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Investigating the reciprocal temporal relationships between tobacco consumption and psychological disorders for youth: an international review

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ABSTRACT

Objective To investigate reciprocal temporal relationships between tobacco consumption and psychological disorders for youth.

Design: Review

Data sources Five databases (PubMed, Embase, Scopus, CINAHL and PsycINFO) on 26 September 2019 and updated on 11 May 2021, indexing tobacco, mental illness and longitudinal.

Study selection: Methods used consensus and multiple reviewers.

Interventions Cohort studies (n=49) examining tobacco and selected psychological disorders (depression, anxiety, bipolar, psychosis, borderline personality disorder) among youth, and systematic reviews (n=4) of these relationships met inclusion criteria.

Primary and secondary outcome measures Effect of tobacco on psychological disorders and effect of psychological disorders on tobacco.

Data extraction and synthesis Independent extraction by the first author and checked by final author. Joanna Briggs Institute Critical Appraisal Tools were used for all studies.

Included studies had moderate-to-high appraisal scores. We synthesised findings using vote counting for effect direction and descriptive data.

Results Fifty-three studies were included in the review. Thirteen of 15 studies showed a positive effect direction of tobacco on depression ($p<0.001$). Six of 12 studies showed a positive effect direction of depression on tobacco ($p=0.016$). Six of eight studies showed a positive effect direction of tobacco on anxiety ($p=0.016$). Eleven of 18 studies showed a positive effect direction of anxiety on tobacco ($p=0.003$). No effect between tobacco and bipolar, or tobacco and psychosis was found. No studies examined tobacco and borderline personality disorder.

Conclusions Reciprocal relationships existed between tobacco and both depression and anxiety for youth, though causality is unconfirmed. No positive effect direction was found between tobacco and psychosis, perhaps because nicotine has conflicting effects on psychosis. For other relationships examined, evidence was weak because of low number of studies. More research to inform prevention and early intervention is needed.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This review has synthesised, in-depth, 53 studies for evidence of the reciprocal temporal relationships between tobacco consumption and psychological disorders for youth.
⇒ The review has performed an analysis of the quality of the studies and identified knowledge gaps and methodological concerns that require further research.
⇒ The included studies were very heterogeneous, preventing meta-analysis of the results.
⇒ Psychological disorders were classified into broad categories; however, it is possible that young people's experiences of these disorders differ in how they relate to tobacco use.

INTRODUCTION

Tobacco consumption is associated with a myriad of economic, social and health problems for young people.[1] One of the health problems associated with tobacco consumption is psychological disorders, and their co-occurrence can dramatically worsen the overall clinical course, physical health and psychosocial outcomes for the person.[2–4] Nicotine dependence per se is a psychological disorder with comorbid conditions being common. Tobacco contributes substantially to the reduced life expectancy observed among people who experience mental health disorders. Furthermore, people living with mental illness have shorter life expectancy than those without, and this is largely attributable to smoking-related illnesses.[5 6] Youth (10–24 years of age) with psychological disorders are overrepresented among those who consume tobacco.[7] However, it is unclear if the relationship between tobacco and psychological disorders is causal or merely associational. If the relationship is indeed causal, the direction of this relationship is poorly understood.[8] Furthermore, it is unclear whether

the 'tobacco–psychopathology' relationship is different depending on the specific type of psychological disorder experienced by the young person (eg, perhaps tobacco use causes depression but not anxiety).

Several reviews have attempted to evaluate the relationship between tobacco and psychopathology,[9–12] but these have several limitations including: (1) a lack of focus on youth, (2) the sample is mostly or entirely from North America, (3) only a small number of psychological disorders are examined and (4) the existing studies and reviews are now quite dated. Given these limitations, we sought to produce an updated review that focuses specifically on youth and samples from a broader international population. Furthermore, we included more psychological disorders to facilitate comparison: anxiety, depression, bipolar disorder, psychosis and borderline personality disorder (BPD). We chose these psychological disorder categories because they affect a substantial percentage of youth.[13] The broad objective of our review was to examine the reciprocal temporal relationship between tobacco consumption and the selected psychological disorders for youth.

