity score and co-relative analyses

In the IV analysis, the association between resilience and DA was calculated as HR = 3.07 (2.44–3.85), producing an unrealistically large estimated proportion of causal effect: 133.3% (95% CIs 108.3–159.5). Among Swedish men born in 1951 (who had predictors of resilience sufficient for propensity score analysis), the raw HR between resilience and risk for DA was very similar to that seen in our entire sample (2.27, 2.12–2.43) and the HR estimated from the propensity analysis was 1.40 (1.28–1.53). For these analyses, our estimate of the proportion of the resilience–DA relationship which is causal equaled 41.0% (32.9–47.9).

Results from the co-relative analyses (Table 2) demonstrate the expected, and substantial, monotonic decline from the general population to MZ twins. Also, as expected, because of heterogeneous sample sizes, HRs were more precise when examining the general population, cousins, and siblings, and much less accurate among MZ twins. Our co-relative model fits the observed results quite well for the general population and full-siblings but modestly overestimated the HRs for cousins. However, because of the large number of cousin pairs, this produced a considerable deterioration in fit, as indexed by AIC. Also, as expected, the model produced a considerable increase in the precision of the most important HR in the model – that derived from MZ twins – which is predicted to equal 1.34 (1.28–1.39). That is, this model predicts that one s.d. difference in resilience in a pair of MZ twins predicts a 34% greater risk for DA in the low *v.* high scoring twin. From these results, we estimated the proportion of causal effects of the resilience-DA relationship at 35.3% (30.1–39.3).

Discussion

We examined the prospective association between resilience, measured in late adolescence, and subsequent risk for DA in a Swedish registry including 1 392 800 men born 1951–1980 evaluated for Swedish army service in 1969–99. We then attempted to quantify the degree to which that association was likely causal. We observed the expected association between low resilience and risk of DA, with each s.d. increase in lowered resilience associated with a 2.3-fold increase in risk of DA. Because standard methods can be biased, three different validated methods for causal analysis were utilized to examine the extent to which this association might be due to causal processes. All three methods confirmed that a substantial amount of resilience-DA association is causal in nature.

In using and reporting the results from three different causal methods selected *a priori* for their potential to answer this critical question, we were confronted with a common problem, comparing the weaknesses and strengths of each method. The first method, utilizing an IV analysis with the month of birth as an IV, suggested that all of the resilience-DA association was causal. The second method, propensity score matching, suggested, more plausibly, that ∼40% of the association of resilience and DA was causal in nature. The third method, the co-relative design, produced results quite similar to those of the propensity analysis, estimating that ∼35% of the resilience-DA association was causal. While these methods agreed on the nature of the association, they disagreed on the degree to which that relationship was also

Table 1. Linear regression model predicting low resilience scores[a]

