1	Adolescent victimization and self-injurious thoughts and behaviors:
2	A genetically sensitive cohort study
3	
4 5	Jessie R. Baldwin ¹ , MSc, Louise Arseneault ¹ , PhD, Avshalom Caspi ^{1,2,3} , PhD, Terrie E. Moffitt ^{1,2,3} , PhD, Helen L. Fisher ¹ , PhD, Candice L. Odgers ^{4,5} , PhD,
6	Antony Ambler ¹ , MSc, Renate M. Houts ² , PhD, Timothy Matthews ¹ , PhD, Dennis
7	Ougrin ⁷ , MBBS, PhD, Leah S. Richmond-Rakerd ² , PhD, Ryu Takizawa ^{8,9} , MD, PhD &
8	Andrea Danese ^{1, 7,10} , MD, PhD.
9 10	Author Affiliations:
11	¹ Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry,
12	Psychology and Neuroscience, King's College London, London, UK
13	² Department of Psychology and Neuroscience, Duke University, Durham, NC, USA
14	³ Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC,
15	USA
16	⁴ Department of Psychology and Social Behavior, University of California, Irvine,
17	Irvine, CA, USA
18	⁵ Sanford School of Public Policy, Duke University, Durham, NC, USA
19	⁶ Department of Psychological Medicine, Institute of Psychiatry, Psychology and
20	Neuroscience, King's College London, London, UK
21	⁷ Department of Child and Adolescent Psychiatry, Institute of Psychiatry, Psychology
22	and Neuroscience, King's College London, London, UK
23	⁸ Department of Clinical Psychology, Graduate School of Education, The University of
24	Tokyo, Tokyo, Japan
25	⁹ Department of Neuropsychiatry, Graduate School of Medicine, The University of
26	Tokyo, Tokyo, Japan
27	¹⁰ National and Specialist CAMHS Trauma and Anxiety Clinic, South London and
28	Maudsley NHS Foundation Trust, London, UK
29	

- 30 Correspondence: Dr Andrea Danese, Social, Genetic and Developmental Psychiatry
- 31 Centre (MRC), Institute of Psychiatry, Psychology and Neuroscience, De Crespigny
- 32 Park, Denmark Hill, London, SE5 8AF, United Kingdom. Tel: +442078480601. Fax:
- 33 +442078480866, Email: andrea.danese@kcl.ac.uk
- 35 Word count: 2992
- 36 Number of tables: 1
- 37 Number of figures: 3
- 38 Number of references: 38
- 39 Abstract word count: 350
- 40 Key points word count: 99

58 59	Key points:
60	Question: Do pre-existing vulnerabilities contribute to the risk for self-injurious
61	thoughts and behaviors in victimized adolescents?
62	
63	Findings: In stringent analyses of a population-representative cohort of 2,232 twins,
64	we found that the experience of adolescent victimization independently contributed to
65	a small elevation in risk for suicidal ideation and self-harm but not to risk for suicide
66	attempt. A large proportion of the observed risks in victimized adolescents was
67	accounted for by non-causal mechanisms involving pre-existing familial and
68	individual vulnerabilities.
69	
70	Meaning: To prevent self-injurious thoughts and behaviors in victimized adolescents,
71	interventions should both address the experience of victimization and target pre-
72	existing vulnerabilities.
73	
74	
75	
76 77	
78	
79	
80 81	
82	
83	
84	
85	
86	
87	
88	

90	Abstract
91	Importance
92	Victimized adolescents are at elevated risk of self-injurious thoughts and behaviors.
93	However, poor understanding of causal and non-causal mechanisms underlying this
94	association hampers the development of effective interventions to prevent premature
95	death in adolescents.
96	
97	Objective
98	To test the contribution of non-causal mechanisms to the association between
99	adolescent victimization and self-injurious thoughts and behaviors, using co-twin
100	control and propensity score methods.
101	
102	Design
103	Prospective birth-cohort study (the Environmental Risk [E-Risk] Longitudinal Twin
104	Study). Assessments were conducted between 1999 and 2014 when participants
105	were aged 5, 7, 10, 12, and 18 years.
106	
107	Setting
108	Nationally representative sample from Great Britain assessed through home visits.
109	
110	Participants
111	2232 twins (1116 twin pairs) born in England and Wales from January 1, 1994 to
112	December 4, 1995.
113	
114	Exposure
115	Adolescent victimization was assessed through interviews with Study members and
116	co-informant questionnaires at the age 18 assessment.
117	

118 Main outcomes and measures

- 119 Suicidal ideation, self-harm, and suicide attempt in adolescence were assessed
- 120 through interviews with Study members at age 18 years.
- 121