METHODS

Eligibility criteria

The inclusion criteria were studies with: (1) a focus on adolescents and youth 10–24 years of age, (2) systematic review of observational longitudinal studies OR observational longitudinal studies conducted since most recent systematic review OR all longitudinal studies if there is no relevant systematic review for the specific disorder, (3) measured tobacco consumption in any form (eg, smoking, smokeless, snus), (4) measured psychological disorder categories of at least one of anxiety, depression, bipolar, psychosis or BPD, (5) English language and (6) published in a peer-reviewed journal. Under the anxiety category, we included various types including social anxiety, panic, agoraphobia and generalised anxiety. Under the bipolar category, we included mania as this symptom is mostly associated with bipolar. Under the psychosis category, we included schizophrenia and general psychotic symptoms. We included 'nicotine dependence' as a measure of tobacco consumption because these constructs are strongly related.[14 15] Studies were excluded if the methods used meant that tobacco consumption could not be distinguished from other drug use (eg, cannabis) and if the population was very specific (eg, pregnant women). Our search strategy was based on advice from an expert university-based librarian and was also informed by previous systematic reviews identified during the early formulation of the current study.[10 11]

Search strategy and study selection

The original search was conducted by KM using PubMed, Embase, Scopus, CINAHL and PsycINFO on 26 September 2019 and updated by LM on 11 May 2021. Initial searches were very broad and focused on keyword categories of tobacco and psychological disorders (for more information, see online supplemental material 1). The screening and review process were managed within COVIDENCE software. After the initial search and deduplication, JS and SL shared the initial screening and full-text reviews. JS and SL then discussed any conflicts in order to reach consensus about inclusion or exclusion. Where consensus could not be reached or the decision remained uncertain, final eligibility was resolved by CM.

For the updated search SL and JS each screened all new titles/abstracts with CLM resolving conflicts, then SL did all full-text reviews, with JS checking 20% of excluded studies—agreement was 100%.

Quality assessment, data extraction and data synthesis

To assess the quality of the included studies, we used the Joanna Briggs Institute (JBI) Critical Appraisal Tools for cohort studies and systematic reviews.[16] JS appraised all studies while SL appraised a random sample of 20%. Data extraction was conducted by JS and checked by SL in order to produce three tables: (1) online supplemental table S1 for descriptive information about the cohort studies, (2) table 1 for vote counting of the direction of effects for cohort studies and (3) table 2 for descriptive information about the systematic reviews. For the 'results' column of online supplemental table S1, we extracted the most adjusted results in order to reduce the risk of confounding.[17] We did vote counting for effect direction (table 1; counting the number of studies with positive vs negative effect direction) based on recent recommendations by Cochrane on conducting synthesis without meta-analysis.[18] To use this approach, we combined similar predictors (eg, nicotine dependence, cigarette smoking and other tobacco use combined into 'tobacco') and outcomes (eg, social anxiety, panic and agoraphobia combined into 'anxiety') and classified effect direction as one of the following: (1) a positive/negative effect direction if at least 70% of findings showed consistency in this direction, (2) a conflicting effect if consistency was less than 70% or (3) an 'unclear' effect if direction was not reported (for a similar method, see Thompson *et al*[19]). For data synthesis, we evaluated each relationship individually (eg, tobacco >depression; depression >tobacco; tobacco >anxiety, etc, where the '>' symbol refers to the direction of the relationship). In this synthesis, we attempted to integrate all information from both the cohort and review studies (eg, descriptive information and vote counting).

