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Original Investigation

Depressive Symptoms and Cigarette Smoking in Adolescents and Young Adults: Mediating Role of Friends Smoking

Christian W. Mendo MSc[1,2], Marine Maurel MSc[3], Isabelle Doré PhD[1,2,4], Jennifer O'Loughlin PhD[1,2], Marie-Pierre Sylvestre PhD[1,2]

[1]Centre hospitalier de l'Université de Montréal Research Center, Montréal, Québec, Canada; [2]School of Public Health, Université de Montréal, Montréal, Québec, Canada; [3]Institute of Public Health, Epidemiology and Development, Université de Bordeaux, Bordeaux, France; [4]School of Kinesiology and Physical Activity Sciences, Université de Montréal, Montréal, Québec, Canada

Corresponding Author: Marie-Pierre Sylvestre, PhD, Centre hospitalier de l'Université de Montréal Research Center 850 Saint-Denis, Montreal, QC H2X 0A9, Canada. Telephone: 1-514-890-8000 extn. 31473; E-mail: marie-pierre.sylvestre@umontreal.ca

Abstract

Introduction: We examined the mediating role of friends smoking in the association between depressive symptoms and daily/weekly cigarette smoking from adolescence into adulthood.
Methods: Data were drawn from the Nicotine Dependence In Teens study (NDIT, Canada) and the Avon Longitudinal Study of Parents and Children (ALSPAC, UK) studies. Three age groups were investigated in NDIT: age 13–14 (n = 1189), 15–16 (n = 1107), and 17–18 (n = 1075), and one in ALSPAC (n = 4482, age 18–21). Multivariable mediation models decomposed the total effect (TE) of depressive symptoms on smoking into a natural direct effect (NDE) and natural indirect effect (NIE) through friends smoking.
Results: The odds ratios (ORs) for the TE were relatively constant over time with estimates ranging from 1.12 to 1.35. Friends smoking mediated the association between depressive symptoms and smoking in the two youngest samples (OR [95% confidence interval [CI] 1.09 [1.01,1.17] in 13- to 14-year-olds; 1.10 [1.03,1.18] in 15- to 16-year-olds). In the two older samples, NDE of depressive symptoms was close to the TE, suggestive that mediation was absent or too small to detect.
Conclusion: Friends smoking mediates the association between depressive symptoms and daily/weekly cigarette smoking in young adolescents.
Implications: If young adolescents use cigarettes to self-medicate depressive symptoms, then interventions targeting smoking that ignore depressive symptoms may be ineffective. Our results also underscore the importance of the influence of friends in younger adolescents, suggestive that preventive intervention should target the social environment, including social relationships.

Introduction

Adolescents and young adults with depressive symptoms are twice as likely to smoke cigarettes compared to their peers without symptoms (40% vs. 25%).[1] While numerous studies report that youth smoke to self-medicate depressive symptoms and alleviate negative mood,[2–4] the mechanisms underpinning this association are poorly understood.[2,3] Two recent systematic reviews suggested that, to identify possible mechanistic underpinnings,[2] researchers should better address confounding bias[3] and use longitudinal data with longer, more frequent follow-up.

Friends plays a critical role during adolescence and young adulthood by influencing well-being and risk-taking behaviors such as smoking.[5] However, the hypothesis that friends smoking mediates

the depressive symptoms—smoking association has received little attention.[6] In adolescents, friends smoking is a key risk factor for smoking initiation and progression,[7,8] and friends tend to exhibit similar smoking patterns.[9] Similarly, adolescents tend to select friends with similar levels of depressive symptoms, and they may influence one another's depressive symptoms over time[10] in a process referred to as depression contagion.[11] Contagion may be particularly salient in friendships characterized by self-disclosure, provision of emotional support, and co-rumination.[11] Because adolescents with depressive symptoms are more likely to smoke[1] and friends smoking is an established risk factor for smoking onset and intensity,[12] friends smoking is hypothesized herein as a pathway through which depressive symptoms affect smoking.