122 Results

- 123 Of 2232 participants in the E-Risk Study, 2055 were included in the analysis.
- 124 Victimized adolescents showed elevated risk for suicidal ideation (odds ratio [OR]=
- 125 2.17, 95%CI=1.93-2.44), self-harm (OR=2.38, 95%CI=2.10-2.69), and suicide
- attempt (OR=3.14, 95%CI=2.54-3.88). These associations were largely attenuated
- 127 after accounting for pre-existing familial and individual vulnerabilities through co-twin
- 128 control and propensity score analyses, respectively. Nevertheless, in the most
- 129 stringent analyses using propensity scores within the monozygotic co-twin control
- design, victimized adolescents still showed elevated risk for suicidal ideation
- 131 (OR=1.36, 95%CI=1.06-1.76) and self-harm (OR=1.50, 95%CI=1.18-1.91), but not
- 132 suicide attempt (OR=1.28, 95%CI=0.83-1.98).
- 133

134 Conclusion and Relevance

Over and above pre-existing familial and individual vulnerabilities, exposure to 135 victimization in adolescence was independently associated with a small elevation in 136 risk for suicidal ideation and self-harm. However, a substantial proportion of the 137 observed risk for self-injurious thoughts and behaviors in victimized adolescents was 138 accounted for by non-causal mechanisms involving such prior vulnerabilities. This 139 suggests that primary prevention of adolescent victimization and targeted therapeutic 140 141 interventions could partly reduce risk for suicidal ideation and self-harm. 142 Furthermore, secondary preventative strategies addressing pre-existing 143 vulnerabilities have the potential to substantially reduce risk for premature death in 144 victimized adolescents.

145

Adolescent victimization and self-injurious thoughts and behaviors:

147 148

A genetically sensitive cohort study

149 Suicide is the third leading cause of death among adolescents worldwide.¹ Suicide

attempts are often preceded by suicidal ideation and self-harm,² which are

151 particularly prevalent in adolescents.³ To prevent self-injurious thoughts and

behaviors in adolescence, it is important to identify proximal risk factors that can be

153 modified through intervention.^{4,5}

154 Here we consider the role of adolescent victimization. One in three adolescents

155 experiences severe victimization,⁶ due to exposures both in the community (e.g.,

156 crime, sexual victimization, and bullying) and in the family (e.g., maltreatment).⁷⁻⁹

157 Furthermore, these stressful experiences may be particularly harmful to adolescents

because of the major neurobiological, emotional, and social changes that take place

during this period.^{10,11} Previous studies have suggested that victimized adolescents

160 have elevated risk for self-injurious thoughts and behaviors.¹²⁻¹⁵ However, confusion

about the relative contribution of causal and non-causal mechanisms complicates the

162 interpretation of these findings and hampers the development of effective

163 interventions.¹⁶

Victimized adolescents might be at high risk for self-injurious thoughts and behaviors
by virtue of exposure to maltreatment, bullying, or crime. Alternatively, their risk might

be high due to pre-existing liability and earlier experiences. This alternative, non-

167 causal interpretation is plausible because both family-wide factors (e.g., family history

168 of psychopathology, socio-economic disadvantage) and individual factors (e.g.,

169 childhood victimization, cognitive deficits, stress-reactive personality traits) can

170 predispose adolescents to experience victimization^{6,17,18} and also influence risk for

171 self-injurious thoughts and behaviors.¹⁹

- 172 Here we report a stringent test of these non-causal interpretations capitalizing on
- design and analytical features with complementary strengths. To account for family-
- 174 wide factors, we used a co-twin control design²⁰ to test whether adolescents with the
- same genotype and rearing environment but different exposure to adolescent
- 176 victimisation had different risk for self-injurious thoughts and behaviors.
- 177 Furthermore, to account for individual factors, we used propensity score matching²¹
- to test whether adolescents with similar individual propensity to experience
- 179 victimization but different exposure to adolescent victimisation had different risk for
- 180 self-injurious thoughts and behaviors.