RESULTS

Publication dates of included studies

We found four systematic reviews for depression and tobacco in youth.[9–11 20] The most recent of these reviews[20] included studies up to 1 November 2018. So, in order to be comprehensive, we also collected depression cohort studies from 2018 onwards. We found two systematic reviews for anxiety and tobacco in youth; but, given the

Table 1 Vote counting of the direction of effects for cohort studies

Authors (year)—country	Tobacco >depression	Depression >tobacco	Tobacco >anxiety	Anxiety >tobacco	Tobacco >bipolar	Bipolar >tobacco	Tobacco >psychosis	Psychosis >tobacco
Ajdacic-Gross *et al*[38] (2009)—Switzerland					◄►			
Ames *et al*[39] (2018)—Canada	▲							
Berk *et al*[40] (2010)—Australia							▼	
Bierhoff *et al*[22] (2019)—USA		◄►		▲				
Borges *et al*[41] (2018)—Mexico	▲	▲		▲				
Buchy *et al*[42] (2014)—USA and Canada							▼	
Buchy *et al*[43] (2015)—USA and Canada							Unclear	
Bulhões *et al*[44] (2020)—Portugal	▲							
Chen *et al*[45] (2017)—USA	▲		▲					
Crane *et al*[46] (2021)—USA		Unclear						
Davies *et al*[47] (2018)—UK		▲						▲
Ferdinand *et al*[48] (2004)—Netherlands								▲
Fonseca *et al*[49] (2021)—Brazil	▲							
Gauge *et al*[50] (2014)—UK							▲	
Gårdvik *et al*[51] (2020)—Norway	▼		▲					
Goodwin *et al*[52] (2004)—New Zealand[52]				▲				
Goodwin *et al*[53] (2013)—Germany		◄►		◄►		◄►		
Griesler *et al*[54] (2008)—USA	◄►	▲	◄►	◄►				
Griesler *et al*[55] (2011)—USA	▲	◄►	◄►	▲				
Hu *et al*[56] (2012)—USA				▲				
Hui *et al*[57] (2013)—China							▲	
Isensee *et al*[27] (2003)—Germany			▲	◄►				
Johnson *et al*[36] (2000)—USA			▲	Unclear				
Jones *et al*[35] (2018)—UK							◄►	◄►
Kalan *et al*[58] (2020)—Lebanon		◄►						
Kendler *et al*[59] (2015)—Sweden							▲	
King *et al*[60] (2004)—USA		◄►		◄►				
MacKie *et al*[61] (2011)—UK							▲	
Marmorstein *et al*[62] (2010)—USA				▲				
Marsden *et al*[63] (2019)—USA	▲							

Continued

Table 1 Continued

Authors (year)—country	Tobacco >depression	Depression >tobacco	Tobacco >anxiety	Anxiety >tobacco	Tobacco >bipolar	Bipolar >tobacco	Tobacco >psychosis	Psychosis >tobacco
Moylan *et al*[28] (2013)—Norway			▲	Unclear				
Mustonen *et al*[64] (2018)—Finland							▲	
Okeke *et al*[65] (2013)—USA				▲				
Pedersen *et al*[66] (2009)—Norway			▲	▲				
Purborini *et al*[67] (2021)—Indonesia	▲							
Raffetti *et al*[24] (2019)—Sweden	▲							
Ranjit *et al*[25] (2019)—Finland	▲							
Ranjit *et al*[26] (2019b*)—Finland	▲	▲						
Savage *et al*[68] (2016)—Finland				▼				
Shete *et al*[23] (2017)—USA				▲				
Smith *et al*[69] (2014)—USA		▲		▲		▲		
Swendsen *et al*[34] (2010)—USA		▲		▲		▲		
Tomita *et al*[70] (2020)—South Africa	▲							
Trotta *et al*[71] (2020)—UK								Unclear
Ward *et al*[31] (2019)—USA and Canada							◄►	
Weiser *et al*[30] (2004)—Israel							▲	
Wilens *et al*[72] (2016)—USA					▲			
Zammit *et al*[32] (2003)—Sweden							▼	
Zhang *et al*[73] (2018)—Germany	▲							

*Testing the reciprocal association between smoking and depressive symptoms from adolescence to adulthood: a longitudinal twin study.
▼, negative effect direction; ▲, positive effect direction; ◄►, conflicting effect directions; unclear, unclear effect direction.

