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Understanding and preventing the multi-fold health problem of smoking in youth: The role of socioeconomic status, depressive symptoms and cultural factors

Depressive symptoms, major depression, and smoking among adolescents: A review

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Abstract

Background The longitudinal relationship between smoking, depressive symptoms, and major depression among adolescents was reviewed. There are four hypothesized relationships between smoking and depression: self-medication; smoking as reward; bi-directionality; and shared vulnerability. **Method** Literature searches were conducted in the following databases: PsycInfo; Scopus; Medline; General Science Abstracts; ERIC; and Web of Science. An ancestry search was also conducted. A total of 450 studies were individually reviewed, and an additional 375 studies were selected and individually reviewed from the ancestry search. To be included in the review, studies had to meet 11 selection criteria: published in a peer-reviewed, English language publication; published between January 1996 and August 2006; the focus was not exclusively on either smoking initiation, maintenance or cessation; adolescents were the index case; included representative, community-based samples; had an intake sample size that was at least 200; assessed more than just the construct 'stress'; included at least one follow-up assessment; was focused in part on determining the nature of the relationship between smoking and depression; was not a primarily genetics- or biologically-based study; and measured either depressive symptoms or major depression using a validated diagnostic instrument. **Findings** A total of 16 independent longitudinal studies were included in the review. Of the four studies that assessed major depression, each hypothesis—except shared vulnerability—was supported, with only one of the sixteen studies failing to uncover a relationship between smoking and depression. Among the twelve studies that assessed depressive symptoms, the smoking as reward and self-medication hypotheses were each supported in five studies. The bi-directionality hypothesis was supported in only two of sixteen studies. **Conclusions** Several conclusions can be drawn from the review. First, the smoking-depression relationship among adolescent populations varies to an important extent as a function of: (a) the type of depression measure that is used and (b) participants' smoking status. Second, unobserved factors do not completely explain away the smoking-depression relationship, but attenuate its strength. Third, smoking exerts different effects depending on the severity and length of depressive symptoms or depressive episode and vice versa. Implications of the findings are discussed and a select list of recommendations for future research is outlined. These recommendations are derived from individual studies that were retrieved while searching the literature.

Depressive Symptome, klinisch manifeste Depression und Rauchen bei adoleszenten Jugendlichen: eine Übersicht

Zusammenfassung

Hintergrund: Der längsschnittliche Zusammenhang zwischen Rauchen, depressiver Symptomatik und klinisch manifester Depression wurde untersucht. Vier verschiedene Ansätze versuchen den Zusammenhang zwischen Rauchen und Depression zu erklären: Selbstmedikation, Rauchen als Belohnung, bidirektionale Kausalität, und gemeinsame Vulnerabilität. **Methodik:** Die formale Literatursuche umfasste die folgenden Datenbasen: PsycInfo; Scopus; Medline; General Science Abstracts; ERIC; and Web of Science. Weiterhin wurden Literaturhinweise aus gefundenen Quellen berücksichtigt. Insgesamt wurden 450 Studien in der formalen Literatursuche gefunden, plus 375 Studien durch die erweiterte Quellensuche. Die folgenden 11 Einschlusskriterien wurden geprüft: Erscheinen in einer peer-reviewed Zeitschrift, englische Sprache, Publikation zwischen Januar 1996 und August 2006, kein ausschliesslicher Fokus auf Rauchverhalten, individuelle Erhebung bei adoleszenten Jugendlichen, repräsentative Erhebung der Allgemeinbevölkerung, Stichprobengrösse von mindestens 200, Erhebung depressiver Symptomatik, die über die Erhebung von Stress hinausging, mindestens eine Nachbefragung, die Beziehung zwischen Rauchen und Depression war ein Fokus der Untersuchung, keine rein genetische oder biologische Studie, Messung von depressiver Symptomatik oder Depression mit standardisierten Messinstrumenten. **Hauptergebnisse:** 16 Studien erfüllten die Einschlusskriterien. Alle Studien mit einer Ausnahme fanden einen Zusammenhang zwischen Rauchen und depressiver Symptomatik bzw. manifester klinischer Depression. Die vier Studien, die manifeste Depression untersuchten, belegten drei der vier Erklärungsansätze, mit gemeinsamer Vulnerabilität als Ausnahme. Von den restlichen 12 Studien unterstützten je 5 die Selbstmedikationshypothese und den Erklärungsansatz von Rauchen als Belohnung. Zwei Studien fanden Belege für die Hypothese einer bidirektionalen Kausalität. **Weitere Ergebnisse und Schlussfolgerungen**: Es besteht ein Zusammenhang zwischen Rauchen und Depression bei adoleszenten Jugendlichen, der auch in längsschnittlichen Studien aufgefunden werden kann. Die Stärke dieses Zusammenhangs hängt aber von der jeweiligen Erhebungsmethodik ab. Potentielle Konfundierung durch nicht gemessene Drittfaktoren ist nicht wahrscheinlich. Hinsichtlich der Erklärung des Zusammenhangs sind weitere Studien notwendig. In der Diskussion werden Empfehlungen für die Durchführung solcher Studien aufgezeigt.

Epidemiology of Adolescent Smoking and Depression

Smoking remains one of the most important causes of chronic disease world wide.[1,2] It is well established that initiation of smoking is most likely to occur during adolescence[3-8] and can lead to symptoms of nicotine dependence long before transition to regular smoking has occured.[9,10] (for a review, see ref[11]). Smoking accounts for a number of adverse health consequences, including lung cancer deaths as well as heart disease and emphysema.[12] Because these health consequences vary as a function of intensity and duration of smoking behavior, earlier onset of smoking provides greater time and opportunity for the development of illness in later life,[13] which represents a critical window of opportunity for preventive interventions. Preventing smoking initiation and administering smoking interventions for adolescents requires collecting detailed and current tobacco surveillance data.[14]

Collection of such data has been facilitated by several large-scale surveillance projects. For example, bringing together researchers from the WHO, the Canadian Public Health Association, and the U.S. Centers for Disease Control and Prevention, the Global Youth Tobacco Survey (GYTS) was used to assess 747,603 13 to 15 year-old adolescents' smoking behavior in 131 countries. Results indicate that 17.5% and 17.9% of respondents in the Americas and European regions respectively were current smokers; the highest prevalence rates of all six WHO regions.[15] In the United States, data from the 2006 Monitoring the Future Study[16] and 2005 Youth Risk Behavior Survey[17] indicate that the decline in current smoking has halted among some adolescent cohorts. Despite concerted effort by public health authorities and governments in responding to the problem of adolescent smoking, some groups of adolescents continue to smoke at consistently high rates. These adolescents appear to be resistant to current public health intervention and prevention programs; a finding that supports the hardening hypothesis.[18-23]

Several prospective studies of adolescent depression indicate that mean levels of depressive symptoms rise in middle adolescence from generally low levels in childhood.[24-27] Researchers generally distinguish between 'depressive symptoms' and 'depressive disorder' (i.e., major depression), noting that several underlying differences characterize both constructs. Indeed, both reflect different assumptions about the nature of psychopathology and depressive phenomena,[28-30] and serve different purposes (see ref[31] for a review). Importantly, the prevalence of depressive symptoms is generally higher than depressive disorder.[32] Using adolescent-specific cut-offs, the prevalence of depressive

symptoms, through the use of depressive symptom scales like the Center for Epidemiological Studies Depression Scale (CES-D),[33] ranges from 9% to 31%.[34-36] These scales, although not designed to diagnose clinical depression, provide meaningful insights into the construct during adolescence. For studies that have examined clinical adolescent depression in the United States and Europe, the lifetime prevalence estimates of major depressive disorder (MDD) range from 13% to 22% by age 18.[37,38] According to one review,[39] there is up to a six-fold increase in rates of clinical depression from early (3% prevalence at age 15) to late (17% prevalence at age 18) adolescence (see also ref[40]).