182 Method

183 Study sample

184 Participants were members of the Environmental Risk (E-Risk) Longitudinal Twin Study, which tracks the development of a birth cohort of 2232 British children. The 185 sample was drawn from a larger birth register of twins born in England and Wales in 186 1994-95.²² Full details about the sample are reported elsewhere.²³ Briefly, the E-Risk 187 sample was constructed in 1999-2000, when 1,116 families (93% of those eligible) 188 189 with same-sex 5-year-old twins participated in home-visit assessments. This sample comprised 56% monozygotic (MZ) and 44% dizygotic (DZ) twin pairs; sex was evenly 190 191 distributed within zygosity (49% male). Families were recruited to represent the U.K. 192 population of families with newborns in the 1990s, on the basis of residential location 193 throughout England and Wales and mother's age. Teenaged mothers with twins were over-selected to replace high-risk families who were selectively lost to the register 194 195 through non-response. Older mothers having twins via assisted reproduction were under-selected to avoid an excess of well-educated older mothers. The study sample 196 represents the full range of socioeconomic conditions in Great Britain, as reflected in 197 198 the families' distribution on a neighborhood-level socioeconomic index (ACORN [A 199 Classification of Residential Neighbourhoods], developed by CACI Inc. for commercial use in Great Britain)²⁴: 25.6% of E-Risk families live in "wealthy achiever" 200 neighborhoods compared to 25.3% nationwide; 5.3% vs. 11.6% live in "urban 201 prosperity" neighborhoods; 29.6% vs. 26.9% live in "comfortably off" neighborhoods; 202 203 13.4% vs. 13.9% live in "moderate means" neighborhoods; and 26.1% vs. 20.7% live 204 in "hard-pressed" neighborhoods. E-Risk underrepresents "urban prosperity" neighborhoods because such households are likely to be childless. 205 206 Follow-up home visits were conducted when the children were aged 7 (98% 207 participation), 10 (96%), 12 (96%), and 18 (93%). Home visits at ages 5, 7, 10, and

208 12 years included assessments with participants as well as their mother (or primary caretaker); the home visit at age 18 included interviews only with the participants. 209 210 Each twin participant was assessed by a different interviewer. The average age of 211 the twins at the time of the assessment was 18.4 years (SD = 0.36); all interviews 212 were conducted after the 18th birthday. There were no differences between the 2,066 participants who took part at age 18 and those who did not in terms of socioeconomic 213 status (SES) assessed when the cohort was initially defined (χ^2 =0.86, p=0.65), age-5 214 215 IQ scores (t=0.98, p=0.33), age-5 internalizing or externalizing behavior problems 216 (t=0.40, p=0.69 and t=0.41, p=0.68, respectively), or childhood victimization (z=0.51, 217 p=0.61). Of the Study members who participated in the age-18 assessment, 99.5% 218 (2055) had complete data on adolescent victimization and self-injurious thoughts and 219 behaviors.

The Joint South London and Maudsley and the Institute of Psychiatry Research
Ethics Committee approved each phase of the study. Parents gave informed consent
and twins gave assent between 5-12 years and then informed consent at age 18.

223 Adolescent victimization

These measures have been described previously⁶ and details are provided in the 224 eMethods of the Supplement. Briefly, at age 18, participants were interviewed about 225 exposure to a range of adverse experiences between 12-18 years using the Juvenile 226 227 Victimization Questionnaire 2nd revision (JVQ-R2)²⁵ adapted as a clinical interview. 228 Each co-twin was interviewed by a different research worker, and each JVQ question 229 was asked for the period 'since you were 12'. Age 12 is a salient age for our 230 participants because it is the age when British children leave primary school to enter 231 secondary school. The JVQ has good psychometric properties²⁶ and was used in the 232 U.K. National Society for the Prevention of Cruelty to Children (NSPCC) national survey^{27,28}, thereby providing important benchmark values for comparisons with our 233

cohort. Our adapted JVQ-R2 comprised 45 questions covering 7 different forms of
victimization: maltreatment, neglect, sexual victimization, family violence, peer/sibling
victimization, cyber-victimization, and crime victimization. Exposure to each type of
adolescent victimization was coded by trained raters using a 3-point scale, in which
"0" indicated "no exposure," "1" indicated "probable" or "less severe" exposure, and
"2" indicated "definite" or "severe" exposure.

- 240 The adolescent poly-victimization variable was derived by summing all victimization
- experiences that received a code of "2": (i.e., severe exposure): 64.6% of
- adolescents had zero severe victimization experiences; 19.2% had 1; 9.4% had 2;
- 4.5% had 3; 1.5% had 4; 0.5.% had 5; and 0.2% had 6 severe victimization

experiences. We winsorized the adolescent poly-victimization distribution into a four

- category variable (0, 1, 2, and 3+ severe experiences).
- 246 Informant reports of adolescent victimization. At age 18, each study member's co-
- twin and parent (usually mother) were asked to reply to a confidential questionnaire
- which inquired whether the Study member had ever been the victim of each of the 7
- 249 different forms of victimization assessed in the adapted JVQ-R2 interview. We
- summed affirmative responses to these questions, within each reporter. The
- correlation between co-twin and parental reports was r=0.38; between co-twin and
- 252 Study members' JVQ reports, r=0.38; and between parental and Study members'

253 JVQ reports, r=0.34.

254 Self-injurious thoughts and behaviors

Study members were privately interviewed at age 18 about suicidal ideation, selfharm and suicide attempts since age 12 using a life history calendar. To assess suicidal ideation, participants were asked whether they thought a lot about death; thought it would be better if they were dead; or thought about a plan to commit suicide. We defined suicidal ideation as an affirmative answer to any of these

questions. To assess self-harm, participants were asked if they had tried to hurt
themselves to cope with stress or emotional pain. To assess suicide attempt,
participants were asked if they had tried to kill themselves. No Study member
completed suicide. Participants who reported self-harm or suicide attempt were

