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# EARLY-ONSET TOBACCO USE AND SUICIDE-RELATED BEHAVIOR – A PROSPECTIVE STUDY FROM ADOLESCENCE TO YOUNG ADULTHOOD

Tellervo Korhonen*, PhD[1, 2, 3], Elina Sihvola*, MD, PhD[1,4], Antti Latvala, PhD[1], Danielle M. Dick, PhD[5], Lea Pulkkinen, PhD[6], John Nurnberger[7], MD, PhD, Richard J. Rose, PhD[8], Jaakko Kaprio MD, PhD[1, 2]

*Drs. Korhonen and Sihvola contributed equally to this article.

[1] Department of Public Health, University of Helsinki, Helsinki, Finland
[2] Institute for Molecular Medicine Finland, FIMM, University of Helsinki, Helsinki, Finland
[3] Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland
[4] Department of Psychiatry, Helsinki University Central Hospital, Helsinki, Finland
[5] Department of Psychology, Virginia Commonwealth University, Richmond, United States
[6] Department of Psychology, University of Jyvaskyla, Jyvaskyla, Finland
[7] Departments of Psychiatry and Medical and Molecular Genetics, Indiana University, Indianapolis , United States
[8] Department of Psychological and Brain Sciences, Indiana University, Bloomington, United States

**Corresponding author:**
Tellervo Korhonen, Institute for Molecular Medicine Finland, FIMM, University of Helsinki, P.O. Box 20, 00014 University of Helsinki, Finland;
e-mail: tellervo.korhonen@helsinki.fi.

## Abstract

### Background

Developmental relationships between tobacco use and suicide-related behaviors (SRB) remain unclear. Our objective was to investigate the longitudinal associations of tobacco use in adolescence and SRB in adulthood.

### Methods

Using a prospective design, we examined whether tobacco use in adolescence is associated with SRB (intentional self-injury, suicide ideation) in young adulthood in a population-based sample of 1330 twins (626 males, 704 females). The baseline and follow-up data were collected by professionally administered semi-structured poly-diagnostic interviews at ages 14 and 22, respectively.

### Results

After adjusting for multiple potential confounders, those who reported early-onset of regular tobacco use had a significantly increased risk for intentional self-injury, such as cutting or burning, at age 22 (adjusted odds ratio [AOR] 4.57, 95%CI 1.93-10.8) in comparison to those who had not at all initiated tobacco use. Also, daily cigarette smoking at baseline was associated with future intentional self-injury (AOR 4.45, 95%CI 2.04-9.70). Early-onset tobacco use was associated with suicidal ideation in females (AOR 3.69, 95%CI 1.56-8.72) but not in males. Considering any SRB, baseline daily smokers (AOR 2.13, 95%CI 1.12-4.07) and females with early onset of regular tobacco use (AOR 3.97, 95%CI 1.73-9.13) had an increased likelihood. Within-family analyses among twin pairs discordant for exposure and outcome controlling for familial confounds showed similar, albeit statistically non-significant, associations.

### Conclusion

Early-onset tobacco use in adolescence is longitudinally associated with SRB (intentional self-injury and/or suicide ideation) in young adulthood, particularly among females. Further investigation may reveal whether this association has implications for prevention of SRB in adolescence and young adulthood.

**Keywords**: self-injury, suicidal ideation, tobacco, smoking, twins

## 1. Introduction

Suicide-related behaviors (SRB), such as intentional self-injury and suicide ideation, are associated with distress and trauma to the patients, their families, and with economic costs to the community (Kidger et al., 2012; Swahn et al., 2002). Preventing of self-injury is important, since it is also a potential precursor for subsequent suicide (Cooper et al., 2005, Hawton et al., 2003). Non-suicidal but intentional, planned or deliberate self-injury, such as cutting, burning, or chafing oneself, represents individual psychopathology, not just common adolescent trends (Levenkron, 1998). These behaviors are often documented in the history of patients with borderline personality disorder, and impulse-control disorders as well as substance use disorders and depression (Hu et al., 2016). In the 5$^{th}$ edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2013), non-suicidal self-injury (NSSI) and suicidal behavior disorder are introduced as clinical conditions (Zetterqvist et al., 2013).