For over a decade, several published reviews from a number of disciplinary frameworks have consistently found a relationship between adolescent smoking and depression.[4,6,8,41-47] This consensus, however, has been tempered by lingering uncertainty over the causal and consequential mechanisms that underlie this relationship. For instance, whether smoking precedes the development of depression is dependent in part on methodological issues, including: the characteristics of the cohort under investigation (e.g., ethnicity; community vs. clinical sample; geographical location, etc); how constructs are measured; timing and spacing of follow-up; and choice of statistical analyses. Moreover, this uncertainty has not been clarified by reviews of the literature, since such reviews have their own limitations. For instance, some reviews have only assessed the relationship in passing and failed to specify what selection criteria were used (example refs[4,8,44]), while others have completely ignored the distinction between depressive symptoms and depressive disorder in assessing the nature of the relationship (example refs[4,43]). With the benefit of the extant literature, our review was restricted to assessing the smoking-depression relationship within a framework that encompassed a strictly defined subset of studies and hypothesized pathways in an attempt to preserve conceptual clarity.

Smoking and Depression: Four Hypothesized Relationships

Four hypotheses[48] have been developed to account for the relationship between smoking and depression. To varying degrees, although developed mainly in adult populations, each has received some empirical support in adolescent populations. Each hypothesis assumes that smoking and depression are correlated with each other. The difference lies in the specific causal and consequential pathways that are used to explain how smoking and depression interact. First, the 'self-medication'[49-60] hypothesis suggests that those already

experiencing depression use nicotine—through cigarettes—as a coping mechanism.[53,55,61-63] It is expected that a person who experiences depression is at increased risk for smoking and decreased likelihood of smoking cessation. Second, the 'smoking as reward' hypothesis focuses on the influence of nicotine on mood regulation through reward.[64-69] According to this view, because nicotine affects mood through alteration of neurochemicals such as, but not limited to, dopamine, norepinephrine, and acetylcholine in the regulatory systems, smoking is expected to precede the onset of depression.[66,68] A third hypothesis postulates a reciprocal relationship (i.e., 'bi-directionality') between smoking and depression.[48,62,70] This view suggests that a person who experiences depression is at increased risk of smoking and a person who smokes is at increased risk of developing depression. Specifically, initiation of smoking is the result of attempts to alleviate depression, while maintenance of smoking is reinforced by the desire to prevent reoccurrence of depression. This hypothesis has emerged as a result of the growing recognition of the complexity of the smoking-depression relationship, and various attempts to account for contradictory research findings. Finally, the 'shared vulnerability' hypothesis[†] proposes that a cluster of shared factors (e.g., genetics, psychosocial, etc.) explains the smoking-depression relationship.[54,71-76] However, the origin and characteristics of the etiological factors are not well established, and testing this hypothesis requires gathering detailed genetic data.[77,78] Not surprisingly, only a limited number of studies have tested this hypothesis.

Approach to the Review

Searching the Literature

Given the unsettled nature of the evidence available in the literature, our goal was to review longitudinal studies that assessed the adolescent smoking-depression relationship by considering research published during the past decade (i.e., 1996-2006). In selecting studies for the review, we were careful to preserve the distinction between those studies using depressive symptoms versus depressive disorder as a measure of the construct 'depression'. Additionally, because a large proportion of research in this area also focuses on 'negative affect', which includes stress-based measures, in relation to adolescent smoking, (see ref[46] for a discussion) the decision was made to exclude from the review those studies that included only stress-based measures.

[†] This hypothesis was not tested in any of the 16 studies that were evaluated in this review.

To gather an initial set of articles, we conducted literature searches in the following databases: PsycInfo; Scopus; Medline; General Science Abstracts; ERIC; and Web of Science. Boolean combinations of the following keywords were inputted into each of the databases: smoking; smoking behavior; tobacco; nicotine; tobacco use; cigarettes; predictors; adolescents; teens; youth; adolescence; young; teenagers; longitudinal; prospective; depressive disorder; depression; depressive symptoms; psychopathology; depressive episode; mood disorders; major depression; mechanisms; processes; mediator; and moderator. Using the Boolean combinations within each database generated over 800 hits, with the majority being false positives and repeat citations from other databases. As a preliminary relevance check, study abstracts were individually scanned, and relevant studies were retrieved and reviewed. To ensure comprehensiveness, an ancestry search was conducted on studies that were deemed relevant to the review. A total 450 studies were individually reviewed, and an additional 375 studies were selected and individually reviewed from the ancestry search.

Selection Criteria

To be included in the review, studies had to meet the following 11 criteria: published in a peer-reviewed, English language publication; published between January 1996 and August 2006; the focus was not exclusively on either smoking initiation, maintenance or cessation; adolescents were the index case (for a definition, see refs[79,80]); included representative, community-based samples; had an intake sample size that was at least 200; assessed more than just the construct 'stress'; included at least one follow-up assessment; was focused in part on determining the nature of the relationship between smoking and depression; was not a primarily genetics- or biologically-based study; and measured either depressive symptoms or major depression using a validated diagnostic instrument.

Review of Findings

With our selection criteria, 16 independent longitudinal studies were included in the review. Of the 16 studies, 12 measured depressive symptoms [48,61,67,69,74,77,78,81-85] while the remainder used major depression.[66,86-88] The majority of studies were conducted in the United States [48,61,66,67,69,74,77,78,82,87,88] while others were conducted in Canada,[81,84] Finland,[85] New Zeland,[86] and China.[83] In comparison to cross-sectional studies, there have been fewer longitudinal studies that have assessed the adolescent smoking-depression relationship using rigorous statistical procedures that are able to control for a

variety of observed and unobserved factors. Because of the complexity and variability of the depression-smoking relationship, it is difficult to interpret cross-sectional findings in terms of developmental pathways, stability, and strength of the association. Consequently, numerous authors have recommended the use of a longitudinal design (example refs[6-8,11,45,77,89]) to study such relationships. We have chosen to review this select body of research for its ability to overcome the limitations of cross-sectional research, although we recognize that a longitudinal design in and of itself is at best a marginal proxy of methodological rigor in any given study. In fact, it is unlikely that the use of a longitudinal design can alone provide a necessary and sufficient explanation of the smoking-depression relationship.[90]

Major Depression and Smoking

There was considerable variation in the types of hypotheses that were supported in the four of 16 studies that assessed major depression. The self-medication hypothesis was supported in a study by Fergusson[86] and his colleagues. Using an unselected birth cohort of 1,265 children—derived from the Christchurch Health and Development Study (CHDS)—and conducting more than 14 follow-ups, it was found that at ages 16, 18, and 21 years, participants with major depression had significantly higher rates of daily cigarette use and nicotine dependence than those without major depression. These participants had odds of daily cigarette use that were between 1.70 to 2.19 times higher than those who did not meet diagnostic criteria for major depression, which was assessed by the Diagnostic Interview Schedule for Children (DISC-1) at age 16 and the Composite International Diagnostic Interview (CIDI) at ages 18 and 21 years. After controlling for 10 fixed and confounding factors, major depression was significantly associated with a 19% increased risk in average daily cigarette use.

The smoking as reward hypothesis was supported in a study by Brook et al.[88] The study's baseline sample, which was derived from two counties in upstate New York, contained 975 participants who were followed across three time points. Heavy cigarette use at the second follow-up was significantly associated with development of major depression at the third follow-up, which was assessed by the DISC-1, and was only slightly attenuated after controlling for prior major depression and conduct disorder. Furthermore, the large confidence interval (0.76 to 7.14) for the association between adolescent depression (T_2) and young adult smoking (T_3) made the prediction unstable, which ruled out the self-medication hypothesis.

In a mixed cross-sectional-longitudinal study, Brown et al.[66] found support for the bi-directionality hypothesis. A total of 1,709 participants from western Oregon were

assessed at baseline with an average follow-up interval close to 14 months. Major depression was assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS), including the Present Episode version (K-SADS-E). Two patterns emerged. First, in the cross-sectional analysis, the relationship between smoking and major depression was explained by smokers who had other psychiatric disorders along with major depression. Second, when the sample was studied prospectively, smoking was a risk factor for development of major depression. Indeed, smokers were twice as likely as non-smokers to develop major depression within twelve months. Moreover, major depression was significantly associated with the onset of smoking after controlling for several other psychiatric disorders.