- further queried about the types of self-injurious behavior that they engaged in.
- 265 Individual characteristics included in the propensity score
- 266 In order to account for pre-existing individual differences between victimized and
- 267 non-victimized adolescents, we derived a propensity score for adolescent
- victimization. The propensity score included 11 child-specific characteristics
- 269 prospectively measured before age 12 years and selected based on previous
- findings^{6,18,29,30}: childhood victimization, social isolation, IQ, internalizing problems,
- externalizing problems, self-harm, and traits comprising the five-factor model of
- 272 personality (openness to experience, conscientiousness, extraversion,
- agreeableness, and neuroticism) (see eTable 1 in the Supplement for details).
- 274 Participants with missing data for these covariates (N=119) did not differ from those
- with complete data (N=1936) according to adolescent victimization and self-injurious
- thoughts and behaviors (see eTable 2 in the Supplement).

277 Statistical analysis

- 278 We first calculated prevalence rates, sex differences in prevalence, and heritability
- estimates for data on suicidal ideation, self-harm, and suicide attempt. Sex
- 280 differences in outcomes were estimated using Generalized Estimating Equations
- 281 (GEE) with binomial function (logistic regression) and an exchangeable correlation
- structure to account for familial clustering in Stata 15 (StataCorp). Heritability
- estimates were calculated using 'Open Mx' in R.

284 We next used GEE analyses to test [1] the associations of adolescent poly-

victimization with self-injurious thoughts and behaviors; [2] the sensitivity of the

findings across informants to examine common-method bias;³¹ and [3] the sensitivity

of the findings across different measure components (seven individual victimizationtypes).

To test whether family-wide factors confounded the associations, we used a co-twin control design with GEE to parse the effect of adolescent poly-victimization on selfinjurious thoughts and behaviors into *between-twin pair effects* and *within-twin pair effects*.³² Because co-twins share their rearing environment as well as half (dizygotic twins) or all (monozygotic twins) their genes, significant *within-twin pair effects* would indicate that adolescent poly-victimization is associated with self-injurious thoughts and behaviors independent of latent, family-wide factors.

To test whether individual factors confounded the associations, we used two 296 297 propensity-score analyses. First, we used the Stata command 'teffects psmatch' (with 298 robust standard errors) to derive a propensity score for adolescent victimization (i.e., 299 exposure to 1, 2, or 3+ types) versus no victimization, and matched victimized and 300 non-victimized adolescents with a similar propensity score. We then estimated the 301 average treatment effect (ATE), which reflects the excess prevalence of self-injurious 302 thoughts and behaviors in victimized adolescents versus non-victimized adolescents 303 matched for the propensity score. Second, to estimate the joint bias owing to family-304 wide and individual effects, we expanded the above monozygotic co-twin control 305 regression model by also accounting for the propensity score.

Further details of the statistical analyses are provided in the eMethods of theSupplement.

308

309 **Results**

310 Self-injurious thoughts and behaviors in adolescence

Nearly a quarter (22.9%) of Study members described some form of self-injurious

thoughts and behaviors, with 18.4% (N=379) reporting suicidal ideation, 13.4%

313 (N=275) reporting self-harm, 3.8% (N=79) reporting suicide attempt, and substantial

overlap between groups (Figure 1, Panel A). Among those who reported self-harm or

suicide attempt, cutting was the most prevalent self-injurious behavior (76.1%),

followed by overdosing (22.2%), and burning (13.5%) (Figure 1, Panel B). The overall

prevalence of self-harm was greater in females than males (OR=1.79, 95%CI=1.34-

2.39, p<0.001), but there were no significant sex differences in the prevalence of

suicidal ideation (OR=1.04, 95%CI=0.81-1.33, p=0.77) or suicide attempt (OR=1.34,

320 95%CI=0.82-2.22, p=0.25). Finally, the occurrence of self-injurious thoughts and

321 behaviors was partly explained by genetic influences, with heritability estimates of

48% (95%CI=6%-67%) for suicidal ideation, 58% (95%CI=28%-70%) for self-harm,

and 62% (95%CI=0%-80%) for suicide attempt (eFigure 1 in the Supplement).

Are victimized adolescents at greater risk for self-injurious thoughts and behaviors?