In the only longitudinal study to date that investigated mediation by friends smoking, depressive symptoms were associated with friends smoking which in turn, contributed to smoking progression from mid- to late adolescence.[6] Using data from two longitudinal studies, we reexamined this association, addressing two gaps in this literature. First, we investigated the mediating effect of friends smoking during the transition from adolescence to adulthood as peer influence weakens.[13] Second, based on evidence suggesting that peer smoking moderates the association between depressive symptoms and smoking escalation in youth, we considered a possible exposure-mediator interaction.[14,15] Specifically, we used the counterfactual approach for mediation analysis, which decomposes direct and indirect effects while taking exposure-mediator interaction into account.[16] Investigating possible interaction in mediation analyses has been recommended[17] to better characterize the dynamics of mediation[16] and, when interaction is present, to avoid bias and loss of power in estimating indirect effects.[18]

Methods

We considered four age periods, including young (age 13–14), middle (age 15–16), and older (age 17–18) adolescence and young adulthood (18–21). Data for the three adolescent samples were drawn from the longitudinal Nicotine Dependence In Teens (NDIT) study, which describes the natural course of cigarette smoking among adolescents in Montreal, Canada.[19] 1293 students were recruited in 1999 from all grade 7 classes in 10 Montreal-area high schools purposively selected to include French and English schools, urban, suburban and rural schools, and schools located in neighborhoods of high, moderate and low socioeconomic status (SES). Participants were surveyed four times during each of the 5 years of high school (ie, total of 20 cycles). The study was approved by the ethics review board at the University of Montreal Hospital Research Centre.

The young adult sample was drawn from the Avon Longitudinal Study of Parents and Children (ALSPAC), a population-based birth cohort following the babies of 15 247 pregnant women in Avon, UK with delivery dates from April 1991 to December 1992.[20,21] 7729 (52%) of the 14 775 live-born babies had data from age 16 into adulthood.[20] The ALSPAC website describes the data available in a fully searchable data dictionary and variable search tool (www.bristol.ac.uk/alspac/reasearchers/our-data/). Ethics approval for use of ALSPAC data was obtained from the ALSPAC Ethics and Law Committee.

Variables

Depressive Symptoms

In NDIT, depressive symptoms in the past 3 months were measured using the 6-item Kandel depression scale.[22,23] In ALSPAC, past 2-week depressive symptoms were measured with the 13-item Mood and Feeling Questionnaire (SMFQ), a short self-report[24,25] checklist. The reliability of both the Kandel and SMFQ scores in adolescents is high (Cronbach's $\alpha = 0.91$ and 0.84, respectively).[25,26] Higher scores in both scales correspond to more frequent symptoms. To enhance comparability across samples, scores were standardized by subtracting the mean and dividing by the standard deviation (SD).

Daily/Weekly Cigarette Smoking

In NDIT, cigarette smoking was assessed by: *What describes you best? (I have never smoked, I have smoked but not in the last year, I have smoked once or a couple of times last year, I smoke once or couple of times each month, I smoke once or couple of times each week*, and *I smoke every day*). In ALSPAC, smoking was assessed by: *Do you smoke every day?* (*yes*, *no*), and *Do you smoke every week?* (*yes*, *no*). Smoking was dichotomized in both studies to compare daily/weekly smokers to monthly-, occasional- and non-smokers.

Friends Smoking

In NDIT, participants were asked: *How many of the people whom you usually hang out with smoke cigarettes?* In ALSPAC, participants were asked: *Between the ages of 18 to 21, how many of your friends would have ever smoked cigarettes?* In both studies, response options included *none, some, about half, more than half, most or all*. Participants who reported *about half, more than half, most* or *all* were coded as yes. Participants reporting *none* or *some* were coded no (ie, no friends smoking).