Using a cohort of 1,242 mainly African American participants from Woodlawn, Chicago—followed from the first grade to age 32—Juon et al.[87] found no relationship between any of the smoking trajectory groups and lifetime major depression, which was assessed at young adulthood using the Michigan version of the CIDI. However, participants who had co-morbidity of major depression and drug problems were more likely to be current smokers/early adopters than non-smokers, compared to those who had no problems. It appears that, short of those participants who were found to be co-morbid for smoking and drug problems, Juon et al.'s study does not support any of the four hypothesized relationships between smoking and depression.

Depressive Symptoms and Smoking

Self-Medication

Five of the 16 studies were found to support the self-medication hypothesis. In a sample of 623 African American adolescents followed annually over six years, Repetto, Caldwell, and Zimmerman[77] found an interaction between sex and the smoking-depression relationship. Male, but not female, participants with higher levels of depressive symptoms—assessed by the Brief Symptom Inventory (BSI)—in ninth grade, were more likely to use cigarettes in 10th grade. This relationship persisted after controlling for prior cigarette use, prior depressive symptoms, other substance use, and socioeconomic status (SES). A similar pattern was found in a study by Costello et al.[61] The sample comprised 1,420 participants in the Great Smoky Mountains Study (GSMS) who were assessed for depressive symptoms using the Child and Adolescent Psychiatric Assessment (CAPA). Males with higher rates of depressive symptoms had significantly elevated rates of every type of substance use, including smoking, than non-depressed males. Females who had higher rates of depressive symptoms also had elevated rates of every type of substance use, but the

difference was not significant possibly due to inadequate power. Controlling for parental drug problems, parental mental illness, including current maternal depression, was not associated with prevalence or onset of any substance use.

Stress was found to be an important risk factor for smoking in a study by Koval et al.[84] The baseline sample contained 1,598 participants from Scarborough, Ontario who were in the sixth grade (approximately age 11) and were followed to the eighth grade (approximately age 13). Depressive symptoms were measured using a version of the CES-D developed for use with adolescent populations. For males and females, increased stress was associated with increased likelihood of smoking, although, surprisingly, the presence of depression did not modify this relationship (i.e., the stress-depression interaction was not significant). For males only, the effect of stress on depression was lower for those who smoked than for those who did not smoke, which suggests that male smokers used cigarettes as a coping mechanism. The CES-D was also used in a study by Rodriguez et al.[82] General Growth Mixture Modeling was used to identify depressive symptoms trajectories in a sample of 925 participants attending one of five Northern Virginia high schools. Three trajectories were identified: 'high', 'moderate', and 'low' depressive symptoms groups. Significant differences were found between the high and moderate groups when the effects of baseline smoking on depressive symptoms were examined. For participants in the high group, baseline smoking was associated with an overall deceleration in the rate of increase in depressive symptoms. Conversely, for adolescents in the moderate group, baseline smoking was associated with an overall acceleration in the rate of increase in depressive symptoms. Thus, participants in the high group tended to use smoking as a form of self-medication. Furthermore, adolescents in the high group had the highest rates of current smoking in the ninth and 12th grades, but it is unclear whether smoking or depression came first because data prior to the ninth grade were not available.

A Finnish study[85] of 1,098 participants between the ages of 14 and 15 (at follow-up) supports the self-medication hypothesis, but only for females, which runs contrary to the findings from three U.S.-based studies (see refs[61,77,84]). The Finnish study was based on data collected from the National Epidemiological Child Psychiatry Study (NECP). When assessed by the Children's Depression Inventory (CDI), females who had elevated levels of depressive symptoms at age eight were more likely to be occasional smokers than non-smokers at the age of 14 to 15 years. Additionally, regular smoking was associated with elevated levels of depressive symptoms among males, but this finding was not significant possibly due to the small proportion of depressed males in the sample, which

suggests inadequate power; a limitation that was also observed in the Costello et al. study.[61]

Smoking as Reward

The smoking as reward hypothesis was supported in five of the 16 studies reviewed. Goodman and Capitman[69] analyzed baseline and one year follow-up data from the National Longitudinal Study of Adolescent Health (Add Health). Two samples were identified, and for both, depressive symptoms were assessed using the CES-D. The effects of cigarette smoking on the development of depressive symptoms were studied in a sample of 8,704 adolescents who did not have elevated levels of depressive symptoms at baseline. Multiple logistic regressions revealed that smoking in the past 30 days before the baseline survey was a robust predictor of developing high depressive symptoms at the one year follow-up. The odds of developing high depressive symptoms for baseline current smokers were nearly four times higher than the odds for non-smokers; the relationship remained after controlling for several confounding factors. Additionally, 6,947 adolescents who had not smoked in the 30 days prior to the baseline survey were assessed on the effects of high depressive symptoms on moderate to heavy cigarette smoking at the one year follow-up. Using hierarchical logistic regression and controlling for sociodemographic factors, previous experimentation with smoking, and high depressive symptoms at follow-up, it was found that high depressive symptoms at baseline more than doubled the odds of becoming a heavy smoker. Nonetheless, after covariates were included in the regression analysis, high depressive symptoms at baseline and current high depressive symptoms were not significant.

In a thirteen year longitudinal study with five follow-ups, Brook, Schuster, and Zhang[78] examined the smoking-depression relationship in a sample of 688 participants representative of the population of New York State in terms of SES and related demographic variables. Depressive symptoms were measured at each wave using the Hopkins Symptom Checklist (HSCL). Cumulative history of cigarette smoking (a score representing the sum of T_2, T_3, and T_4) was significantly associated with elevated depressive symptoms at T_5, both with and without controlling for previous depressive symptoms at T_4. A similar analysis was conducted to examine the relationship between a cumulative history of depressive symptoms and cigarette smoking at T_5 with and without controlling for previous cigarette smoking (at T_2, T_3, and T_4). Although a history of depressive symptoms was associated with later cigarette smoking, when previous smoking at T_4 was controlled, the findings were not significant.

A Canadian study by Galambos, Leadbeater, and Barker[81] used 1,322 adolescents between the ages of 12 and 19 years at baseline to study the depression-smoking relationship across three data waves, with data collection occurring every second year. The sample was derived from Canada's National Population Health Survey (NPHS). The CIDI was used to measure depressive symptoms. Adolescents who smoked at baseline (1994) were 1.4 times more likely to report elevated levels of depressive symptoms in 1996 or 1998, with smoking being an especially robust predictor of depression in the younger cohort. In addition, among the younger, but not older, cohort, there was a significant correlation between earlier depressive symptoms and later smoking.

There were two U.S.-based longitudinal studies that used a validated six item depressive symptoms scale developed by Kandel and Davies.[91] Choi et al.[67] studied 6,863 adolescents between the ages of 12 and 18 years who participated in the 1989 National Teenage Attitudes and Practices Survey and its follow-up in 1993 (TAPS I and II), and who did not have elevated levels of depressive symptoms at baseline. Smoking significantly predicted development of depressive symptoms across sex, although the relationship was stronger for females. Males who were established smokers at baseline were nearly twice as likely as never-smokers at baseline to develop elevated levels of depressive symptoms. There was a dose-response relationship between smoking and depressive symptoms among females, with those who were current smokers at baseline being two times as likely as those who were never-smokers to develop high levels of depressive symptoms; females who were experimenters had an intermediate risk. Adolescents who stopped smoking at any time during the four year period decreased their chances of developing depressive symptoms as opposed to those who either continued or established a smoking habit. For example, among current established smokers at baseline who quit during follow-up, only 12.2% developed high levels of depressive symptoms compared to participants who remained current established smokers at follow-up (18.8% of this latter group developed depressive symptoms at follow-up). Similarly, Albers and Biener[67,74] used data from 522 adolescents who participated in the Massachusetts Tobacco Survey of Youth 1993 and 1997. The adolescents who comprised the sample were selected because they did not have high depressive symptoms at baseline. Results indicate that rebelliousness accounted for nearly 15% of the relationship between smoking and depressive symptoms. Moreover, adolescents who scored high on rebelliousness were two times as likely as those who scored low on rebelliousness to develop high depressive symptoms. At

least in this sample, it appears that rebelliousness is an important factor that affects the relationship between smoking and depression.