326 Adolescents reporting exposure to more victimization types were at greater risk for

327 suicidal ideation (OR=2.17, 95%CI=1.93-2.44), self-harm (OR=2.38, 95%CI=2.10-

328 2.69), and suicide attempts (OR=3.14, 95%CI=2.54-3.88) between ages 12-18

329 (Table 1, Model 1; black triangles on Figure 2). Risk estimates in victimized

adolescents were similar in males and females (eTable 3 in the Supplement) and,

thus, we hereafter present analyses in the overall sample. In sensitivity analyses, we

found that adolescents identified by their co-twin or parent as having been victimized

also showed elevated risk for self-injurious thoughts and behaviors (Table 1, Models

2 and 3), suggesting that the findings were not due to biased self-reports of

victimization by adolescents who experienced self-injurious thoughts and behaviors.
Furthermore, adolescents reporting exposure to each of the seven individual types of
victimization showed greater risk for self-injurious thoughts and behaviors compared
to unexposed adolescents (eTable 4 in the Supplement).

339 Does greater risk for self-injurious thoughts and behaviors in victimized

340 adolescents reflect confounding by family-wide characteristics?

341 We next turned to examine the mechanisms underlying these associations.

342 Adolescents experience victimization⁶ and develop self-injurious thoughts and behaviors partly because of family-wide characteristics, such as genotype and the 343 344 rearing environment (eFigure 1 in the Supplement). Therefore, family-wide characteristics are plausible non-causal mechanisms underlying the observed 345 associations. We tested the role of these family-wide characteristics by examining 346 the association between adolescent victimization and self-injurious thoughts and 347 348 behaviors within twin pairs who shared their rearing environment as well as half (dizygotic twins) or all (monozygotic twins) of their genes. Twins exposed to more 349 350 victimization types were at greater risk for suicidal ideation, self-harm, and suicide 351 attempts compared to their co-twin exposed to fewer victimization types (yellow 352 points in Figure 2; eTable 5, Panel B in the Supplement), although these effect sizes 353 were smaller than phenotypic associations in the overall sample. In the more 354 stringent monozygotic co-twin design (red points in Figure 2; eTable 5, Panel D in the 355 Supplement), adolescents exposed to more victimization types were at greater risk 356 for suicidal ideation and self-harm, but not suicide attempt, compared to their co-twin 357 exposed to fewer victimization types.

358 Does the greater risk for self-injurious thoughts and behaviors in victimized

359 adolescents reflect confounding by individual characteristics?

360 Although the co-twin control design accounts for family-wide characteristics, it cannot account for characteristics not shared within the family (i.e., individual 361 362 characteristics). Victimized and non-victimized adolescents differed on several pre-363 existing individual characteristics (Figure 3, Panel A; eTable 6, Panel A and eTable 7 364 in the Supplement), which also predicted self-injurious thoughts and behaviors 365 (eTable 8 in the Supplement) and were, thus, plausible non-causal mechanisms 366 underlying the observed associations. We tested the role of these individual 367 characteristics through propensity score methods.

368 First, we re-estimated the associations after matching victimized adolescents to non-

369 victimized adolescents with similar propensity for adolescent victimization based on

individual characteristics (Figure 3, Panel B; eTable 6, Panel B in the Supplement).

371 Victimized adolescents showed greater risk for suicidal ideation (ATE=20.14%,

372 95%CI=15.50%-24.79%), self-harm (ATE=19.73%, 95%CI=15.33%-24.14%), and

suicide attempt (ATE=8.06%, 95%CI=5.43%-10.68%) than matched non-victimised

adolescents, although risk was on average 10% lower than in the original, non-

375 matched analyses (eTable 9 in Supplement).

Finally, to estimate the joint bias owing to family-wide and individual characteristics,

377 we expanded the co-twin control analysis to include the above propensity score.

378 Even when accounting for within-pair differences in individual characteristics,

379 monozygotic twins exposed to more victimization types were at greater risk for

suicidal ideation and self-harm than their co-twins exposed to fewer victimization

types (blue points in Figure 2; eTable 5, Panel E in the Supplement).

383 Discussion

We found that victimized adolescents were more likely to engage in self-injurious thoughts and behaviors than their non-victimized peers, consistent with previous research.¹²⁻¹⁵ This risk was marked - exposure to each additional victimization type doubled the odds of suicidal ideation and self-harm and tripled the odds of attempting suicide - and was consistent across different informants and victimization types. Therefore, adolescent victimization is an important risk indicator for self-injurious thoughts and behaviors in young people.

To better understand the contribution of non-causal mechanisms to this association 391 392 and, thus, inform intervention development, we used a co-twin control design to account for pre-existing family vulnerabilities and propensity score methods to 393 394 account for pre-existing individual vulnerabilities. Taken together, our results both strengthen the evidence for high risk of self-injurious thoughts and behaviors in 395 396 victimized adolescents and challenge conventional interpretations. Even in these 397 most stringent analyses, victimized adolescents showed elevated risk for suicidal ideation and self-harm, consistent with likely causal effects of adolescent 398 victimization on psychopathology.³³ However, these analyses also highlighted the 399 400 role of pre-existing familial and individual vulnerabilities, and suggested that previous 401 studies may have overestimated the causal association between adolescent 402 victimization and self-injurious thoughts and behaviors.