Table 2 Descriptive information about systematic reviews (n=4)

Authors (year)	Target population and study designs (n)	Tobacco measure/s	Psychological measure/s	Relationship/s examined (n)	Result	Quality score %	Limitations
Ahun *et al* (2020)[20]	Youth (n=43)	Cigarette smoking	Unclear	Depression >tobacco (N=7); anxiety >tobacco (N=1)	Six of the depression studies had a significant association with cigarette smoking, while the one anxiety study did not	72.7	No statistics reported, only significance of association; only one anxiety study examined;
Cairns *et al* (2014)[9]	Youth aged 12–18 (n=17)	Any form	Unclear	Tobacco/depression	Tobacco associated with increased depression with small effect size (r=0.09, CI=0.06 to 0.12)	90.9	Directionality unclear
Chaiton *et al* (2009)[10]	Non-clinical youth aged 13–19 (n=15)	Mostly 'smoking onset' operationalised as ever having had a 'puff' or 'one cigarette'	Various but mostly CES-D	Tobacco >depression (n=6); depression >tobacco (n=12)	Smoking predicted depression (PE=1.73, CI=1.32 to 2.40); depression predicted smoking (PE=1.41, CI=1.21 to 1.63)	81.8	Low number of tobacco >depression studies
Esmaeelzadeh *et al* (2018)[11]	Youth from USA and Canada (N=17)	Various (eg, ever smoked; current smoker; regular smoker)	Various for depression but mostly CES-D; various for anxiety (eg, SIAS, DISC-IV)	Depression >tobacco (n=7); tobacco >depression (n=4); anxiety >tobacco (n=1); tobacco >anxiety (n=1)	Depression predicted tobacco use (OR=1.22, CI=1.09 to 1.37); tobacco use predicted depression (OR=1.87, CI=1.23 to 2.85); anxiety did not predict tobacco use (OR=1.38, CI=0.83 to 2.29); tobacco use predicted anxiety (OR=1.88, CI=1.47 to 2.41)	81.8	Low number of studies especially for anxiety; only USA and Canada; different types of anxiety pooled together

CES-D, Centre for Epidemiology Depression Scale; DISC-IV, Diagnostic Interview Schedule for Children, version IV; SIAS, Social Interaction Anxiety Scale.

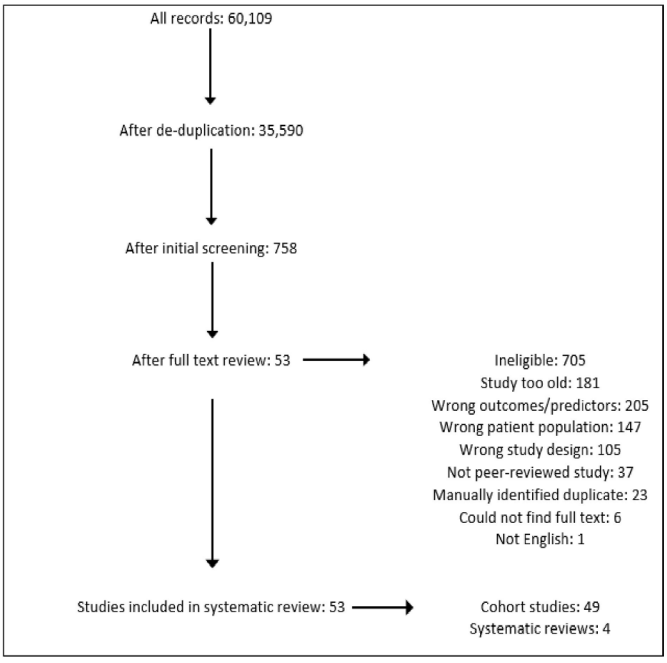

Figure 1 PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

low sample size of anxiety studies in these reviews,[11 20] we included anxiety cohort studies from any period. We did not find any systematic reviews for bipolar, psychosis or borderline personality and tobacco in youth, so no publication date inclusion constraints were applied to studies involving youth who experience these disorder categories.