Bi-directionality

Only two of 16 studies supported the bi-directionality hypothesis. Windle and Windle[48] obtained data from 1,218 adolescents who participated in the Middle Adolescent Vulnerability Study (MAVS); a four wave longitudinal study based in Western New York. Depressive symptoms were measured using the CES-D. After controlling for alcohol, other substance use, and delinquent activity, it was found that heavy cigarette use predicted increases in depressive symptoms across a 1.5 year interval. Also, persistently high levels of depressive symptoms predicted increases in smoking across a 1.5 year interval. The bi-directional influence findings emerged only for both heavy cigarette use and high levels of depressive symptoms.

A study by Lam et al.[83] is the first in Asia to examine the smoking-depression relationship using a longitudinal design (two wave), which contained a one year interval between baseline and follow-up. The sample comprised 1,894 Chinese adolescents from Hong Kong. The mean age at baseline was 12.7 years. Depressive symptoms were measured using a 13 item scale (Cronbach's alpha= .86 for the overall scale) developed by two of the investigators. Several important findings emerged. Participants who were never smokers at T_1, but who had high levels of depressive symptoms, were more likely to smoke at the follow-up. When sex and age were controlled, never-smokers who experienced high levels of depressive symptoms at baseline were nearly 50% more likely to smoke at follow-up than those who reported low levels of depressive symptoms at baseline. As well, participants who had low levels of depressive symptoms at T_1, and were never-smokers, were less likely to have elevated levels of depressive symptoms than both ex- and current smokers at T_2. After controlling for sex and age, ever smoking at T_1 predicted high depressive symptoms at T_2.

Discussion

As statistical methods and longitudinal research designs become increasingly complex, one clear benefit is the ability to provide more comprehensive explanations of relationships between variables. Both these developments have greatly contributed to our understanding of the natural history of smoking. They have also benefited research in the area of depression. A large body of evidence linking both areas has been accumulated over the past three decades, with the

majority of studies published in the past fifteen years. Such research supports a relationship between smoking and depression among adults and, more recently, adolescents. In this review, we assessed the strength of this relationship in adolescent populations by examining longitudinal studies published between 1996 and 2006.

Applying a stringent set of criteria for inclusion in our review achieved two purposes. First, it ensured that the more methodologically rigorous studies were used as a basis for drawing qualitative conclusions across disparate samples, contexts, and time periods. Second, it enabled us to conduct a theoretically-driven review by separating findings according to the type of hypothesis supported in a given study. This latter approach is new to the literature, and was conducted with the aim of promoting theory-based research and development. When researchers approach a study with explicitly defined hypotheses, results are situated within a defined context, which helps to make better sense of the findings. It also simplifies the process of replication and extension. Unfortunately, a number of studies we reviewed either did not consider all the relevant hypothesized relationships between smoking and depression or did not explicitly discuss them (for notable exceptions, see refs[48,77,78,84]). This can be avoided in the future by more focused literature searches, with particular emphasis on reviews, and explicit mention of what specific hypotheses, derived from which theoretical frameworks, are being tested. Thus, we encourage subsequent reviews to adopt a thematic approach similar to ours.

In terms of findings from this review, of the four studies that assessed major depression, each hypothesis—except shared vulnerability—was supported. Also, only one of the sixteen studies failed to uncover a relationship between smoking and depression.[87] Among the twelve studies that assessed depressive symptoms, the smoking as reward and self-medication hypotheses were each supported in five studies. The bi-directionality hypothesis was supported in only two of the sixteen studies. Overall, there is little evidence to doubt that there is a meaningful relationship between smoking and depression not completely explained by unobservable factors (cf. refs[90,92-94]). Thus, despite the relatively small number of studies included in the review, several conclusions can be drawn from the available data. First, the smoking-depression relationship among adolescent populations varies to an important extent as a function of: (a) the type of depression measure (major depression vs depressive symptoms) that is used and (b) participants' smoking status (i.e., occasional vs regular smoker). The smoking-depression relationship is most likely to be found among participants who are regular smokers, and who are diagnosed with major depression; a

finding confirmed by this review. However, a relationship of similar strength is also likely to be found among regular smokers who experience elevated levels of depressive symptoms. Second, a variety of unobserved factors (e.g., adolescents' home environment; genetic predisposition) does not completely explain away the smoking-depression relationship, but attenuate its strength. However, because different studies account for different unobservable factors, it is difficult to assess which factors are more prominent 'third variables' than others. Third, smoking exerts different effects depending on the severity and length of depressive symptoms or depressive episode and vice versa. Although this would seem to support the bi-directionality hypothesis—and at least one review has reached such a conclusion[95]—it does not preclude support for any of the other three hypotheses because, at different developmental time points, different mechanisms could be influencing either smoking or depression or both. Thus, we caution against searching for the *one* hypothesis that can best explain the smoking-depression relationship across the developmental life course. Indeed, such an explanation may be too simplistic to fully account for all contingencies.

Knowing that there is a meaningful relationship between smoking and depression is only part of the story. Indeed, as McMahon[44 (p49)] suggests, "[w]hat are the 'active ingredients' of various psychopathologies that put these youth at risk for tobacco use?…[W]hat are the *mechanisms* and *processes*?" According to recent research, nicotine exposure, through smoking, alters neurochemicals in the brain. With prolonged exposure, depressive mood may result since nicotine may adversely affect dopamine or norepinephrine levels, making it difficult to cope with stressful life events.[78,96,97] Parrot[98] proposes one explanation for the tendency to find a strong association between smoking and depression among regular smokers. To prevent withdrawal symptoms, including irritability and tension, regular smokers must maintain their nicotine intake. Smokers' brains have significantly less monoamine oxidase B (MAO-B) than non-smokers and former smokers.[45] MAO-B is implicated in the breaking-down of dopamine, a neurotransmitter that affects pleasurable feelings associated with substance use. The reduction of MAO-B levels in smokers has a synergistic effect with nicotine by substantially increasing dopamine levels, which makes nicotine more addictive by slowing the breakdown of dopamine.[99] Because adolescents' brains are still in the process of development, these neurobiological mechanisms open the possibility that adolescents' smoking behavior actually modifies the development of brain reward pathways.[47,100] Similarly, Balfour and Ridley[101] suggest that chronic exposure to tobacco smoke may elicit serotonin-related alterations in the brain, which potentially cause increased depression when smoking ceases.

These explanations represent an attempt to elucidate the mechanisms and processes that underlie the smoking-depression relationship. Nonetheless, more research—across diverse samples—is needed to clarify the exact processes and pathways.

As with any qualitative review, certain limitations inherent in the review method exist. For one, we were not able to report on quantitative measures of sensitivity, specificity, and positive predictive value, as would ordinarily be the case in a meta-analysis. Additionally, although our conclusions are supported by rigorous longitudinal studies with large, representative community-based samples, we were only able to review a small proportion of the available literature. Consequently, we encourage future reviews to conduct comparative analyses between longitudinal and cross-sectional methodologies.

Implications

Smoking is a disease with a pediatric age of onset.[11,102,103] The first step to developing efficacious intervention and prevention programs is to have a thorough understanding of the natural history of smoking, whether that understanding is by way of a series of stages or developmental trajectories (for a review, see ref[104]). For researchers examining stage theories of smoking, an important implication is that the difference between smoking initiation and progression in relation to depression is critical. Findings from cross-sectional and longitudinal studies suggest that the causal pathways linking smoking and depression differ depending on an adolescent's smoking status. For instance, social influences might be more prominent factors that affect an adolescent's tendency to initiate smoking while progression to regular smoking might be more likely to be precipitated by neurochemical influences, which manifest as depression.[105,106] Conversely, studies examining developmental trajectories of smoking and depression—like the Rodriguez et al.[82] study—have focused on subpopulations of adolescents at particular risk, and most in need of targeted smoking intervention programs. The implication flowing from this latter body of research is that the unstated assumption of a single population of adolescents at risk for smoking and depression, which guides the majority of studies, is questionable. Not all adolescents are equally influenced by depression and smoking. Identification of subpopulations of at-risk adolescents remains challenging from a methodological perspective, but is nonetheless a promising avenue for future research.