Our study has limitations. First, assessment of victimization and self-injurious thoughts and behaviors spanned the same observational period, and therefore the direction of effects is unclear. However, the findings were independent of childhood self-harm (included in the propensity score) and are thus unlikely to be explained by continuity in self-injury. Second, adolescent victimization and self-injurious thoughts and behaviors were measured via self-report, potentially giving rise to common-

method bias.³¹ Nevertheless, adolescent victimization remained associated with self-409 410 injurious thoughts and behaviors when victimization was reported by co-informants. 411 Third, the effect estimates were less precise for suicide attempt because it is rarer than suicidal ideation and self-harm. Therefore, the non-significant association 412 413 between victimization and suicide attempts in monozygotic twin analyses might reflect low statistical power, as effect sizes were similar to those observed for other 414 415 outcomes. Finally, findings in our twin sample may not generalize to singletons. 416 However, the prevalence estimates for victimization and self-injurious thoughts and behaviors reported here are similar to estimates in singleton samples.³³ Despite 417 418 these limitations, our findings have implications for research and interventions.

With regard to future research, our findings suggest the need to better understand 419 420 the mechanisms linking adolescent victimization to self-injurious thoughts and 421 behaviors. The experience of victimization might directly evoke negative self-views 422 and, in turn, trigger suicidal ideation and self-harm as a means of escaping negative feelings or punishing oneself.³⁴ Furthermore, future research should identify pre-423 existing familial and individual vulnerabilities that contribute to the elevated risk of 424 self-injurious thoughts and behaviors in victimized adolescents. These vulnerabilities 425 might include partly heritable individual traits such as poor emotion regulation, 426 impulsivity, and low self-esteem, 35,36 as well as unsupportive family environments. 37,38 427

With regard to interventions, our findings suggest that primary prevention of
adolescent victimization and targeted therapeutic interventions could partly reduce
risk for suicidal ideation and self-harm. Furthermore, secondary preventative
strategies addressing pre-existing vulnerabilities to self-injurious thoughts and
behaviors in victimized adolescents could substantially reduce risk for premature
death.

434

435 Acknowledgements:

- 436 The E-Risk Study is funded by the Medical Research Council (grant
- 437 G1002190). Additional support was provided by National Institute of Child Health
- and Development (grant HD077482), the Jacobs Foundation, the Nuffield
- 439 Foundation, the National Society for Prevention of Cruelty to Children (NSPCC) and
- the Economic and Social Research Council (ESRC). J.R.B is funded by the ESRC.
- L.A is the Mental Health Leadership Fellow for the UK ESRC. H.L.F is supported by
- an MQ Fellows Award (MQ14F40). C.O is a Jacobs Foundation and Canadian
- 443 Institutes for Advanced Research Fellow. R.T. is funded by the JSPS (JP16H05653),
- the Royal Society, and the British Academy as a Newton International Fellow
- Alumnus. We report no conflict of interests. We are grateful to the study mothers and
- fathers, the twins, and the twins' teachers for their participation and to members of
- the E-Risk team for their dedication, hard work, and insights.

448

- 451 <u>References</u>
- 452 453
- 454 **1.** World Health Organisation. *Global Accelerated Action for the Health of*
- 455 Adolescents (AA-HA!): guidance to support country implementation. Geneva:
 456 World Health Organisation;2017.
- 457 **2.** Nock MK. Self-injury. *Annu. Rev. Clin. Psychol.* 2010;6:339-363.
- 458 3. Ross S, Heath N. A study of the frequency of self-mutilation in a community
 459 sample of adolescents. *J Youth Adolesc*. 2002;31(1):67-77.
- 460 **4.** Turecki G, Brent DA. Suicide and suicidal behaviour. *The Lancet.*461 2016;387(10024):1227-1239.
- 462 5. Brent DA, McMakin DL, Kennard BD, Goldstein TR, Mayes TL, Douaihy AB.
 463 Protecting adolescents from self-harm: a critical review of intervention
- 464 studies. J. Am. Acad. Child Adolesc. Psychiatry. 2013;52(12):1260-1271.
- **6.** Fisher HL, Caspi A, Moffitt TE, et al. Measuring adolescents' exposure to
- 466 victimization: The Environmental Risk (E-Risk) Longitudinal Twin Study. *Dev.*
- 467 *Psychopathol.* 2015;27(4pt2):1399-1416.
- 468 **7.** Brown SL, Birch DA, Kancherla V. Bullying perspectives: Experiences,
- 469 attitudes, and recommendations of 9 to 13 year olds attending health
- education centers in the United States. J. Sch. Health. 2005;75(10):384-392.
- 471 8. Sickmund M, Puzzanchera C. Juvenile offenders and victims: 2014 national
 472 report. Pittsburgh, PA: National Center for Juvenile Justice;2014.
- 473 9. Peskin MF, Tortolero SR, Markham CM. Bullying and victimization among
 474 Black and Hispanic adolescents. *Adolescence*. 2006;41(163):467.
- 475 **10.** Blakemore S-J, Mills KL. Is adolescence a sensitive period for sociocultural
 476 processing? *Annu. Rev. Psychol.* 2014;65:187-207.