Early-onset use of psychoactive substances, such as tobacco, may have neurotoxic and neuromodulatory effects, which can be related also with SRB. Especially, the age of smoking initiation may be an important determinant for risk of various somatic and mental adverse health outcomes (DeBry & Tiffany., 2008). Part of the association between tobacco use and SRB may be explained by the confounding effects of these well-known risk factors, such as depression or abuse of other addictive substances. However, another part of the association may be the result of the effect of tobacco use itself, especially cigarette smoking that may increase the risk of SRB through a biological pathway. Cigarette smoking has been suggested to have implications also for brain neurobiology. For example, smoking can significantly decrease the activity of the serotonergic system of the human hippocampus and may reduce brain serotonin function which is negatively related to risk of suicide. Furthermore, nicotine, the addictive substance in all kinds of tobacco products, is a potent activator of the hypothalamic-pituitary-adrenal (HPA) axis and is able to activate the attenuated responsiveness of the HPA axis to psychological stress. On the other hand, hyperactivity of the HPA axis is supposed to be a risk factor for suicidal behaviors (DeBry & Tiffany, 2008; Durazzo et al., 2010; van Heeringen & Mann, 2014).

Considering empirical evidence, in cross-sectional studies, early smoking initiation and nicotine dependence have been associated with suicidal behavior (Hockenberry et al., 2010; Dong-Sik & Hyun-Sun., 2010; Swahn et al., 2012), but the associations may differ by sex (Cho et al., 2007; Brunner et al., 2007). Genetically informed designs, such as twin studies, have found risk factors for self-injury, such as alcohol use and bullying victimization (Few et al., 2015; Fisher et al., 2012). Studies among adults have confirmed an association between smoking and suicide in cross-sectional, clinical and prospective studies (Covey et al., 2012, 2009; Breslau et al., 2005), even after adjusting for confounders (Kessler et al., 2009). Smoking is longitudinally associated also with suicidal ideation, suicide attempts, and completed suicide among adults (Li et al., 2012, Evins et al., 2017). Smoking may increase the risk for future SRB independently of psychiatric comorbidity (Hintikka et al., 2001, Oquendo et al., 2007).

Adolescence is an important period of risk for the development of lifelong smoking behaviors and nicotine addiction, but limited data are available on smoking in relation to SRB in this age-group (McGee et al., 2005; Hockenberry et al., 2010). Smoking is associated with increased risk for subsequent suicide ideation and attempts in adolescence (Riala et al., 2009). However, other studies, also following adolescents into young adulthood, have found no association (Fergusson et al., 2000, Dugas et al., 2012, Wilcox & Anthony, 2004). Moran et al. (2012) suggested that self-injury is independently associated with smoking and depression. Outcomes are poor also among those who have intentionally harmed themselves without suicidal intent (Mars et al., 2014). Previous findings warrant prospective studies to understand the relationships between smoking and SRB, and to identify risk groups who benefit most from preventive actions. However, complex behaviors, such as smoking and SRB, may be difficult to assess reliably and ethically at a young age.

The association may not be causal and could be explained common underlying factors for smoking and SRB. Thus, it is important to enhance the understanding of the role of familial factors, such as childhood environment or dispositional genetic factors, which might underlie these relationships. One approach is to study these associations among discordant twin pairs. By design, this approach controls for potential familial confounds shared by the twins such as family structure, socioeconomic status, and medical history.

The first aim of this study was to examine the developmental relationships of early–onset tobacco use in adolescence with SRB (intentional self-injury, suicidal ideation) in young adulthood. The second aim was to test whether these relationships are replicated when controlling for shared genetic and other familial influences.