Covariates

Potential confounders measured in both NDIT and ALSPAC (Figure 1) included age, sex, socioeconomic status (SES), parents smoke, alcohol consumption and physical activity.[2,4,6,27] Mother graduated high school *(yes, no)* in NDIT, and mother's social class (*high, medium, low*) in ALSPAC were used as proxy indicators of SES. In NDIT, alcohol consumption was assessed by: *During the past 3 months, how often did you drink alcohol?* (*never, a bit to try, once or a couple of times a month, once or a couple of times a week, usually every day),* and responses were recoded no (ie, never) or yes (ie, all other responses). In ALSPAC, participants were asked: *How many drinks do you consume each day when you drink alcohol?* (*0–2, 3–6, ≥7)*. In NDIT, physical activity was assessed as mean minutes/day of moderate and vigorous intensity physical activity (MVPA).[28] In ALSPAC, weekly physical activity frequency was assessed as: *>5, 4–5, 1–3 times/week* or *never*. Models in NDIT were further adjusted for nicotine dependence measured by: *How mentally/physically addicted to smoking cigarettes are you*? (*not at all* vs. *a little, quite, very*). Participants were considered addicted if they responded being *quite* or *very* mentally/physically addicted. No equivalent measure of nicotine dependence was available in ALSPAC. Drug use and number of cigarettes smoked lifetime (available in ALSPAC only), was assessed respectively by: *Have you ever used cannabis or other drugs*? (*yes*, *no*) and *total number of cigarettes that respondent has smoked* were assessed as potential confounders in the ALSPAC models.

We considered four analytical samples: the first three samples were drawn from cycles 5–8, 11–14, and 17–20 in NDIT (ie, age 13–14, 15–16, and 17–18, respectively). We excluded cycles 1–4 because frequency of daily/weekly smoking was too low to estimate a multivariable model at this age. Cycles 5–20 were divided into three time periods: the young adolescent sample included 1189

participants not lost-to-follow-up by cycle 8; the mid- and older adolescent samples included 1107 and 1075 participants not lost-to-follow-up at cycle 14 and 20, respectively. The young adult sample comprised 4482 participants age 18–21 not lost-to-follow-up at age 21 in ALSPAC. Supplementary Figures S2–S5 describe these samples.

We estimated a mediation model in each sample, in which the exposure was depressive symptoms, the outcome was daily/weekly smoking and the mediator was friends smoking. To minimize reverse causation bias, we used consecutive measures of the exposure, mediator, and outcome (ie, depressive symptoms were measured at time t, friends smoking at time t+1, and daily/weekly smoking at time t+2). Confounding variables were assessed at time t-1 so that temporally, the measured values were less likely to lie on the causal pathway between exposure and outcome. Figure 1 shows the directed acyclic graph (DAG) for the mediation models and the mean age at which each variable was measured.

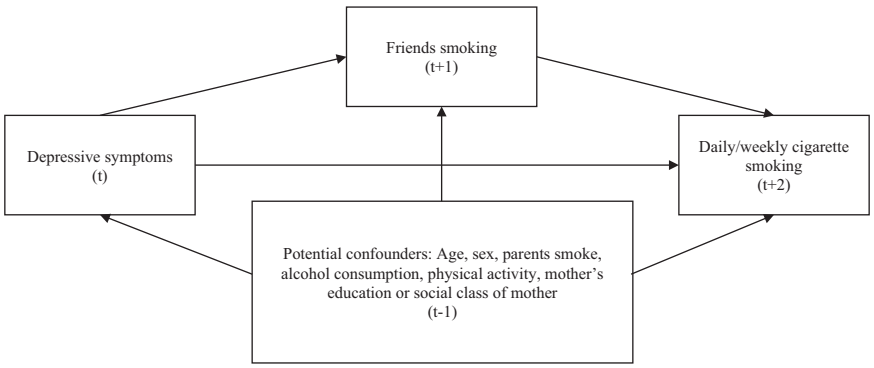
Analysis

Descriptive analyses assessed distributions, identified outliers and computed proportions, means and SDs.We used natural effect models which rely on the counterfactual approach in the causal inference framework, to estimate the total effect (TE) of depressive symptoms on daily/weekly cigarette smoking and its decomposition into natural direct effects (NDE) and natural indirect effects (NIE) through friends smoking.[29] The counterfactual approach, including natural effect models, take interaction between the exposure and the mediator into account. This interaction is generally ignored in traditional mediation analyses using the product or difference method, which may result in invalid inferences.[30]