After canvassing the literature, there are several general implications that flow from this review and cut across the different areas of research. First, school administrators, counsellors, family members, and doctors ought to be aware of depressive symptoms/major depression in adolescents, especially for those who smoke. Furthermore, intervention and prevention programs ought to screen for depression among adolescent populations. Part of the reason why relapse occurs may be traced to sub-clinical vulnerability to depression, which may adversely affect attempts to change smoking behavior. Finally, intervention and prevention programs must be initiated early in the life-course (i.e., before age 13).

Recommendations for Future Research

Conducting a comprehensive literature search has enabled us to compile a select list of recommendations for future research on the relationship between smoking and depression among adolescents. The list along with the study that proposes the recommendation(s) are contained below.

- Longitudinal investigation of whether conduct problems mediate the relationship between adolescent smoking and depression[107]
- Assessing the extent to which diagnostic instruments, especially ones that are used to assess depression, are valid[32]
- Smoking cessation or prevention programs should be tailored to stage/trajectory of smoking, while taking into account the person's age (childhood, adolescence, young adulthood)[108]
- Smoking and depression should be measured with the same referent time[108]
- Protective factors that deter adolescents from smoking ought to be studied[109]
- Adolescent smokers who are in cessation programs should be screened for depression prior to and throughout treatment[110,111]
- The influence of parents, parenting styles, peer relations, and self-esteem should be studied as a moderator of the relationship between adolescent smoking and depression[112,113]
- Alternative data collection methods, such as ecological momentary assessment (EMA), ought to be used[114]

Table 1. ***Description of Studies Included in the Review***

Authors	Name of longitudinal study	Location; age/grade; and *N*‡ (at baseline)	Depression measure; name of depression scale	Hypothesis supported	Important finding(s)
Albers & Biener[74]	Massachusetts Tobacco Survey of Youth 1993 and 1997	United States 12-15 year-olds *N*= 1,606	Depressive symptoms Kandel & Davies 6-Item Depressive Symptoms Scale[91]	Smoking as reward	Rebelliousness accounted for close to 15% of the relationship between smoking and depressive symptoms. Also, participants who scored high on rebelliousness were two times as likely as participants who scored low on rebelliousness to develop elevated levels of depressive symptoms.
Brook, Schuster, & Zhang[78]	Population-based	United States 14 year-olds *N*= 688	Depressive symptoms Hopkins Symptom Checklist (HSCL)	Smoking as reward	Whether prior depressive symptoms (T_4) were controlled or not, cumulative history of cigarette smoking was significantly associated with elevated depressive symptoms at T_5. Further, when prior cigarette smoking at T_4 was controlled, the relationship between depressive symptoms and later cigarette smoking was not significant.
Brook, Cohen, & Brook[88]	Population-based	United States 1-10 year-olds (at baseline) *N*= 975	Major depression Diagnostic Interview Schedule for Children Version 1 (DISC-1)	Smoking as reward	Heavy cigarette use at T_2 was significantly associated with major depression at T_3. This relationship was reduced, but remained significant, when prior major depression and conduct disorder were controlled. Also, when prior adolescent smoking was controlled, major depression during adolescence was not associated with young adult smoking.
Brown, Lewinshon, Seeley, & Wagner[66]	Population-based	United States Mean age= 16.6 years *N*= 1,709	Major depression Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-	Bi-directionality	First, participants who were smokers at T_1 were twice as likely as non-smokers to develop major depression. Second, after controlling for a number of psychiatric disorders, only major depression retained statistical significance as a risk factor for onset of smoking. Finally, co-morbidity of smoking and major depression was found, but when co-occurrence of other

			SADS), including the Present Episode Version (K-SADS-E)		psychiatric disorders was controlled, the relationship was not significant.
Choi, Patten, Gillin, Kaplan, & Pierce[67]	1989 and 1993 Teenage Attitudes and Practices Survey (TAPS I and II)	United States 12-18 year-olds *N*= 9,965	Depressive symptoms Kandel & Davies 6-Item Depressive Symptoms Scale[91]	Smoking as reward	Current established smokers at baseline developed a rate of depressive symptoms of 17.3% by follow-up while experimenters and never-smokers had a rate of 12.4% and 10.2% respectively. Additionally, smoking was the most robust predictor of depressive symptoms among both sexes. Males who were established smokers at baseline were nearly two times more likely as never-smokers at baseline to develop depressive symptoms. Females who were current smokers at baseline were twice as likely as never-smokers to develop depressive symptoms. The effect was greater for females and showed a dose-response relationship.
Costello, Erkanli, Federman, & Angold[61]	Great Smoky Mountains Study (GSMS)	United States 9-, 11-, and 13-year-olds *N*= 1,420	Depressive symptoms Child and Adolescent Psychiatric Assessment (CAPA)	Self-medication	Most psychiatric disorders, including depression, showed their first symptoms well before the onset of substance use, which occurred between ages nine to 11. As well, males with elevated rates of depressive symptoms had significantly higher rates of every type of substance use, including smoking, than non-depressed males. This relationship was not significant for females.
Ebeling et al.[85]	1989 National Epidemiological Child Psychiatry Study (NECP)	Finland 14-15 year-olds (at follow-up) *N*= 5,813	Depressive symptoms Children's Depression Inventory (CDI)	Self-medication	Females, but not males, with elevated levels of depressive symptoms at age eight were more likely to be occasional smokers than non-smokers at ages 14 to15 years. A total of 45.1% of previously depressed females smoked regularly compared to non-depressed females (7.9% smoked regularly).
Fergusson, Goodwin, &	Christchurch Health and	New Zealand birth-21 years	Major depression Diagnostic	Self-medication	At ages 16, 18, and 21 years, participants with major depression had significantly higher rates of daily cigarette use as well as

Horwood[86]	Development Study (CHDS)	*N*= 1,265	Interview Schedule for Children (DISC-1); Composite International Diagnostic Interview (CIDI)		nicotine dependence than those without major depression. Participants with major depression had rates of daily cigarette use that were between 1.70 to 2.19 times higher than those who did not have major depression. Moreover, the following factors were associated with both smoking and depression: novelty-seeking; ethnicity; childhood adversity; neuroticism; early conduct problems; parental attachment; anxiety disorders; alcohol abuse/dependence; adverse life events; peer affiliations; previous cigarette smoking; and nicotine dependence. Controlling for these factors reduced the strength of the relationship between smoking and depression.
Galambos, Leadbeater, & Barker[81]	National Population Health Survey (NPHS)	Canada 12-19 year-olds *N*= 1,322	Depressive symptoms Composite International Diagnostic Interview (CIDI)	Smoking as reward	Participants who smoked at baseline were 1.4 times more likely to have elevated levels of depressive symptoms in 1996 or 1998 than non-smokers, with the relationship being especially strong in the younger cohort. Furthermore, a significant correlation was found among the younger cohort between earlier depressive symptoms and later smoking, which supports the self-medication hypothesis.
Goodman & Capitman[69]	National Longitudinal Study of Adolescent Health (Add Health)	United States Non-depressed sample mean age= 15.48; non-current smokers sample mean age= 15.32 *N*= 8,704 (non-depressed); *N*= 6,947 (non-current smokers)	Depressive symptoms Center for Epidemiological Studies Depression Scale (CES-D)	Smoking as reward	In the non-depressed sample, smoking in the thirty days prior to the baseline survey significantly predicted development of depressive symptoms at the one year follow-up. For baseline current smokers, the odds of developing depressive symptoms were almost four times higher than for baseline non-smokers, and the relationship persisted after controlling for a variety of factors. In the non-smokers sample, high depressive symptoms at baseline more than doubled the odds of becoming a heavy smoker. After controlling for confounding factors, high depressive symptoms at baseline and current high depressive symptoms were not significant.
Juon, Ensminger, & Sydnor[87]	Woodlawn Longitudinal Study (WLS)	United States Grade 1 *N*=1,242	Major depression Composite International	None	There was no relationship between any of the smoking trajectory groups and lifetime major depression. However, participants who had co-morbidity of major depression and drug problems were