**2. Participants and data collection**

FinnTwin12 is a longitudinal twin study launched in 1994 to investigate the developmental epidemiology of health-related behaviors (Rose et al., 2001). From 1994 to 1998, all Finnish families with twins born in 1983-1987 were identified from Finland's Population Register Centre and enrolled into a two-stage sampling design (Kaprio et al., 2002). The first stage included questionnaire assessments of all twins and parents at baseline (87% participation rate, 2,724 families) conducted during the year in which the consecutive twin cohorts reached age 11, with follow-up of all twins at ages of 14 and 17½ years, and as young adults (age 22).

Nested within this population study was an intensive assessment targeting 1035 families, comprising about 40% of all twins, most (72.3%; 748 families) selected at random. About one-quarter of the families (27.7%; 287 families) were assumed to be at elevated familial risk for alcoholism, based on one or both parents' scores on an 11-item lifetime version of the Malmö-modified Michigan Alcoholism Screening Test (Seppä et al., 1990). Details about these families have been described earlier (Rose et al., 2001).

Both co-twins in this sub-sample were interviewed at ages of 14 and 22 using the Semi-Structured Assessment for the Genetics of Alcoholism (Bucholz et al., 1994), a widely-used, reliable instrument providing detailed assessments of tobacco use, SRB, and lifetime diagnoses (DSM-IIIR, DSM-IV) for several disorders, including alcohol dependence and major depressive disorder (MDD). The twins at age 14 were administered the adolescent version of SSAGA (C-SSAGA-A) whereas the adult SSAGA was administered at age 22. All interviewers were trained by personnel from Indiana University's Institute of Psychiatric Research using standard COGA-interview training procedures (Edenberg 2002).

The mean age at baseline was 14.2 years, with 75% of interviews completed between 14.0 and 14.3 years of age, and all interviews completed before age 15. The final baseline interview sample (n=1852) consisted of 945 males (51%) and 907 females (participation rate 90%). Data collection procedures were approved by the Ethics Committee of Helsinki University, Finland and the Institutional Review Board of Indiana University, Bloomington, USA.

The fourth wave of data collection was started by inviting the twins from the intensive sample to participate in an in-laboratory protocol at a mean age of 22 years (range 20 – 26). For those unable to participate in the full protocol (in-lab assessments conducted in Helsinki; in Oulu or Turku for some participants), we offered an abbreviated protocol. This protocol included the SSAGA interview via telephone, postal questionnaires and providing a DNA sample. Zygosity was originally determined using well-validated questionnaires in adolescence and young adulthood (Sarna et al. 1978, Goldsmith 1991). For more than 90% of the same-sex twins in the intensive sample, zygosity was confirmed from DNA and found to be correct in 94% of cases.

We report analyses of the full intensively studied sample to retain statistical power. Based on our sensitivity analyses, the type of sampling (random versus non-random) did not attenuate estimates of the associations between tobacco use and SRB variables. The intensively studied sample analyzed for this study included 1330 individual twins (626 males, 704 females) who provided sufficient data on tobacco use and SRB. Non-respondents at follow-up did not significantly differ from the respondents at baseline in terms of depression status, sex, age or tobacco use status. However, due to missing values in potential confounders, the final sample sizes varied in the multiple adjusted analyses from 1266 (592 males, 674 females) to 1269 (594 males, 675 females).

## 3. Measures

### *3.1 Tobacco use*

We analyzed two tobacco use variables, which were assessed at baseline (age 14) and at follow-up (age 22). At age 14, a specific question about frequency of cigarette smoking was asked. Based on the responses, the adolescents were categorized into four groups:

never, experimenting, occasional and daily cigarette smokers. For those reporting never use, confirmatory questions were asked, such as: “So, have you never tried any tobacco products, not even cigarettes?” Those who had smoked at least once, but less than 5 packs of cigarettes lifetime, were considered experimenters. Further, among those who had smoked at least 5 packs, those who reported smoking 3-4 days a week or less often, were categorized as occasional smokers, whereas those who smoked daily or almost daily were categorized as daily smokers.