Variable	Univariate regression models	Multivariate regression model	Proportional reduction of error (%)
Fathers alcohol consumption (Mid *v.* Low)	−0.036 (−0.058; −0.0143)	−0.073 (−0.090; −0.056)	0.23
Fathers alcohol consumption (High *v.* Low)	0.599 (0.551; 0.646)	0.057 (0.019; 0.095)	
Parental education (Low *v.* High)	0.422 (0.453; 0.390)	0.112 (0.087; 0.138)	0.17
Parental education (Mid *v.* High)	0.166 (0.186; 0.147)	0.067 (0.041; 0.093)	
Parental abuse (Sometime *v.* Never)	−0.024 (−0.043; −0.005)	−0.050 (−0.065; −0.036)	0.10
Parental abuse (Occasionally *v.* Never)	0.260 (0.230; 0.291)	−0.024 (−0.047; −0.000)	
Parental abuse (Often *v.* Never)	0.793 (0.713; 0.873)	0.007 (−0.056; 0.070)	
Disruption in family	0.415 (0.392; 0.438)	0.190 (0.171; 0.208)	0.83
Low parental monitoring	0.363 (0.353; 0.374)	0.170 (0.160; 0.180)	2.36
Move during childhood 1 *v.* 0	−0.009 (−0.031; 0.013)	−0.018 (−0.035; −0.002)	0.03
Move during childhood 2 *v.* 0	0.037 (0.006; 0.067)	0.002 (−0.022; 0.025)	
Move during childhood 3 + *v.* 0	0.152 (0.121; 0.188)	0.037 (0.011; 0.063)	
Urbanization *v.* Countryside	0.016 (−0.006; 0.038)	0.046 (0.029; 0.063)	0.06
Sniffing glue	0.494 (0.479; 0.520)	0.046 (0.024; 0.068)	0.03
Low IQ (1 unit)	0.330 (0.322; 0.338)	0.258 (0.250; 0.265)	9.30
Externalizing behavior (1 Std)	0.461 (0.450; 0.473)	0.159 (0.148; 0.170)	1.53
Internalizing behavior (1 Std)	0.609 (0.600; 0.617)	0.523 (0.514; 0.531)	24.20
Drug use score (1 Std)	0.212 (0.203; 0.221)	0.067 (0.059; 0.075)	0.53
Alcohol score (1 Std)	0.147 (0.137; 0.158)	−0.082 (−0.092; −0.073)	0.63
R^2		42.7%	

[a]Standardized with mean 0 and s.d. = 1; high values are low resilience.

Fig. 1. The association (depicted in blue) between the month of birth and resilience assessed at age 18 in our sample of 1 392 800 Swedish male Swedish adolescents. A linear model predicted that being 1-month younger reduced resilience in this sample by an average of 1.15% of a s.d.

influenced by confounders with the IV results being the outlier. How should we interpret these discrepancies?

Theoretically, the IV analyses are the strongest. We have good reason to think that month of birth satisfies the key 'as-if random' assumption (Dunning, 2012) and we showed empirically that it had no appreciable direct association with DA once resilience levels were controlled for. Therefore, like a randomized controlled trial, our IV analyses should have controlled for all known and unknown confounders. The next strongest analysis methodologically was the co-relative design. Its main limitation is that, while it controls for all known and unknown familial confounders, confounding influences that impact on both resilience and risk for DA at the individual level are not controlled for. Propensity score matching is the weakest in that it only controls for measured covariates and does best, as in this situation, where diverse strong potential confounders are assessed.

However, IV analyses that use 'weak instruments' – those with only modest associations with the predictor, here resilience – can produce unstable results which typically underestimate the impact of confounders (Bound, Jaeger, & Baker, 1995). Because of these concerns (Hahn & Hausman, 2003), we performed sensitivity analyses to determine the potential for weak instruments to explain this deviation (online Appendix Table S2). These analyses indeed suggested that our IV estimation was unstable. Despite passing the most common test for weak instruments with a strikingly statistically significant first-stage F-test [$F = 2123.6$ (1/1 392 798), $p < 0.001$], the first-stage R^2 ($R^2 = 0.02$) for this study was well under the explanatory threshold (<0.1) (Hahn & Hausman, 2003). Additionally, while our sample was large, it was far short of the number needed to produce stable estimates (>11 000 000) given our instrument's small effect size (Boef, Dekkers, Vandenbroucke, & Le, 2014). Together, these additional tests led us to conclude that our IV estimate was likely biased and underestimated the impact of confounders on the resilience-DA association. Since sample sizes are increasing rapidly across a range of fields, future analyses may benefit from utilizing thresholds for determining instrument strength that are independent of sample size.