- **11.** Crone EA, Dahl RE. Understanding adolescence as a period of social–
- 478 affective engagement and goal flexibility. *Nat Rev Neurosci.* 2012;13(9):636479 650.
- 480 **12.** Geoffroy M-C, Boivin M, Arseneault L, et al. Associations between peer
- 481 victimization and suicidal ideation and suicide attempt during adolescence:
- 482 results from a prospective population-based birth cohort. *J. Am. Acad. Child*
- 483 *Adolesc. Psychiatry.* 2016;55(2):99-105.
- **13.** Turner HA, Finkelhor D, Shattuck A, Hamby S. Recent victimization exposure
 and suicidal ideation in adolescents. *Arch. Pediatr. Adolesc. Med.*
- 486 2012;166(12):1149-1154.
- 487 14. Klomek AB, Marrocco F, Kleinman M, Schonfeld IS, Gould MS. Bullying,
 488 depression, and suicidality in adolescents. *J. Am. Acad. Child Adolesc.*489 *Psychiatry*. 2007;46(1):40-49.
- 490 **15.** Barker ED, Arseneault L, Brendgen M, Fontaine N, Maughan B. Joint
 491 development of bullying and victimization in adolescence: Relations to
 492 delinquency and self-harm. *J. Am. Acad. Child Adolesc. Psychiatry.*
- 493 2008;47(9):1030-1038.
- 494 16. Silberg J, Kendler KS. Causal and noncausal processes underlying being
 495 bullied. *JAMA Psychiatry*. 2017;74(11):1091-1092.
- **17.** Singham T, Viding E, Schoeler T, et al. Concurrent and longitudinal
- 497 contribution of exposure to bullying in childhood to mental health: The role of
 498 vulnerability and resilience. *JAMA Psychiatry*. 2017;74(11):1112-1119.
- **18.** Danese A, Moffitt TE, Arseneault L, et al. The origins of cognitive deficits in
 victimized children: implications for neuroscientists and clinicians. *Am. J.*
- 501 *Psychiatry*. 2017;174(4):349-361.
- **19.** Hawton K, Saunders KE, O'Connor RC. Self-harm and suicide in
- 503adolescents. The Lancet. 2012;379(9834):2373-2382.

- 504 20. Kendler KS. Causal inference in psychiatric epidemiology. *JAMA Psychiatry*.
 505 2017;74(6):561-562.
- Heckman JJ. Sample selection bias as a specification error. *Econometrica*.
 1979;47(1):153-161.
- Trouton A, Spinath FM, Plomin R. Twins early development study (TEDS): a
 multivariate, longitudinal genetic investigation of language, cognition and
 behavior problems in childhood. *Twin Res.* 2002;5(5):444-448.
- 511 23. Moffitt TE, E-Risk Study Team. Teen-aged mothers in contemporary Britain. J
 512 *Child Psychol Psychiatry*. 2002;43(6):727-742.
- 513 **24.** Odgers CL, Caspi A, Russell MA, Sampson RJ, Arseneault L, Moffitt TE.
- 514 Supportive parenting mediates neighborhood socioeconomic disparities in
- 515 children's antisocial behavior from ages 5 to 12. *Dev. Psychopathol.*

516 2012;24(3):705-721.

- 517 **25.** Finkelhor D, Hamby S, Turner H, Ormod R. *The Juvenile Victimization* 518 *Questionnaire: 2nd Revision (JVQ-R2).* Durham, NH: Crimes Against
- 519 Children Research Center; 2011.
- 520 26. Finkelhor D, Hamby SL, Ormrod R, Turner H. The Juvenile Victimization
 521 Questionnaire: reliability, validity, and national norms. *Child Abuse Neglect*.
 522 2005;29(4):383-412.
- 523 27. Radford L, Corral S, Bradley C, et al. *Child abuse and neglect in the UK*524 *today.* London: NSPCC;2011.
- Radford L, Corral S, Bradley C, Fisher HL. The prevalence and impact of
 child maltreatment and other types of victimization in the UK: Findings from a
 population survey of caregivers, children and young people and young adults. *Child Abuse Neglect.* 2013;37(10):801-813.
- Rogosch FA, Cicchetti D. Child maltreatment and emergent personality
 organization: Perspectives from the five-factor model. *J. Abnorm. Child Psychol.* 2004;32(2):123-145.