At age 22, there was a detailed interview about use of various tobacco products, including cigarettes, cigars, pipe and smokeless tobacco. First, the respondents were asked if they had ever used those products daily or almost daily for one month. Those who replied ‘no’ to all these items were categorized as never users (245 males, 367 females). For those who had replied ‘yes’ to at least one of the items, the following question was asked: “At what age did you start using tobacco on daily basis?” Based on the responses, the ever users were categorized into two categories of regular tobacco use initiation, i.e. ‘late onset’ (14-22 years of age; 306 males, 271 females) and ‘early onset’ (<14 years of age; 43 males, 36 females). Cotinine measurements in a sample of never smokers confirmed the absence of recent tobacco use.

*3.2 Suicide-related behaviors*

We analyzed two SRB (intentional self-injury, suicide ideation). The questions assessing these behaviors were as follows: ’Have you ever intentionally injured yourself, for example by cutting or burning?’ and ‘Have you ever had any thoughts of suicide?’, respectively. For each behavior, a ‘no’ (0) or ‘yes’ (1) response was recorded. We also created a variable considering whether any of the previously mentioned SRB was observed, where ‘none’ was coded 0 (512 males, 499 females) and ‘any’ was coded 1 (82 males, 175 females).

*3.3 Confounders*

Based on previous literature (e.g. Dugas et al., 2012; Dumais et al., 2005; Few et al., 2015; Hawton et al., 2003), we considered several variables as potential confounders in the association between tobacco use and SRB. Here, we took into account several baseline variables, namely school achievement, MDD (DSM-IV), impulsivity, and alcohol

dependence symptoms, as well as parental education. School achievement was assessed at age 14 when the teachers responded to questionnaire items on school performance, including grade point average (GPA) (Latvala et al., 2014). An adolescent version of the SSAGA (C-SSAGA-A) was used to assess presence or absence of DSM-IV MDD. We assessed impulsivity at age 14 using teacher rating forms of the Multinomial Peer Nomination Inventory (MNPI), which has high reliability, internal consistency and discriminative validity (Pulkkinen et al., 1999). The MPNI covers a wide spectrum of behaviors; the scales for hyperactivity-impulsivity, aggression, and inattention may be used to form a factor for externalizing problem behaviors (Pulkkinen et al., 1999). For our analysis, we utilized the scale for hyperactivity-impulsivity ('impulsivity' below). Further, the SSAGA provided diagnoses and symptom counts for alcohol abuse and dependence; the number of alcohol dependence symptoms was used instead of the full diagnosis, as the latter was rare at this age. Finally, parental education was assessed for mothers and fathers, with categories ranging from compulsory schooling only to tertiary education. The highest education of either parent was used as a covariate. A more detailed description of the potential confounders is shown in the Supplement 1.

**4. Statistical analysis**

Logistic regression was used to test the associations of the tobacco use variables with the SRB The odds ratios (OR) and adjusted odd ratios (AOR) with 95% confidence intervals (95%CI) were computed first adjusting for age and sex. Sex-by-tobacco use interactions were tested for all SRB. If such interaction was observed ($p<.10$), we conducted the subsequent analyses separately by sex. Otherwise, females and males were pooled together. The final analyses were adjusted for age, sex (if no interaction), school achievement, DSM-IV MDD, impulsivity, and number of alcohol dependence symptoms at baseline, as well as for parental education. When assessing the association of early onset tobacco use with later suicide ideations, we conducted an incidence analysis where we removed those reporting any baseline suicidal thoughts. In these analyses we treated the twins as individuals using robust estimators of variance when estimating standard errors (Williams 2000). For all these individual-based analyses, we conducted sensitivity analyses, where we added the variable reflecting type of sampling (random versus non-random) into the final multiple adjusted models. None of these sensitivity analyses

suggested confounding by the type of sampling; i.e. the estimates reflecting the association between tobacco use and SRB were not clearly attenuated.