In sum, we suggest one main conclusion from our three statistical models. All three models provided strong statistical support

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Table 2. Results of the co-relative analysis of the association between resilience and drug abuse

	N pairs	Hazard ratio (± 95% Confidence Interval) for drug abuse	
		Observed	Predicted
Population	1 392 800[a]	2.31 (2.28–2.33)	2.29 (2.27–2.31)
Cousin	477 903	2.05 (2.01–2.08)	2.14 (2.13–2.16)
Full sibling	382 732	1.78 (1.75–1.82)	1.75 (1.72–1.78)
Monozygotic twins	2354	1.15 (0.83–1.59)	1.34 (1.28–1.39)
AIC (Akaike, 1987)		1 427 563.8	1 427 582.4

[a]Individuals.

for the hypothesis that a meaningful proportion of the resilience-DA relationship is causal. This would lead us to conclude that an effective intervention aimed at increasing resilience in adolescence would likely produce a meaningful reduction in rates of DA. We think the discrepancy between our three models resulted from methodological limitations of our weak instrument which were not compensated for despite our relatively large sample. We would therefore conclude that a substantial proportion of the association between resilience and DA is not causal and the result of a range of confounders, many of which are likely familial. This, however, would not imply that intervention would not be efficient.

The inference of causal relationships from observational data should always be considered tentative (Ohlsson & Kendler, 2019). But confidence can be considerably increased if similar results are obtained with different methods that have varying strengths and limitations, a method sometimes termed 'triangulation' (Munafo & Davey, 2018). Given our three quite different methodological approaches, we consider it likely that our conclusion is valid.

The interpretation of our findings is also dependent on the nature of the resilience measure obtained by the Swedish Military. We found that, examining a wide range of self-report measures collected at conscription, low resilience was far and away most strongly predicted by internalizing symptoms of anxiety, depression and somatization, followed by low IQ and low parental monitoring which indirectly assesses the closeness and quality of parent–child relationships (Crouter & Head, 2002; Stattin & Kerr, 2000). These results are consistent with prior evidence that resilience is associated with individual assets such as IQ, self-esteem, self-efficacy, problem-solving and the ability to cope with negative affect, often produced by stress (Fergus & Zimmerman, 2005; Rudzinski et al., 2017; Rutter, 1985). External protective factors, such as close relationships with parents or other adults, can also promote resilience (Fergus & Zimmerman, 2005; Luthar, Cicchetti, & Becker, 2000).

Through what possible mechanisms could month of birth impact on resilience? Dixon et al. (Dixon, Horton, & Weir, 2011) proposed a model of what they term the 'relative age effect' in which older children in each school year develop a spiral of an accumulated advantage as a result of increased maturity and opportunity → positive self-concept → increased motivation. The effect works in the opposite direction for the younger children. Key to this hypothesis is the consistent evidence that within each school year, birthdate impacts appreciably on both academic and sports performance, especially in boys, with older boys performing better in both domains (Bell, Massey, & Dexter, 1997; Dixon et al., 2011; Thompson, Barnsley, & Battle, 2010). Sports participation in school is related to greater resilience (Hawkins & Mulkey, 2005), lower symptoms of depression (Armstrong & Oomen-Early, 2009) and in several studies, including in Swedish elementary, middle and high-school students, higher self-esteem (Taylor, 1995; Wagnsson, Lindwall, & Gustafsson, 2014; Weiss & Ebbeck, 1996). However, younger boys in each school year are more likely to drop out of sports (Crane & Temple, 2015; Delorme, Chalabaev, & Raspaud, 2011; Lemez, Baker, Horton, Wattie, & Weir, 2014) and to have lowered levels of self-esteem and self-efficacy (Thompson et al., 2010).

Finally, the results of this study support the likely efficacy of interventions implemented in childhood or adolescence to reduce risk for DA by increasing resilience. Such programs are typically offered to vulnerable youth to enhance the individual assets and environmental supports associated with resiliency. For example, Cognitive Behavioral Intervention for Trauma in Schools (CBITS) builds coping skills and improves peer and parental relationships among youth experiencing adversities like exposure to violence (Stein et al., 2003). However, it can be challenging to identify eligible students and to avoid stigmatizing them with service delivery, so these programs usually reach only a small percentage of youth who could benefit from them.