Quality appraisal

As per the Preferred Reporting Items for Systematic reviews and Meta-Analyses flow diagram (figure 1),[21] our search identified 49 cohort studies and four systematic reviews, giving a total of 53 included studies. For the quality appraisal of included studies, we converted scores on the JBI into percentages in order to facilitate interpretation. Higher percentage scores indicated higher quality studies, while a score ≤50% reflects low quality. For the cohort studies, there was a relatively low level of agreement between the authors (66.2%), whereas the systematic reviews had comparatively high agreement (84.1%). The main issues contributing to disagreement were different interpretations of the JBI criteria, particularly for cohort questions one, four, five and six as well as systematic review question four. These differences were resolved through discussion.

Overall, the included studies had moderate-to-high appraisal scores. The quality appraisal of included cohort studies (n=49) is displayed in online supplemental table S1 and in more detail in online supplemental table S2. Five of the cohort studies were classified as low quality, with the lowest score being 36.4%.[22 23] The remaining appraisal scores ranged from 45.5% to 81.8%, with four studies scoring above 75% (ie, high quality). In terms of common strengths, all studies used a sufficient follow-up time (Q8) and appeared to use appropriate statistical analysis (Q11). More than 89% of studies measured the exposures and outcomes in a valid and reliable way (Q3 and Q7). Most studies addressed confounders appropriately (Q4 and Q5). In terms of common weaknesses, only 14.3% of studies had samples that were free of the outcome at first assessment (eg, below cut-off on a depression scale; Q6). Only asmall minority of studies divided the sample into groups based on tobacco or psychological symptoms in order to make baseline comparisons, and, thus, the studies scored very low on Q1 and Q2. Few studies (44.9%) clearly explained strategies to address incomplete follow-up (Q10). These limitations should be considered when interpreting the review findings.

The quality appraisal of included review studies (n=4) is displayed in table 2 and online supplemental table S2. Three reviews were appraised as high quality with percentage scores above 80%. In terms of strengths, all reviews met 8 of the 11 criteria, including: stating the review question clearly and explicitly (Q1), selecting appropriate inclusion criteria (Q2), using a comprehensive search strategy (Q3 and Q4), using appropriate criteria to appraise studies (Q5), using appropriate methods to combine studies (Q8) and making evidence-based recommendations for policy/practice (Q10) as well as future research directions (Q11). In terms of weaknesses, no reviews clearly stated that critical appraisal was conducted by at least two reviewers independently (Q6) and only one review clearly outlined methods to minimise errors in data extraction (Q7).[9]

Overview of included cohort studies

As per online supplemental table S1, the vast majority of the 49cohort studies were either from North America (n=20, with 18 from USA) or Europe (n=21). Most studies used a non-clinical youth sample (n=40), with the remaining nine using a clinical sample (youth in receipt of clinical mental health services) or a pseudo-clinical sample (eg, youth with elevated anxiety sensitivity). Sample sizes ranged widely from 117 to 233 879 (M=8162.53, Mdn=14 000, SD=33 738.60). Youth age at baseline ranged from 6.2 to 23.5 (M=16.09, SD=3.59). Follow-up periods with youth participants ranged from 1 to 27 years (M=6.43, SD=5.15). Of the 46 studies that provided this longitudinal follow-up information, the number of waves ranged from 2 to 15 (M=3.93, SD=2.40). In terms of the types of tobacco measures used, numerous studies used a binary measure (n=25; for example, cigarette user vs non-user, nicotine user vs non-user), while others used a categorical (ordinal) measure (n=22; for example, non vs moderate vs heavy smoker), while only five studies used a continuous measure. Nine studies used 'nicotine dependence' as the tobacco-related measure, while five used 'onset' (eg, age of smoking onset), and four studies also included consumption of tobacco more broadly than cigarettes (eg, cigarillos, snus, smokeless tobacco). Twelve studies used multiple measures of tobacco use. Only one study examined smoking cessation as the tobacco-related variable. Most studies (n=30) used