Finally, if there was a significant association between a tobacco use and a SRB variable, we further explored the association by controlling for confounds shared by the twins using a discordant twin design. Such within-pair analysis controls for familial factors constant within twin pairs, such as environmental factors shared by the co-twins (e.g. family environment) and shared genetic liability for both tobacco use and SRB (Kujala et al., 2002). Thus, if an analysis among twin pairs discordant for tobacco and SRB provides similar results as provided by the individual-based analysis, the association between tobacco and SRB is not confounded by underlying familial (shared genetic or environmental factors) liability. All analyses were conducted using the statistical software Stata (version 13) (StataCorp. 2013).

## 5. Results

### *5.1 Descriptive results*

Self-injurious behaviors were uncommon among males. At age 22, three percent of males, but 13% of females reported intentional self–injury, such as cutting or burning themselves on purpose. Thirteen per cent of males and 20% of females reported suicidal ideation. Proportions and numbers of these SRBs (intentional self-injury, suicide ideation) in each tobacco use categories are shown in the Supplemental Table (Supplement 2).

### *5.2 Tobacco use and self-injury*

When the association between age of regular tobacco use initiation (reported retrospectively as a young adult) and intentional self-injury was assessed, those who had initiated regular tobacco use before age 14 had a higher likelihood for intentional self-injury at young adulthood compared to never users. When adjusted for age, sex, baseline school achievement, depression, impulsivity and alcohol dependence symptoms, as well as for parental education, such 'early-onset' tobacco use remained significantly associated with self-injury (AOR 4.57, 95%CI 1.93-10.8, p=.001). However, also those who had started regular tobacco use between the ages of 14 and 22 had an elevated risk compared to

never users (AOR 3.24, 95%CI 2.02-5.21, p=1.2e-06). Daily cigarette smoking reported at age 14 was associated with age 22 intentional self-injury. When adjusted for multiple confounders, daily smokers at age 14 had an elevated risk (AOR 4.45, 95%CI 2.04-9.70, p=1.8e-04) compared to never smokers at age 14 (Table 1).

*5.3 Tobacco use and suicidal ideation*

For age of regular tobacco use initiation, there was a sex interaction (Likelihood-ratio test LR $chi^2$ (2) = 5.21; p= .074), so that the association of early onset tobacco use was significant among females only. Females with early-onset regular tobacco use had a higher liability to suicidal ideation at the age of 22 compared to never users. When adjusted for multiple confounders early onset tobacco use remained significantly associated with subsequent suicidal ideation (AOR 3.69, 95%CI 1.56-8.72, p=.003) (Table 1).

As an incidence analysis, we examined the association of early onset tobacco use with suicide ideation among those 615 females who did not report any suicidal thoughts at baseline. Those with early regular tobacco use had a higher liability to incident suicidal ideation at the age of 22 compared to never users. In the fully adjusted model early-onset tobacco use remained significantly associated with incident suicidal ideation (OR 2.72, 95%CI 1.05-7.06, p=.039) (not shown in tables).

*5.5 Tobacco use and any suicide related behavior*

When using any SRB (no/yes) as the binary variable, there was a sex interaction (Likelihood-ratio test LR $chi^2$ (2) = 7.08; p=.029), so that the association of early onset regular tobacco use was significant among females only. When adjusted for school achievement, age, depression, impulsivity and alcohol dependence symptoms, as well as for parental education, those females who started regular tobacco use at an age younger than 14 had a significantly higher likelihood for any SRB (AOR 3.97, 95%CI 1.73-9.13, p=.001). However, as seen in Table 2, those who started tobacco use between ages of 14 and 22 also had an elevated risk compared to never users (AOR 1.92, 95%CI 1.27-2.92, p=.002). Considering baseline smoking status, daily smokers had over two-fold likelihood for any SRB compared to never smokers (AOR 2.13, 95%CI 1.12-4.07, p=.022).