The counterfactual approach specifies four key assumptions related to confounding that are required for a causal interpretation of natural effects.[31] In our context, the first three assumptions translate into no unmeasured confounding of: (1) the association between depressive symptoms and friends smoking; (2) the association between depressive symptoms and daily/weekly smoking; and (3) the association between friends smoking and daily/weekly smoking. The fourth assumption is no intermediate confounding (ie, no confounders of the association between friends smoking and daily/weekly smoking are affected by depressive symptoms. We assumed a common set of confounders for each of the three associations in our mediation model (see DAG in Figure 1). Confounders were selected based on the literature and included age, sex, SES, parents smoke, alcohol consumption, and physical activity.[2,4,6,27]

NDE expresses the change in the odds of being a daily/weekly smoker if the depressive symptoms score increased by one SD when friends smoking is set at the level naturally observed in the absence of depressive symptoms. NIE expresses the change in the odds of being a daily/weekly smoker in the absence of depressive symptoms, when the value of the mediator changes from the value it naturally takes in the absence of depressive symptoms to the value it naturally takes if depressive symptoms are increased by one SD. NIE is thus equivalent to suppressing the direct effect of depressive symptoms on daily/weekly cigarette smoking. Standard errors and CIs were obtained using nonparametric bootstrap resampling. Mediation analyses were conducted using parametric logistic regression models with the *medflex*[30] package in R version 3.5.1.

Missing values in the four samples ranged from 5% to 15%. We used multiple imputation by chained equations with 10 imputation sets to impute missing values using the *mice* package.[32] Imputation models included all variables considered in the mediation models and, in NDIT, included auxiliary variables that were correlated with those in the mediation model, thus improving the imputation process by adding information and making the "missing at random" assumption more tenable.[33,34] These variables (ie, stress, screen time [ie, computer use, television]) and sociodemographic descriptors (ie, single-parent family, born in Canada) are described in Supplementary Table S4.



Timing of measurement of exposure, mediator, outcome and potential confounders in each sample

	Young adolescents (age 13-14)		Mid adolescents (age 15-16)		Older adolescents (age 17-18)		Young adults (age 18-21)	
	Cycle	Mean age	Cycle	Mean age	Cycle	Mean age	Period	Mean age
Potential confounders	5	13.1	11	14.7	17	16.5	16	16.0
Exposure: Depressive symptoms	6	13.6	12	15.0	18	16.7	18	18.6
Mediator: Friends smoking	7	13.9	13	15.3	19	17.0	20	20.0
Outcome: Daily/weekly smoking	8	14.1	14	15.9	20	17.1	21	21.2

Figure 1. Directed Acyclic Graph displaying the hypothesized causal associations between depressive symptoms and cigarette smoking directly and indirectly through friends smoking.

Sensitivity Analysis

We first compared results obtained in the complete datasets to those using multiple imputations. In a second sensitivity analysis, we re-estimated the models using the same set of potential confounders in NDIT and ALSPAC (ie, not adjusting for nicotine dependence in NDIT and not adjusting for drug use in ALSPAC). We computed E-values, which assess how strong the association between unmeasured confounders and each of the exposure, mediator, and outcome would need to be to nullify the estimated TE, NIE, and NDE.[35]

Results

Table 1 presents participant characteristics in each sample in the imputed dataset (Supplementary Table S1 reports these same characteristics in the complete datasets). Supplementary Table S3 shows the differences between adolescents retained and not retained (due to attrition) for the analyses. The only substantively meaningful differences were apparent in the older adolescent sample (age 17–18). Specifically, compared to participants not included, those included had higher levels of physical activity (mean (SD) 15.3 (11.2) vs. 12.2 (11.9)), a lower proportion consumed alcohol (19.9% vs. 23.6%), more had mothers who were not high school graduates (7.6% vs.5.3%,), fewer had friends who smoke (34.1% vs. 41.2%) and fewer had parents who smoke (25.5% vs. 30.3%). In ALSPAC, relatively fewer young adults included in the analyses consumed <2 alcoholic drinks per day (21.6% vs 27.7%), smoked cigarettes (14.1% vs 23.4 %) and lived in a household with smokers (24.7% vs 28.5%). However, relatively more young adults included in the analyses had friends who smoke (41.5% vs 35.2%).