			Diagnostic Interview (CIDI), Michigan version		more likely to be current smokers/early adopters than non-smokers, compared to participants who had no problems.
Koval, Pederson, Mills, McGrady, & Carvajal[84]	Population-based	Canada Grade 6 *N*= 1,598	Depressive symptoms Center for Epidemiological Studies Depression Scale (CES-D)	Self-medication	For both sexes, increased stress was associated with increased likelihood of smoking, although the presence of depression did not modify this relationship. Furthermore, for males only, the effect of stress on depression was lower for those who smoked than for those who did not smoke.
Lam et al.[83]	Population-based	China Grade 7 *N*= 1,894	Depressive symptoms 13-Item Depressive Symptoms Scale	Bi-directionality	Participants who were never-smokers at baseline, but who had high levels of depressive symptoms, were more likely to smoke at follow-up. When sex and age were controlled, never-smokers who experienced high levels of depressive symptoms at baseline were almost 50% more likely to smoke at follow-up than those who reported low levels of depressive symptoms at baseline. Finally, participants who reported not wanting to quit and those who had been unsuccessful at quitting had higher levels of depressive symptoms at follow-up than those who successfully quit.
Repetto, Caldwell, & Zimmerman[77]	Population-based	United States Grade 9 *N*=850	Depressive symptoms Brief Symptom Inventory (BSI)	Self-medication	Male, but not female, participants with higher levels of depressive symptoms at baseline were more likely to use cigarettes at follow-up. Additionally, this relationship persisted after controlling for prior cigarette use, prior depressive symptoms, other substance use, and socioeconomic status.
Rodriguez, Moss, & Audrain-McGovern[82]	Population-based	United States Grade 9 *N*= 925	Depressive symptoms Center for Epidemiological Studies Depression	Self-medication	For participants who were in the high depressive symptoms trajectory group, baseline smoking was associated with an overall deceleration in the rate of increase in depressive symptoms. However, for adolescents in the moderate depressive symptoms trajectory group, baseline smoking was associated with an overall

			Scale (CES-D)		acceleration in the rate of increase in depressive symptoms. Finally, participants in the high group had the highest rates of current smoking in the ninth and 12th grades.
Windle & Windle[48]	Middle Adolescent Vulnerability Study (MAVS)	United States Grades 10-11 *N*= 1,218	Depressive symptoms Center for Epidemiological Studies Depression Scale (CES-D)	Bi-directionality	Heavy cigarette use predicted increases in depressive symptoms across a 1.5 year interval after controlling for alcohol, other substance use, and delinquent activity. Moreover, persistently high levels of depressive symptoms predicted increases in smoking across a 1.5 year interval.

‡The baseline sample may not represent the actual sample that was analyzed in a given study.

References

(1) Peto R, Lopez AD, Boreham J, Thun M, Heath C. *Mortality from smoking in developed countries 1950-2000: Indirect estimation from National Vital Statistics*. Oxford: Oxford University Press; 1994.

(2) Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. *Journal of the American Medical Association.* 2004;291:1238-1245.

(3) Galea S, Nandi A, Valhov D. The social epidemiology of substance use. *Epidemiologic Reviews.* 2004;26:36-52.

(4) Schepis TS, Rao U. Epidemiology and etiology of adolescent smoking. *Current Opinion in Pediatrics.* 2005;17:607-612.

(5) Geckova A, van Dijk JP, van Ittersum-Gritter T, Groothoff JW, Post D. Determinants of adolescents' smoking behaviour: A literature review. *Central European Journal of Public Health.* 2002;10:79-87.

(6) Turner L, Mermelstein R, Flay BR. Individual and contextual influences on adolescent smoking. *Annals of the New York Academy of Sciences.* 2004;1021:175-197.

(7) Flay BR, Petraitis J, Hu FB. Psychosocial risk and protective factors for adolescent tobacco use. *Nicotine & Tobacco Research.* 1999;1:S59-S65.

(8) Jamner LD, Whalen CK, Loughlin SE et al. Tobacco use across the formative years: A road map to developmental vulnerabilities. *Nicotine & Tobacco Research.* 2003;5:S71-S87.

(9) Gervais A, O'Loughlin J, Meshefedjian G, Bancej C, Tremblay M. Milestones in the natural course of onset of cigarette use among adolescents . *Canadian Medical Association Journal.* 2006;175:255-261.

(10) Klein JD. Adolescents and smoking: The first puff may be the worst. *Canadian Medical Association Journal.* 2006;175:262-263.

(11) Eissenberg T, Balster RL. Initial tobacco use episodes in children and adolescents: Current knowledge, future directions. *Drug & Alcohol Dependence.* 2000;59:41-60.

(12) American Cancer Society. Cancer facts and figures 2005. http://www.cancer.org/downloads/STT/CAFF2005f4PWSecured.pdf . 2005. 9-1-2006.
Ref Type: Electronic Citation

(13) Krainuwat K. Smoking initiation prevention among youths: Implications for community health nursing practice. *Journal of Community Health Nursing.* 2006;22:195-204.

(14) World Health Organization. WHO framework convention on tobacco control. http://www.who.int/gb/ebwha/pdf_filesWHA56/ea56r1.pdf . 2003. 7-26-2006.
Ref Type: Electronic Citation

(15) Warren CW, Jones NR, Eriksen MP, Asma S. Patterns of global tobacco use in young people and implications for future chronic disease burden in adults. *Lancet.* 2006;367:749-753.

(16) Johnston, L. D., O'Malley, P. M., Bachman, J. G., and Schulenberg, J. E. National press release: Decline in daily smoking by younger teens has ended. http://www.monitoringthefuture.org/pressreleases/06cigpr_complete.pdf . 2006. 12-27-2006.
Ref Type: Electronic Citation

(17) US Centers for Disease Control and Prevention. Youth Risk Behavior Surveillance - United States, 2005. http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5505a1.htm . 2006. 8-6-2006.
Ref Type: Electronic Citation

(18) Hughes JR. Comorbidity and smoking. *Nicotine & Tobacco Research.* 1999;1:S149-S152.

(19) Hughes JR. The case for hardening. In: National Cancer Institute, ed. Rockville, MD: US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Cancer Institute; 2003.
(20) Irvin JE. The increasing recalcitrance of smokers in clinical trials. *Nicotine & Tobacco Research.* 2000;5:13-25.
(21) McCormick D, Bor DH. Smoking and mental illness: A population-based prevalence study. *Journal of the American Medical Association.* 2000;284:2606-2610.
(22) Warner KE, Burns DM. Hardening and the hard-core smoker: Concepts, evidence, and implications. *Nicotine & Tobacco Research.* 2003;5:37-48.
(23) Johnson EO, Breslau N. Is the association of smoking and depression a recent phenomenon? *Nicotine & Tobacco Research.* 2006;8:257-262.
(24) Cole DA, Martin JM, Peeke LA, Serocznski AD, Fier J. Children's over and underestimation of academic competence: A longitudinal study of gender differences, depression, and anxiety. *Child Development.* 1999;
70:459-473.
(25) Ge X, Lorenz FO, Conger RD, Elder GH. Trajectories of stressful life events and depressive symptoms during adolescence. *Developmental Psychology.* 1994;30:483.
(26) Wade TJ, Cairney J, Pevalin DJ. Emergence of gender differences in depression during adolescence: National panel results from three countries. *Journal of the American Academy of Child & Adolescent Psychiatry.* 2002;41:190-198.
(27) Wichstrom L. The emergence of gender differences in depressed mood during adolescence: The role of intensified gender socialization. *Developmental Psychology.* 1999;35:232-245.
(28) Compas BE, Ey S, Grant KE. Taxonomy, assessment, and diagnosis of depression during adolescence. *Psychological Bulletin.* 1993;114:323-344.
(29) Cantwell DP, Baker L. Manifestations of depressive affect in adolescents. *Journal of Youth & Adolescence.* 1991;20:121-133.
(30) Kazdin AE. Childhood depression. In: Mash EJ, Terdal LG, eds. *Behavioral assessment of childhood disorders*. 2 ed. New York: Guilford; 1988:157-95.
(31) Petersen AC, Compas BE, Brooks-Gunn J, Stemmler M, Ey S, Grant KE. Depression in adolescence. *American Psychologist.* 1993;48:155-178.
(32) Poulin C, Hand D, Boudreau B, Santor D. Gender differences in the association between substance use and elevated depressive symptoms in a general adolescent population. *Addiction.* 2005;100:525-535.
(33) Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement.* 1977;1:385-401.
(34) Roberts RE, Andrews JA, Lewinsohn PM, Hops H. Assessment of depression in adolescents using the Center for Epidemiologic Studies Depression Scale. *Psychological Assessment.* 1990;2:122-128.
(35) Steinhausen HC, Winkler MC. Adolescent self-rated depressive symptoms in a Swiss epidemiological study. *Journal of Youth & Adolescence.* 2000;29:427-440.
(36) Rushton JL, Forcier M, Schectman RM. Epidemiology of depressive symptoms in the National Longitudinal Study of Adolescent Health. *Journal of the American Academy of Child & Adoelscent Psychiatry.* 2002;41:199-205.
(37) Lewinsohn PM, Hops H, Roberts RE, Seeley JR, Andrews JA. Adolescent psychopathology I: Prevalence and incidence of depression and other DSM-III-R disorders in high school students. *Journal of Abnormal Psychology.* 1993;102:133-144.
(38) Kessler RC, Walters EE. Epidemiology of DSM-III-R major depression and minor depression among adolescents in the National Comorbidity Survey. *Depression & Anxiety.* 1998;7:3-14.
(39) Hankin BL. Adolescent depression: Description, causes, and interventions. *Epilepsy & Behavior.* 2006;8:102-114.