532	30.	Turner HA, Finkelhor D, Ormrod R. Child mental health problems as risk
533		factors for victimization. Child Maltreat. 2010;15(2):132-143.
534	31.	Podsakoff PM, MacKenzie SB, Lee J-Y, Podsakoff NP. Common method
535		biases in behavioral research: a critical review of the literature and
536		recommended remedies. J. Appl. Psychol. 2003;88(5):879-903.
537	32.	Carlin JB, Gurrin LC, Sterne JA, Morley R, Dwyer T. Regression models for
538		twin studies: a critical review. Int. J. Epidemiol. 2005;34(5):1089-1099.
539	33.	Schaefer JD, Moffitt, T.E., Arseneault, L., Danese, A., Fisher, H.L., Houts, R.,
540		Sheridan, M.A., Wertz, J., Caspi, A. Adolescent victimization and early-adult
541		psychopathology: Approaching causal inference using a longitudinal twin
542		study to rule out non-causal explanations. Clin Psychol Sci. 2017.
543		doi.org/10.1177/2167702617741381.
544	34.	Hooley JM, Franklin JC. Why Do People Hurt Themselves? A New
545		Conceptual Model of Nonsuicidal Self-Injury. Clin Psychol Sci. 2017.
546	35.	Brent DA, Mann JJ. Family genetic studies, suicide, and suicidal behavior.
547		American Journal of Medical Genetics Part C: Seminars in Medical Genetics.
548		2005;133(1):13-24.
549	36.	Hawton K, Rodham K, Evans E, Weatherall R. Deliberate self harm in
550		adolescents: self report survey in schools in England. BMJ.
551		2002;325(7374):1207-1211.
552	37.	Ougrin D, Tranah T, Stahl D, Moran P, Asarnow JR. Therapeutic
553		interventions for suicide attempts and self-harm in adolescents: systematic
554		review and meta-analysis. J. Am. Acad. Child Adolesc. Psychiatry.
555		2015;54(2):97-107.
556	38.	Asarnow JR, Hughes JL, Babeva KN, Sugar CA. Cognitive-behavioral family
557		treatment for suicide attempt prevention: a randomized controlled trial. J. Am.
558		Acad. Child Adolesc. Psychiatry. 2017;56(6):506-514.
559		

560 Figure 1. Distribution of self-injurious thoughts and behaviors in adolescence. LEGEND: Panel A shows the overlap between adolescent suicidal ideation, self-561 562 harm, and suicide attempt. The size of the circles and their overlap is proportional to 563 the number of participants (total N=2,055). Suicidal ideation was correlated with self-564 harm (r = 0.77, p<0.001) and suicide attempt (r = 0.84, p<0.001). Self-harm was correlated with suicide attempt (r = 0.79, p<0.001). Panel B shows the prevalence of 565 self-injurious behaviors endorsed by >1% of those who reported self-harm or suicide 566 567 attempt. Females and males did not differ in the types of self-injury reported, except 568 for cutting/stabbing self (more prevalent in females: OR=1.94, p=0.021), and hitting 569 self/object (less prevalent in females: OR=0.24, p<0.001). 570 571 572 Figure 2. Association between adolescent victimization and self-injurious thoughts and behaviors. LEGEND: Note. MZ=monozygotic; DZ=dizygotic. 573 574 575 576 Figure 3. Propensity score for adolescent victimization in non-victimized and victimized adolescents based on child-specific characteristics. LEGEND: The 577 propensity score was derived based on the following child-specific characteristics: 578 childhood victimization, social isolation, IQ, internalizing problems, externalizing 579 problems, self-harm, openness to experience, conscientiousness, extraversion, 580 agreeableness, and neuroticism. We used 1:1 nearest neighbor matching with 581

replacement to match each Study member to a Study member with a similar propensity score in the opposite "treatment" group (e.g., victimization [N=671] or no 583

victimization [N=1265]). 584

582

(self-report of (co-twin report of (pau victimization) victimization) vion Victimization) vietimization
Suicidal ideation 2.17 (1.93-2.44) 2.00 (1.71-2.34) 2.0
Self-harm 2.38 (2.10-2.69) 1.99 (1.68-2.36) 2.0
Suicide attempt 3.14 (2.54-3.88) 2.73 (2.21-3.39) 2.0

 Table 1. Association between adolescent victimization and self-injurious thoughts and behaviors.



Figure 1. Distribution of self-injurious thoughts and behaviors in adolescence



Figure 2. Association between adolescent victimization and self-injurious thoughts and behaviors







Figure 3. Propensity score for adolescent victimization in non-victimized and victimized adolescents based on child-specific characteristics