Table 2 presents the odds ratios (ORs) and 95% confidence intervals (CIs) for the NDEs, NIEs, and TEs in each sample. TEs for depressive symptoms on the odds of daily/weekly cigarette smoking were relatively stable across adolescence (ie, ORs ranged between 1.12 and 1.24), suggesting that an increase of one SD in depressive symptoms was associated with a 12–24% increase in the odd of being a daily/weekly smoker. Although the precision of the OR was relatively constant during adolescence, only the OR for the TE in the sample of 15-16-year-olds excluded the null (OR [95% CI] = 1.24 [1.01,1.53]). In young adults, the TE was larger and more precise (OR [95% CI] = 1.35 [1.28,1.42]) because of the larger sample size in ALSPAC. Friends smoking appears to mediate the association between depressive symptoms and daily/weekly smoking as shown by the NIE in the sample of young (OR [95% CI] = 1.09 [1.01, 1.17]) and mid-age adolescents (OR [95% CI] = 1.10 [1.03, 1.18]). In older adolescents as well as in young adults, the OR for NIE was close to the null and estimated with precision, suggesting that there was no mediation by friend smoke (OR [95% CI] of 1.02 [0.95, 1.10] and 1.03 [0.85, 1.05], respectively).

Sensitivity Analyses

Results were similar in the complete data samples, with slight attenuation of the ORs after multiple imputations. Adjusting for the same potential confounders across the two studies altered the results slightly (Supplementary Table S1). Supplementary Figure S1 shows

Table 1. Charcteristics of Participants in Each Sample (Imputed Data)

Characteristics	Young Adolescents (Age 13–14) (*n* = 1189)	Mid Adolescents (Age 15–16) (*n* = 1107)	Older Adolescents (Age 17–18) (*n* = 1075)	Young Adults (Age 18–21) (*n* = 4482)
Age (y), mean (95%CI)	13.6 (13.6,13.7)	15.0 (15.0,15.0)	16.5 (16.5,16.5)	18.8 (18.8,18.9)
Female, % (95%CI)	52.0 (49.1,54.8)	52.5 (49.5,55.4)	52.9 (49.9,55.9)	60.9 (60.5,61.3)
Daily or weekly smoker, % (95% CI)	13.3 (10.8,15.8)	14.5 (12.1,16.8)	16.9 (14.5,19.4)	19.7 (19.5,20.0)
Depression score, mean (95% CI)				
Kandel (NDIT)	2.0 (1.9,2.0)	2.0 (2.0,2.1)	2.3 (2.2,2.3)	-
SMFQ (ALSPAC)	-	-	-	5.8 (5.6,7.0)
Parents smoke (yes), % (95% CI)	35.0 (32.2,37.9)	30.4 (27.2,33.6)	29.7 (26.9,32.6)	27.8 (26.5,28.1)
Friends smoking (yes), % (95% CI)	30.9 (27.9,33.8)	35.4 (32.3,38.6)	40.5 (37.0,44.0)	36.4 (34.2,36.9)
Nicotine addiction (yes), % (95% CI)	4.2 (3.0,5.3)	5.7 (4.2,7.3)	5.9 (4.3,7.4)	-
Number of cigarettes (total in lifetime), mean (95% CI)	-	-	-	287.5(114.7,315.8)
Drug use (yes), % (95% CI)				6.4 (5.6,7.3)
Alcohol consumption (yes), % (95% CI)	7.7 (6.1,9.2)	13.6 (11.0,16.2)	23.9 (20.9,26.9)	-
Number of drinks per occasion % (95% CI)				
0–2	-	-	-	26.2 (24.1,28.3)
3–6	-	-	-	42.5 (36.0,44.7)
7 or more	-	-	-	31.2 (28.6,35.9)
MVPA (mins/d), mean (95% CI)	18.9 (18.0,19.8)	15.4 (14.6,16.1)	15.5 (14.8,16.2)	-
Team sports (yes), % (95% CI)	62.3 (59.5,65.2)	48.6 (45.3,51.8)	48.4 (44.8,52.0)	-
Physical activity (times/wk) % (95%CI)				
Never			-	16.5 (14.3,17.7)
1 to 3	-	-	-	51.3 (46.1,53.9)
4 to 5	-	-	-	17.1 (15.8,19.2)
More than 5	-	-	-	15.1 (14.3,19.6)
Mother did not graduate high school, % (95% CI)	11.3 (9.4,13.3)	10.5 (8.4,12.5)	10.4 (8.5,12.2)	-
Mother has high social class, % (95% CI)	-	-	-	44.7 (43.2,45.1)