(40) Birmaher B, Ryan ND, Williamson DE. Childhood and adolescent depression: A review of the past 10 years. Part I. *Journal of the American Academy of Child & Adolescent Psychiatry.* 1996;35:1427-1439.
(41) Pederson LL, Koval JJ, McGrady GA, Tyas SL. The degree and type of relationship between psychosocial variables and smoking status for students in grade 8: Is there a dose-response relationship? *Preventive Medicine.* 1998;27:337-347.
(42) Glassman AH. Cigarette smoking: Implications for psychiatric illness. *American Journal of Psychiatry.* 1993;150:546-553.
(43) Derzon JH, Lipsey MW. Predicting tobacco use to age 18: A synthesis of longitudinal research. *Addiction.* 1999;94:995-1006.
(44) McMahon RJ. Child and adolescent psychopathology as risk factors for subsequent tobacco use. *Nicotine & Tobacco Research.* 1999;1:S45-S50.
(45) Mathers M, Toumbourou JW, Catalano RF, Williams J, Patton GC. Consequences and correlates of youth tobacco use: A review of prospective behavioral studies. *Addiction.* 2006;101:948-958.
(46) Kassel JD, Stroud LR, Paronis CA. Smoking, stress, and negative affect: Correlation, causation, and context across stages of smoking. *Psychological Bulletin.* 2003;129:270-304.
(47) Moolchan ET, Ernst M, Henningfield JE. A review of tobacco smoking in adolescents: Treatment implications. *Journal of the American Academy of Child & Adoelscent Psychiatry.* 2000;39:682-693.
(48) Windle M, Windle RC. Depressive symptoms and cigarette smoking among middle school adolescents: Prospective associations and intrapersonal influences. *Journal of Consulting and Clinical Psychology.* 2001;69:215-226.
(49) Khantzian EJ. The self-medication hypothesis of addiction disorder: Focus on heroin and cocaine dependence. *American Journal of Psychiatry.* 1988;142:1259-1264.
(50) Khantzian EJ. The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. *Harvard Review of Psychiatry.* 1997;4:231-244.
(51) Kaplan HB, Martin SS, Robbins C. Pathways to adolescent drug use: Self-derogation, peer influence, weakining of social controls, and early substance use. *Journal of Health and Social Behavior.* 1984;25:270-289.
(52) Kandel DB, Davies M. Adult sequelae of adolescent depressive symptoms. *Archives of General Psychiatry.* 1986;43:255-262.
(53) Breslau N, Kilbey MM, Anderski P. Nicotine dependence, major depression, and anxiety in young adults. *Archives of General Psychiatry.* 1991;48:1069-1074.
(54) Breslau N, Kilbey MM, Anderski P. Nicotine dependence and major depression: New evidence from a prospective investigation. *Archives of General Psychiatry.* 1993;50:31-35.
(55) Killen JD, Robinson TN, Haydel KF et al. Prospective study of risk factors for the initiation of cigarette smoking. *Journal of Consulting and Clinical Psychology.* 1997;65:1011-1016.
(56) Cicchetti D, Toth SL. The development of depression in children and adolescents. *American Psychologist.* 1998;3:221-241.
(57) Escobedo LG, Reddy M, Giovino GA. The relationship between depressive symptoms and cigarette smoking in U.S. adolescents. *Addiction.* 1998;93:433-440.
(58) Lerman C, Main D, Audrain J et al. Depression and self-medication with nicotine: The modifying influence of the dopamine D4 receptor gene. *Health Psychology.* 1998;17:56-62.
(59) Ludman EJ, Curry SJ, Grothaus LC, Graham E, Stout J, Lozano P. Depressive symptoms, stress, and weight concerns among African American and European American low-income female smokers. *Psychology of Addictive Behaviors.* 2002;16:68-71.
(60) Carmody TP. Affect regulation, nicotine addiction, and smoking cessation. *Journal of Psychoactive Drugs.* 1989;24:111-122.

(61) Costello EJ, Erkanli A, Federman E, Angold A. Development of psychiatric co-morbidity with substance abuse in adolescents: Effects of timing and sex. *Journal of Clinical Child Psychology.* 1999;28:298-311.
(62) Lerman C, Audrain J, Orleans CT et al. Investigation of mechanisms linking depressed mood to nicotine dependence. *Addictive Behaviors.* 1996;21:9-19.
(63) Patton GC, Hibbert M, Rossier M, Carlin JB, Caust J, Bowes G. Is smoking associated with depression and anxiety in teenagers? *American Journal of Public Health.* 1996;86:225-230.
(64) Pomerleau OF, Pomerleau CS. Neuroregulators and the reinforcement of smoking: Towards a biobehavioral explanation. *Neuroscience and Biobehavioral Reviews.* 1984;8:503-513.
(65) Pontieri FE, Tanda G, Orzi F, Di Chiara G. Effects of nicotine on the nucleus accumbens and similarity to those of addictive drugs. *Nature.* 1996;382:255-257.
(66) Brown RA, Lewinsohn PM, Seeley JR, Wagner EF. Cigarette smoking, major depression, and other psychiatric disorders among adolescents. *Journal of the American Academy of Child and Adoelscent Psychiatry.* 1996;35:1602-1610.
(67) Choi WS, Patton CA, Gillin JC, Kaplan RM, Pierce JP. Cigarette smoking predicts development of depressive symptoms among U.S. adolescents. *Annals of Behavioral Medicine.* 1997;19:42-50.
(68) Wu L, Anthony JC. Tobacco smoking and depressed mood in late childhood and early adolescence. *American Journal of Public Health.* 1999;89:1837-1840.
(69) Goodman E, Capitman J. Depressive symptoms and cigarette smoking among teens. *Pediatrics.* 2000;106:748-755.
(70) Wang MQ, Fitzhugh EC, Turner LW, Fu Q, Westerfield RC. Association of depressive symptoms and school adolescents' smoking: A cross-lagged analysis. *Psychological Reports.* 1996;79:127-130.
(71) Kendler KS, Neale MC, MacLean CJ, Heath AC, Eaves LJ, Kessler RC. Smoking and major depression: A causal analysis. *Archives of General Psychiatry.* 1993;50:36-43.
(72) Gilbert DG, Gilbert BO. Personality, psychopathology, and nicotine response as mediators of the genetics of smoking. *Behavior Genetics.* 1995;25:133-147.
(73) Fergusson DM, Lynskey MT, Horwood J. Comorbidity between depressive disorders and nicotine dependence in a cohort of 16-year-olds. *Archives of General Psychiatry.* 1996;53:1043-1047.
(74) Albers AB, Biener L. The role of smoking and rebelliousness in the development of depressive symptoms among a cohort of Massachusetts adolescents. *Preventive Medicine.* 2002;34:625-631.
(75) Kendler KS, Neale MC, Sullivan P, Corey LA, Gardner CO, Prescott CA. A population-based twin study in women of smoking initiation and nicotine dependence. *Psychological Medicine.* 1999;29:299-308.
(76) Kandel DB, Johnson JG, Bird HR et al. Psychiatric disorders associated with substance use among children and adolescents: Findings from the Methods for the Epidemiology of Child and Adolescent Mental Disorders (MECA) study. *Journal of Abnormal Child Psychology.* 1997;25:121-132.
(77) Repetto PB, Caldwell CH, Zimmerman MA. A longitudinal study of the relationship between depressive symptoms and cigarette use among African American adolescents. *Health Psychology.* 2005;24:209-219.
(78) Brook JS, Schuster E, Zhang C. Cigarette smoking and depressive symptoms: A longitudinal study of adolescents and young adults. *Psychological Reports.* 2004;95:159-166.
(79) World Health Organization. Global consultation on adolescent friendly health services: A consensus statement. World Health Organization . 2001. 8-20-2006.
Ref Type: Electronic Citation