structured interviews with youth (eg, World Health Organization World Mental Health - Composite International Diagnostic Interview (WHO WHM-CIDI), Psychosis-like symptoms semi-structured interview (PLIKSi)) to assess the relevant psychological variable (eg, anxiety), and a moderate number of studies (n=19) used self-report measures (eg, PHQ-9, CESD). Only four studies used caregiver-report (teacher or parent) and one study used peer report. As shown in online supplemental table S1, there were zero relevant studies found for BPD. The number of covariates included in analyses ranged from 1 to 19 (M=6.69, SD=4.05). Common covariates included gender, age, SES and other drug use (eg, cannabis and alcohol). Common limitations of the cohort studies included: only using two waves, small sample sizes, not controlling for earlier levels of outcome or later levels of predictor, small cell sizes, and unclear temporal ordering.

Overview of included systematic reviews

As per table 2, one of the four systematic reviews only focused on youth from the USA and Canada,[11] while the other three did not have geographical constraints. Cairns *et al*[9] and Chaiton *et al*[10] specified a target population age range, while Esmaeelzadeh *et al*[11] and Ahun *et al*.[20] broadly referred to 'youth'. All reviews examined a variety of tobacco and psychological measures, and all four examined the relationship between tobacco and depression; whereas, only Esmaeelzadeh *et al*[11] and Ahun *et al*.[20] also examined the relationship between tobacco and anxiety. None of the other psychological disorder categories were evaluated. Two of the reviews were limited by small sample sizes for anxiety analyses.[11 20]

Tobacco>depression

Fifteen cohort studies examined the effect of tobacco use on the development of depression in youth, including only one with a clinical sample and eight with more than two waves. As shown in table 1, there was evidence that tobacco had an effect on depression, with 13 of 15 studies (86.7%) showing a positive effect direction (p<0.001). Only one of these studies was high quality (quality appraisal score >75%), and this study found a positive effect direction. Effect estimates for each cohort study are shown in online supplemental table S1). Additionally, three of the four systematic reviews examined the effect of tobacco on depression and found a positive and significant pooled estimate, as shown in table 2.

Depression>tobacco

Twelve cohort studies examined the effect of depression on development of tobacco use by youth. None of these studies used clinical samples, and seven had more than two waves. There was evidence that depression had an effect on tobacco use, with six of the twelve studies (50.0%) showing a positive effect direction (p=0.016). One of these studies was high quality, and this study showed a positive effect direction. All of the systematic reviews examined the effect of depression on tobacco and the three reviews that reported a pooled estimate found a significant positive effect direction. The fourth review reported individual study results and found that 85.7% of the included depression >tobacco studies had a significant positive effect direction.

Tobacco>anxiety

Eight studies examined the effect of tobacco use on development of anxiety in youth. One of these had a clinical sample, and six had more than two waves. Tobacco appeared to have an effect on anxiety, with six of eight studies (75.0%) showing a positive effect direction (p=0.016). None of these studies were high quality. One systematic review examined the effect of tobacco on anxiety and found a positive and significant effect, but this effect was based on only one study.

Anxiety>tobacco

Eighteen studies examined the effect of anxiety on development tobacco use by youth. None of these used a clinical sample, and 11 had more than two waves. Anxiety appeared to have an effect on tobacco use, with 11 of 18 studies (61.1%) showing a positive effect direction (p=0.003). Two of these studies were high quality, and both showed a positive effect direction. Two systematic reviews examined the effect of anxiety on tobacco use. One of these found a positive non-significant effect, while the other found a non-significant effect and did not report the effect direction. However, both reviews only included one anxiety >tobacco study and thus were extremely underpowered.