CI = confidence interval; Cells indicated with "-" correspond to variables that were not measured in the corresponding dataset.

Table 2. Odds Ratio (OR) and 95% Confidence Interval (CI) for the Natural Direct, Natural Indirect, and Total Effects of Depressive Symptoms On Daily/Weekly Cigarette Smoking Considering Mediation by Friends Smoking (Imputed Data)

	Young Adolescents (Age 13–14) (*n* = 1189)		Mid Adolescents (Age 15–16) (*n* = 1107)		Older Adolescents (Age 17–18) (*n* = 1075)		Young Adults (Age 18–21) (*n* = 4482)	
Effects	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
NDE	1.06	(0.85, 1.32)	1.13	(0.91, 1.39)	1.09	(0.88, 1.35)	1.37	(1.28, 1.49)
NIE	1.09	(1.01, 1.17)	1.10	(1.03, 1.18)	1.02	(0.95, 1.10)	1.03	(0.85, 1.05)
TE	1.15	(0.94, 1.41)	1.24	(1.01, 1.53)	1.12	(0.89, 1.39)	1.35	(1.28, 1.42)

NDE = natural direct effect, NIE = natural indirect effect, TE = total effect, CI = confidence intervals. Models are adjusted for age, sex, household smoking, alcohol, physical activity, mother's education (NDIT), social class of mother (ALSPAC).

E-value plots for each association in Table 2. With one exception (ie, E-value for NIE in mid-adolescents = 1.10), E-values exceeded 1.28, suggestive that unmeasured confounders would need to have a relatively large association (OR≥1.28) to explain away the observed associations.[36]

Discussion

This study used data from two large samples of young persons to investigate the mediating role of friends smoking in the association between depressive symptoms and daily/weekly smoking. Supportive of the hypothesis that youth use cigarettes to self-medicate depressive symptoms and alleviate negative affect,[2,4,37] we observed that higher levels of depressive symptoms are associated with an increased likelihood of daily/weekly smoking. Further, friends smoking mediated this association in early adolescence. In older adolescents and young adults, there was no important mediating role of friends smoking, with NIE close to zero and precise confidence intervals. We first discuss possible mechanisms underpinning mediation by friends smoking. We then discuss advantages of estimating natural effect models using the counterfactual approach over traditional mediation approaches.

Depressive Symptoms Relate to Friends Smoking in Younger Adolescents

In younger adolescents, depressive symptoms were associated with friends smoking, which in turn related to daily/weekly smoking. Several mechanisms support such an association. First, depressive symptoms are associated with social isolation and loneliness, which can compromise social interactions, relationships[38] and alter friend selection. In fact, there is evidence that youth with depressive symptoms select friends with similar levels of depressive symptoms.[39] Similarity in values, traits, and behaviors facilitates communication and increases the likelihood of shared feelings, understanding and belongingness.[40] Second, adolescents with depressive symptoms are more likely to have friends with riskier behaviors such as substance use.[41] Finally, adolescents with depressive symptoms might be more vulnerable to peer influence and social pressure.[40] Simons et al. reported that adolescents with depression who had friends who use substances were more likely to become substance users than adolescents without depression.[42] Although we did not measure depressive symptoms among friends (and therefore cannot verify the notion), a mediation effect of friends smoking supports the hypothesis that having depressive symptoms impacts the composition of the social network (ie, number of friends who smoke).