*5.6 Discordant twin analysis*

In order to explore whether the association between tobacco use and any SRB is confounded by shared familial liability, we conducted conditional logistic regressions among twin pairs discordant for exposure and outcome. The first analysis was conducted among 66 female twin pairs discordant for age of regular tobacco use initiation and for any SRB. The point estimates suggested that those twin sisters with early regular tobacco use onset had higher likelihood for any SRB (OR 1.72, 95%CI 0.27-10.8, p=.56) and so did those who started regular tobacco use between ages 14 and 22 (OR 1.40, 95%CI 0.58-3.40, p=.45), when compared to their twin sisters who did not start tobacco use at all by the age of 22. Another pair-wise analysis included 157 twin pairs discordant for daily smoking status at baseline and any SRB at follow-up. The point estimates suggested that daily smoking co-twins had increased likelihood for any SRB (OR 1.94, 95%CI 0.65-5.75, p=.23) when compared to their never smoking co-twins. However, these associations failed to reach statistical significance. The small number of cases precluded further pair-wise analyses by zygosity (not shown in tables).

## 6. Discussion

The findings of this prospective analysis suggest that early tobacco use, particularly initiation of regular use before age 14, is longitudinally associated with SRB at age 22, especially among females. Namely, daily cigarette smoking at age 14 was associated with intentional self-injury, suggesting that daily smoking adolescents are at higher risk for self-injurious behaviors, such as cutting or burning oneself, compared to never users. Exploring early smoking in a young population sample extends earlier research during an important period of risk for developing these behaviors and may be an opportune time for preventive actions. Results of pairwise comparisons of exposure- and outcome-discordant twin pairs suggest that the associations found in individual-level analyses are not due to complete confounding by familial factors. However, as these within-pair estimates did not reach statistical significance, their interpretation remains speculative. Also, limited samples of discordant twin pairs constrain power and those results are suggestive but not definitive; we cannot confidently dismiss potential confounding.

In some studies, adjustment for baseline psychiatric disorders has eliminated the

association of smoking with suicide ideation (McGee et al., 2005) and with completed suicide (Hemmigsson et al., 2003). We assessed depression with an early age of onset, a disorder with low recognition and treatment-seeking. We also analyzed baseline impulsivity, risk factor for suicide (Dumais et al., 2005) and alcohol dependence symptoms, early onset alcohol use being associated with intentional self-injury (Few et al., 2015). Largely consistent with earlier limited data, early onset tobacco use remained longitudinally associated with suicidal ideation. These findings warrant consideration for routine assessment of early tobacco use along with assessment for major psychiatric disorders, such as depression.

In the case of early onset of regular tobacco use and suicide ideation, we found no association in males, whereas in females the association was strong and statistically significant. Female vulnerability for SRB has been documented previously in clinical and population samples (Moran et al., 2012). For example, in cross-sectional studies, adolescent female smoking is significantly associated with self-injury, but the association may be non-existent among males (Brunner et al., 2007). A possible explanation for the concurrent and prospective findings may be that the development of nicotine dependence among females after the first use of nicotine may be more rapid than among males. This may be partly explained by sex differences in nicotine metabolism, since among females estrogen is known to enhance metabolism. Also, the anxiolytic effects of nicotine are more pronounced among females (Pogun & Yararbas, 2009). These findings may partially explain the fact that early exposure to tobacco and nicotine may be a more hazardous indicator for subsequent SRB among adolescent females compared to males.

At baseline, suicidal thoughts were very rare in this young population and there was a strong overlap with early onset-depression. To explore further, as an incidence analysis, we examined the effect of early onset tobacco use among females, who did not report any suicidal thoughts at baseline. Also here, those with early tobacco exposure had higher liability to incident suicidal ideation compared to those who had not initiated tobacco use by age 22. Thus, in this analysis we were able to control for pre-existing suicidal thoughts occurring before tobacco use assessment at age 14 baseline. However, we acknowledge as a limitation of this prospective study, that we did not have data for pre-existing intentional self-injury at baseline. Thus, for this SRB, we cannot rule out the possibility that lifetime self-injury reported as young adult had actually appeared before the assessment of baseline tobacco use.