Social and emotional learning (SEL) programs are also designed to promote individual assets (Durlak, Weissberg, Dymnicki, Taylor, & Schellinger, 2011), and some multi-component programs target individual and social factors related to resilience (Catalano, Berglund, Ryan, Lonczak, & Hawkins, 2004). Many of these programs can be delivered universally, thereby avoiding stigmatizing at-risk youth. However, broad dissemination of these programs is also lacking, which greatly reduces their potential to prevent DA (Fagan et al., 2019; Greenberg et al., 2003). Moreover, while some have been shown to prevent drug use (Durlak, Weissberg, & Pachan, 2010; Foxcroft & Tsertsvadze, 2011), most have not assessed impact on DA because they do not follow participants into adulthood when DA is more prevalent. Evidence from this study that resilience and DA are causally related suggests that researchers should evaluate universal SEL and multi-component programs and programs for vulnerable youth for long-term effects on DA, as well as shorter-term outcomes like coping skills, parent/child bonds and/or mental health. Researchers should communicate positive findings to potential users to increase demand for and dissemination of these programs, especially in schools given their ability to reach youth of all ages and backgrounds with services that can significantly reduce DA (Fagan et al., 2019).

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Limitations

These results should be interpreted in the context of four potentially significant methodological limitations. First, our assessment of DA was based entirely on data from Swedish registries. Such sources have important methodological advantages (e.g. no refusals or reporting biases), but they do not replicate results of interview-based assessments. On average, our cases are probably more severely ill than those who meet DSM-5 criteria for substance use disorder in an epidemiological sample (Association, 2013). However, the lifetime prevalence of DA/dependence in nearby Norway is only slightly higher than the estimates obtained in Sweden (Kringlen, Torgersen, & Cramer, 2001).

Second, our instrument – month of birth – has some limitations as it is weakly predicted by parental educational and risk for DA. Results did not appreciably differ when we included these variables as covariates. Furthermore, the association in our IV analysis between our instrument and risk factor – resilience – was relatively modest. It is likely that our IV estimates may have been upwardly biased by a weak instrument, potentially implying that IV estimation requires stronger instruments than current guidance suggests.

Third, while our IV analyses should protect us against the impact of reverse causation (i.e. prior drug use predicting both low resilience AA and DA risk) (Cingolani & de Crombrugghe, 2012; Yu, 2018), we evaluated this bias by re-analyzing our data including varying buffer periods in which we censored DA registrations soon after the assessment of resilience, as early drug use should predict early DA registration. Buffer periods of up to 8 years produced no meaningful changes in the causal resilience-DA associations from our IV, co-relative or propensity score analyses (online Appendix Table S2).

Finally, we have, in these analyses, used our resilience measure in an atypical manner – to predict risk for DA rather than linking it, as is more typical, to responses to adversity. Furthermore, our measure is somewhat unusual in construction and it is not easy to compare with the many other resilience measures available in the literature (Windle, Bennett, & Noyes, 2011).

Conclusion

In a national sample of Swedish males, low levels of resilience assessed in late adolescence are strongly associated with future risk for DA. Three different statistical methods – IV, co-relative and propensity score analyses – concur in suggesting that an appreciable proportion of this association, probably around 40%, is causal. Through our large, representative sample, our long-term follow-up and our 'hard' clinical outcome, these results complement and extend prior intervention studies seeking to demonstrate that improved levels of resilience through interventions in adolescence are likely to reduce risk for subsequent DA.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291719003842.

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Conflicts of interest. None of the authors have any conflicts of interest to declare.

Compliance with ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. We secured ethical approval for this study from the Regional Ethical Review Board of Lund University (No. 2008/409).

Informed consent. As approved by Swedish ethical authorities, informed consent was not obtained from individual participants included in this study.

Location of where work was done. Lund University, Virginia Commonwealth University, Stony Brook University Health Sciences Center, University of Florida

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