Friends Smoking Relates to Smoking in Younger Adolescents

Extant evidence also supports associations between friends smoking and smoking initiation and frequency of smoking.[43] Having friends who smoke could facilitate access to cigarettes and promote a normative perception of smoking.[44–46] Because adolescence is characterized by increasing bonds with peers, friendships between adolescents with depressive symptoms likely increase the risk of adopting or modeling health-risk behaviors of friends.[47,48] According to social learning theory,[49] affiliation with friends who engage in risk behavior predicts an adolescent's own health-risk behavior. Friends can have a direct influence on adolescent smoking by acting as role models and providing social reinforcement. Smoking could also be motivated by attempts to avoid exclusion by friends who smoke.[50]

No Mediation by Friends Smoking in Older Samples

In contrast to our findings in younger adolescents, we did not observe a mediating role of friends smoking in older adolescents or young adults, with NIE close to zero and precise confidence intervals. Peer influence may decline as adolescents gain self-mastery and develop social identities during the transition into adulthood.[51] Social learning theory suggests that, compared to older adolescents, younger adolescents are more inclined to reproduce and imitate peer behavior[49] in order to avoid social exclusion.[50,52] Older adolescents and young adults have more assertive social identities, which allow them to detach from peer influences, and act according to personal norms. In addition, irrespective of friends smoking, cravings and withdrawal increase over time with sustained smoking,[53] and could eventually over-ride peer influences on smoking.[54]

Although our study examines mechanisms that may underpin how depressive symptoms affect adolescent smoking, other studies suggest a reverse association in which repeated exposure to nicotine modifies the regulation of brain neurotransmitters[2,38,40] including hypersecretion of cortisol, a hormone important in the psychobiology of depression in adolescents.[44] Two recent systematic reviews suggest that the association is bidirectional, but that effect sizes are generally not well-measured, precluding assessment of the relative importance of each direction of the association. While a recent Mendelian randomization study of 400,000 UK adults supported bi-directionality,[45] it was suggested that long-term smoking exposure was necessary to increase the risk of depression, which could explain why previous Mendelian randomization studies that relied on measures of current smoking frequency and intensity (ie, ignoring long-term exposure[46,47]) did not clearly support a causal effect of smoking on depression. If this tenet holds, it is possible that

exposure to smoking is not of sufficient duration in adolescents to cause depression.

Advantages of Our Modeling Strategy

Our results align with those of Audrain-McGovern et al. who used a different statistical approach (ie, parallel processes latent growth curves models) in a sample with a narrower age range (14–18) than in our study (13–21). Similar to Audrain-McGovern et al., we observed that friends smoking mediates the association between depressive symptoms and smoking in early to mid-adolescence. However, our use of natural effect models in the counterfactual approach framework in four samples ranging in age from 13 to 21 extend Audrain-McGovern et al.'s findings in two important ways. First, by incorporating an exposure-mediator interaction term, we relaxed the assumption of a consistent effect of friends smoking on smoking across levels of depressive symptoms, which is supported by the literature.[14,15,24] Our intent in incorporating moderation was not to provide a mechanistic interpretation, but rather to provide a more flexible and comprehensive depiction of the association in our mediation model.[16] Unlike traditional mediation models, the counterfactual approach framework allows estimation of NDE and NIE that sum to TE in the presence of interaction between the exposure and mediator.[17] Second, we investigated whether the mediating role of friends smoking changes from adolescence into young adulthood, and observed that the influence of friends smoking declines with age, possibly indicative of different mechanisms in younger versus older adolescents or young adults.