One critical issue in follow-up studies is the effect of attrition, i.e. those who participate the baseline assessment but dropout from the follow-up assessment. Such bias would be of great importance if the dropout rate is high, which is not the case in our study. However, we have tested the effect of attrition – i.e. those lost to follow-up as follows: We compared the effects of baseline smoking status and suicide ideation at age 14 according to follow-up participation status as young adult. We found that those who were daily smokers at baseline had lower likelihood for participating the follow-up study at age 22 (OR=0.62, p=0.007). Thus, we acknowledge that there is selective attrition that will bias results; e.g. associations between tobacco use and SRB may actually be under estimations. However, self-reports of suicide ideations at baseline were not associated with follow-up participation status as young adult (p=0.147) and thus that attrition should not bias our findings.

Several intriguing questions remain. Why do children start tobacco use at an early age? What are their relationships with their parents and peers like? Are their family environments characterized by negative attitudes towards life or by avoidance of responsibility? Do these factors correlate with future psychopathology, such as SRB's? (Pulkkinen 1982). Analyses of discordant co-twins represent one way to explore the association of early-onset tobacco use with self-injurious behaviors while taking into account familial confounds. Scherrer et al. (2012) suggested that contributions from familial factors may not significantly alter the association of smoking with SRB. In our study, we did not fully replicate the individual based analyses in the discordant twin design. Thus, longitudinal associations between early-onset tobacco use and SRB may partly be explained by differences in family environments. Other family studies are encouraged to investigate these associations further. If confirmed, these novel findings may have important implications for treatment and prevention programs.

Preventive efforts for SRB should incorporate screening, education and follow-up of youth smoking behavior. For example, screening for tobacco use increases the odds of health care professionals, especially physicians intervening with patients who smoke. However, without appropriate follow-through within health care, screening for tobacco use is not enough to significantly increase cessation rate.

**7. Conclusions**

Early-onset exposure to tobacco and nicotine - even the first experiments followed by development up to daily use in adolescence – should be recognized as a potential warning sign for later SRB. Female vulnerability for SRB suggests implications for designing prevention programs promoting young women's mental health. However, we should take into consideration that in young adulthood, males in general are at highest risk for suicide and, perhaps, are less likely to report risk behaviors and seek help. Further investigation may reveal whether this association has implications for prevention of SRB in adolescence and young adulthood.

**Author Disclosure**

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**Contributors**
Authors Tellervo Korhonen, Elina Sihvola, and Jaakko Kaprio designed the study. Tellervo Korhonen and Elina Sihvola wrote the first draft of the manuscript and conducted the statistical analysis. All authors have contributed to further drafts of the manuscript and have approved the final version of the manuscript for submission.

**Conflicts of Interest**
Jaakko Kaprio has consulted for Pfizer on nicotine dependence in 2011-2015. Tellervo Korhonen has consulted for Pfizer on nicotine dependence in 2011-2017. The other authors have no conflicts to declare.

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**Table 1.**The odds ratios for suicide related behaviors (intentional self-injury, suicide ideation) at age 22 according to tobacco use behavior in a population-based sample of twins.