(80) West P. Health inequalities in the early years: Is there an equalisation in youth? *Social Science & Medicine.* 1997;44:833-858.
(81) Galambos NL, Leadbeater BJ, Barker ET. Gender differences in and risk factors for depression in adolescence: A 4-year longitudinal study. *International Journal of Behavioral Development.* 2004;28:16-25.
(82) Rodriguez D, Moss HB, Audrain-McGovern J. Developmental heterogeneity in adolescent depressive symptoms: Associations with smoking behavior. *Psychosomatic Medicine.* 2005;67:200-210.
(83) Lam TH, Stewart SM, Ho SY et al. Depressive symptoms and smoking among Hong Kong Chinese adolescents. *Addiction.* 2005;100:1003-1011.
(84) Koval JJ, Pederson LL, Mills C, McGrady GA, Carvajal SC. Models of the relationship of stress, depression, and other psychological factors to smoking behavior: A comparison of a cohort of students in grades 6 and 8. *Preventive Medicine.* 2000;30:463-477.
(85) Ebeling H, Moilanen I, Linna S-L et al. Smoking and drinking habits in adolescence: Links with psychiatric distrubance at the age of 8 years. *European Child and Adolescent Psychiatry.* 1999;8:68-76.
(86) Fergusson DM, Goodwin RD, Horwood LJ. Major depression and cigarette smoking: Results of a 21-year longitudinal study. *Psychological Medicine.* 2003;33:1357-1367.
(87) Juon H-S, Ensminger ME, Sydnor KD. A longitudinal study of developmental trajectories to young adult cigarette smoking. *Drug & Alcohol Dependence.* 2002;66:303-314.
(88) Brook JS, Cohen P, Brook DW. Longitudinal study of co-occuring psychiatric disorders and substance use. *Journal of the American Academy of Child and Adolescent Psychiatry.* 1998;37:322-330.
(89) Jackson C, Henriksen L, Dickinson D, Messer L, Robertson SB. A longitudinal study predicting patterns of cigarette smoking in late childhood. *Health Education & Behavior.* 1998;25:436-447.
(90) Duncan B, Rees DI. Effect of smoking on depressive symptomology: A reexamination of data from the National Longitudinal Study of Adolescent Health. *American Journal of Epidemiology.* 2005;162:461-470.
(91) Kandel DB, Davies M. Epidemiology of depressive mood in adolescents. *Archives of General Psychiatry.* 1982;39:1205-1212.
(92) Aldridge K. Letters to the editor. *American Journal of Epidemiology.* 2006;163:779.
(93) Goodman E, Capitman J. Letters to the editor. *American Journal of Epidemiology.* 2006;163:779.
(94) Duncan B, Rees DI. The authors reply. *American Journal of Epidemiology.* 2006;163:780-781.
(95) Upadhyaya HP, Deas D, Brady KT, Kruesi M. Cigarette smoking and psychiatric comorbidity in children and adolescents. *Journal of the American Academy of Child and Adoelscent Psychiatry.* 2002;41:1294-1305.
(96) George TP, Picciotto MR, Verrico CD, Roth RH. Effects of nicotine pretreatment on dopaminergic and behavioral responses to conditioned fear stress in rats: Dissociation of biochemical and behavioral effects. *Biological Psychiatry.* 2001;49:300-306.
(97) Leonard BE. Stress, norepinephrine, and depression. *Journal of Psychiatry & Neuroscience.* 2001;20:S11-S16.
(98) Parrott AC. Does cigarette smoking cause stress? *American Psychologist.* 1999;54:817-820.
(99) Walton R, Johnson E, Manufo M, Neville M, Griffiths S. Genetic clues to the molecular basis of tobacco addiction and progress towards personalized therapy. *Trends in Molecular Medicine.* 2001;7:70-76.
(100) Chambers R, Taylor JR, Potenza MN. Developmental neurocircuitry of motivation in adolescence: A critical period of addiction vulnerability. *American Journal of Psychiatry.* 2003;160:1041-1052.

(101) Balfour DJK, Ridley DL. The effects of nicotine on neural pathways implicated in depression: A factor in nicotine addiction? *Pharmacology, Biochemistry & Behavior.* 2000;66:79-85.
(102) Kessler DA, Natanblut SL, Wilkenfeld JP et al. Nicotine addiction: A pediatric disease. *Journal of Pediatrics.* 1997;130:518-524.
(103) Najem GR, Batuman F, Smith AM, Feuerman M. Patterns of smoking among inner-city teenagers: Smoking has a pediatric age of onset. *Journal of Adolescent Health.* 1997;20:226-231.
(104) Mayhew KP, Flay BR, Mott JA. Stages in the development of adolescent smoking. *Drug & Alcohol Dependence.* 2000;59:S61-S81.
(105) Escobedo LG, Reddy M, Giovino GA. Are baseline depressive symptoms associated with smoking initiation in adolescents? *Western Journal of Medicine.* 2006;170:265.
(106) Breslau N, Peterson EL, Schultz LR, Chilcoat HD, Andreski MA. Major depression and stages of smoking: A longitudinal investigation. *Archives of General Psychiatry.* 1998;55:161-166.
(107) Ritt-Olson A, Unger J, Valente T et al. Exploring peers as a mediator of the association between depression and smoking in young adolescents. *Substance Use & Misuse.* 2005;40:77-98.
(108) Kelder SH, Murray NG, Orpinas P et al. Depression and substance use in minority middle-school students. *American Journal of Public Health.* 2001;91:761-766.
(109) Acierno R, Kilpatrick DG, Resnick H, Saunders B, De Arellano M, Best C. Assault, PTSD, family substance use, and depression as risk factors for cigarette use in youth: Findings from the National Survey of Adolescents. *Journal of Traumatic Stress.* 2000;13:381-396.
(110) Glied S, Pine DS. Consequences and correlates of adolescent depression. *Archives of Pediatrics and Adolescent Medicine.* 2002;156:1009-1014.
(111) Hallfors DD, Waller MW, Ford CA, Halpern CT, Brodish PH, Iritani B. Adolescent depression and suicide risk: Association with sex and drug use. *American Journal of Preventive Medicine.* 2004;27:224-231.
(112) Lloyd-Richardson EE, Papandonatos G, Kazura A, Stanton C, Niaura R. Differentiating stages of smoking intensity among adolescents: Stage-specific psychological and social influences. *Journal of Consulting and Clinical Psychology.* 2002;70:998-1009.
(113) Reynolds MW, Frank C. Smoking and adverse childhood experiences. *Journal of the American Medical Association.* 2000;283:1958-1959.
(114) Whalen CK, Jamner LD, Henker B, Delfino RJ. Smoking and moods in adolescents with depressive and aggressive dispositions: Evidence from surveys and electronic diaries. *Health Psychology.* 2001;20:99-111.