Conditions for causal interpretation of the estimated TE, NDE, and NIE in the counterfactual approach framework include among others, no unmeasured confounding.[55] Our E-values suggest that unmeasured confounders would need to be strongly associated with the exposure, mediator or outcome to negate the estimated associations. While unlikely given the confounders included in our analyses, residual confounding may be present because of unmeasured factors (ie, childhood adversity, self-esteem, academic performance). Additional conditions include that there must be no confounders of the association between friends smoking and cigarette smoking that are affected by depressive symptoms.[55] Use of a longitudinal design that ensured temporal ordering of potential confounders, exposure, mediator, and outcome, maximized the likelihood that this last condition was not violated. We could not investigate the mediating role of friends' depressive symptoms because we did not collect these data in NDIT or ALSPAC. Since evidence supports that youth select friends with similar levels of depressive symptoms, future studies should investigate friends' depressive symptoms and friends smoking as sequential mediators of the association between depressive symptoms and smoking.

Study strengths include the use of two large population-based studies of young people, which permitted investigation of the association at different junctures during the transition from adolescence into young adulthood. Limitations include that adjustment for the same confounders across samples was not possible. However, most potential confounders were measured similarly across studies, and additional adjustment for nicotine dependence in NDIT and drug use in ALSPAC did not alter interpretation of the results. Measures of depressive symptoms differed across studies, but we standardized the measures to enhance comparison. Standardization was not feasible for friends smoking (ie, an ordinal variable referring to number of friends who currently smoke cigarettes in NDIT, and who have "ever smoked" in ALSPAC). However, given possible telescoping effects[56] and varying friendship durations (ie., participants could forget which friends used to smoke in the distant past), responses are more likely to reflect friends who currently smoke than who quit in the distant past). Thus, the ALSPAC measure is likely an acceptable proxy for current friends smoking. This notion is supported by the fact that the proportion of friends smoking in ALSPAC is consistent with trends in NDIT (which used the same measure from age 13 to 18). Finally, while the different frequency of assessments in NDIT (every 3 months) and ALSPAC (annually) may be viewed as a limitation, it is not known how long it takes for depressive symptoms to translate into smoking (ie, a direct effect) or into higher proportions of friends smoking and then into regular smoking (ie, an indirect effect). Although it is possible that the mechanisms under investigation cause changes too rapid to be captured with annual measurements, it is also possible that both ALSPAC and NDIT captured similar associations. Overall, NDIT and ALSPAC results tell a consistent story. Other limitations include that self-report measures are subject to misclassification. Selection bias due to loss-to-follow-up may be an issue in both studies, although comparison of included and excluded participants revealed few differences in the variables of interest.

Implications for Intervention

If, as supported by our results, youth use cigarettes to self-medicate depressive symptoms, then preventive intervention targeting smoking that ignores depressive symptoms may be ineffective.[57] Our results highlight the influence of friends in younger adolescents, suggesting that interventions must not focus solely on individuals, but also target the social environment including social relationships. Interventions targeting the influence of friends smoking that seek to reinforce self-esteem and self-mastery might help young adolescents gain confidence and reduce the adverse influence of friends.[46,47] As underscored by Eisenberg et al., who studied four aspects of perceived social norms in adolescent smoking (ie, perceived prevalence of smoking, belief that adults care about adolescent smoking, frequency of noticing adolescent smoking, perceived adult disapproval of adolescent smoking),[58] social norms in young persons are complex, being influenced by both peers and parents. Because adolescents spend much of their time with peers, having many friends who smoke may make them feel that smoking is normative.[13,49,59]

Conclusion

This study suggests that friends smoking mediates the association between depressive symptoms and daily/weekly cigarette smoking in young adolescents. This mediation role, however, decreases as adolescents age and transition into young adulthood. Interventions to prevent depressive symptoms and daily/weekly cigarette smoking in young adolescents should target peer influences, although this focus may not be as critical in interventions for older adolescents or young adults.

Supplementary Material

A Contributorship Form detailing each author's specific involvement with this content, as well as any supplementary data, are available online at https://academic.oup.com/ntr.

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Declaration of Interests

None declared.

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