| | **Model 1** (Adjusted for age and sex) | | | **Model 2** (Adjusted for age, sex, baseline school achievement, depression, impulsivity, alcohol, and parental education) | | |
|---|---|---|---|---|---|---|
| **Intentional self-injury assessed at age 22** | | | | | | |
| **Age of regular tobacco use initiation (n=1268)** | OR | 95%CI | p-value | AOR | 95%CI | p-value |
| Never | 1.00 | | | 1.00 | | |
| Late onset tobacco use [1] | 3.07 | 1.98,4.75 | 4.6e-07 | 3.24 | 2.02,5.21 | 1.2e-06 |
| Early onset tobacco use [2] | 4.32 | 2.00,9.34 | 2.0e-04 | 4.57 | 1.93, 10.8 | .001 |
| **Cigarette smoking at baseline (n=1265)** | OR | 95%CI | p-value | AOR | 95%CI | p-value |
| Never | 1.00 | | | 1.00 | | |
| Experimenting | 1.16 | 0.73,1.86 | .523 | 1.17 | 0.71,1.92 | .526 |
| Occasional | 1.70 | 0.66,4.40 | .271 | 2.12 | 0.74,6.11 | .163 |
| Daily | 3.41 | 1.83,6.34 | 7.2e-05 | 4.45 | 2.04,9.70 | 1.8e-04 |
| **Suicide ideation assessed at age 22** | | | | | | |
| **Age of regular tobacco use initiation (n=675 females) [3]** | OR | 95%CI | p-value | AOR | 95%CI | p-value |
| Never | 1.00 | | | 1.00 | | |
| Late onset tobacco use [1] | 1.26 | 0.84,1.87 | .264 | 1.34 | 0.86,2.09 | .195 |
| Early onset tobacco use [2] | 3.27 | 1.47,7.25 | .004 | 3.69 | 1.56,8.72 | .003 |
| **Cigarette smoking at baseline (n=1266)** | OR | 95%CI | p-value | AOR | 95%CI | p-value |
| Never | 1.00 | | | 1.00 | | |
| Experimenting | 1.27 | 0.92,1.74 | .149 | 1.33 | 0.93,1.89 | .113 |
| Occasional | 1.01 | 0.50,2.05 | .973 | 1.11 | 0.49,2.51 | .796 |
| Daily | 1.33 | 0.73,2.42 | .347 | 1.68 | 0.83,3.41 | .148 |

[1] Late-onset tobacco use = ≥ 14 years of age
[2] Early–onset tobacco use = <14 years of age
[3] Sex interaction: Likelihood-ratio test LR $chi^2$ (2) = 5.21; p= .074

**Table 2.**The odds ratios for any of the suicide related behaviors (intentional self-injury and/or suicide ideation) at age 22 according to tobacco use behavior in a population-based sample of twins.

| | **Model 1** (Adjusted for age and sex) | | | **Model 2** (Adjusted for age, sex, baseline school achievement, depression, impulsivity, alcohol, and parental education) | | |
|---|---|---|---|---|---|---|
| **Age of regular tobacco use initiation (n=674 females)[3]** | OR | 95%CI | p-value | AOR | 95%CI | p-value |
| Never | 1.00 | | | 1.00 | | |
| Late onset tobacco use [1] | 1.79 | 1.23,2.60 | .002 | 1.92 | 1.27,2.92 | .002 |
| Early onset tobacco use [2] | 3.53 | 1.67,7.45 | .001 | 3.97 | 1.73,9.13 | .001 |
| **Cigarette smoking at baseline (n=1265)** | OR | 95%CI | p-value | AOR | 95%CI | p-value |
| Never | 1.00 | | | 1.00 | | |
| Experimenting | 1.30 | 0.59,1.76 | .091 | 1.33 | 0.96,1.85 | .090 |
| Occasional | 1.23 | 0.64,2.37 | .535 | 1.42 | 0.67,3.00 | .365 |
| Daily | 1.79 | 1.06,3.01 | .029 | 2.13 | 1.12,4.07 | .022 |

[1] Late-onset tobacco use = ≥ 14 years of age
[2] Early–onset tobacco use = <14 years of age
[3] Sex interaction: Likelihood-ratio test LR chi$^2$ (2) = 7.08; p=.029

**Highlights**

- Early-onset tobacco use and daily cigarette smoking are longitudinally associated with intentional self-injury
- Early-onset tobacco use is longitudinally associated with suicidal ideation in females.
- Females with early tobacco use have an increased risk for suicide-related behavior.