Tobacco>bipolar

Two studies examined the effect of tobacco use on development of bipolar in youth. Both of these studies used clinical samples and had more than two waves. Tobacco did not appear to have an effect on bipolar, with just one study (50%) showing a positive effect direction (p=0.500). Neither of these studies was high quality. No reviews examined the tobacco-bipolar relationship.

Bipolar>tobacco

Three studies examined the effect of bipolar on development of tobacco use by youth. None of these used a clinical sample, and one had more than two waves. Bipolar did not appear to have an effect on tobacco use, with two studies (66.7%) showing a positive effect direction (p=0.250). One of the three studies was high quality, and this study showed a positive effect direction. No reviews examined the bipolar-tobacco relationship.

Tobacco>psychosis

Twelve studies examined the effect of tobacco use on development of psychosis in youth. Seven of these used a clinical or pseudo-clinical sample, and seven had more than two waves. Tobacco use did not appear to have an effect on psychosis, with only six studies (50%) showing a positive effect direction (p=0.254). Only one of the twelve studies was high quality, and this study showed

a negative effect direction. No reviews examined the tobacco-psychosis relationship.

Psychosis>tobacco

Four studies examined the effect of psychosis on development of tobacco use by youth. None of these used a clinical sample, and three had more than two waves. Psychosis did not appear to have an effect on tobacco use, with two studies (50.0%) showing a positive effect direction (p=0.250). None of these studies were high quality, and no reviews examined the psychosis-tobacco relationship.

DISCUSSION

The purpose of the current study was to review the reciprocal temporal relationships between youth tobacco consumption and a group of psychological disorder categories including depression, anxiety, bipolar, psychosis, and BPD. This review was justified because existing reviews: (1) are several years old, (2) have biased samples, (3) only examine a narrow range of psychological disorders and (4) lack a dedicated focus on youth.

Synthesising the cohort and review studies, we found evidence that tobacco consumption predicted the development of depression and anxiety for youth, but not bipolar or psychosis. Tobacco might cause depression through certain biological mechanisms (eg, decreasing the cortisol response) and also by eliciting withdrawal symptoms of low mood.[24] However, it is also possible that this longitudinal relationship is not causal. For example, the relationship may become non-significant when certain confounders (eg, familial and genetic factors) are controlled for, as was found by Ranjit *et al*.[25 26] Tobacco use might cause anxiety because it elicits physiological symptoms for the young person similar to anxiety (eg, shortness of breath, increased heart rate and blood pressure), which are then catastrophically misinterpreted.[27] However, similar to depression, this relationship might be better explained by unmeasured confounders and may not be causal.[28] Also, it is important to consider that smoking exerts its adverse effects on a cumulative basis, which means that higher exposure with increasing time will increase the risk of incident mental health events. If specific outcomes do not occur in response to smoking due to restricted timeframe due to younger age, it does not mean that a causal relationship per se can be excluded.

Hahad *et al*[29] recently reviewed the evidence for smoking as a potential risk factor for neuropsychiatric disorders such as depression, anxiety and psychosis, with the aim of identifying central pathophysiological mechanisms that may contribute to these relationships. Readers are referred to this review for a more comprehensive understanding of the evidence for neuropsychiatric pathophysiology. Hahad *et al* emphasise that oxidative stress or inflammatory mediators associated with cigarette smoke can impair proper endothelial (vascular) function essential for a healthy cardiovascular system, with implications for the function of other bodily systems. They stress that prolonged oxidative stress combined with prolonged exposure noxious chemicals from cigarette smoke can lead to chronic inflammation, and that consequent structural and functional alterations in the central nervous system of individuals who smoke may indeed increase the risk of these disorders and other chronic conditions. Hahad *et al* argue, however, that, 'the relationship between smoking, oxidative stress, inflammation, and neuropsychiatric diseases is not always clear. This stems from the fact that neuropsychiatric diseases also increase the chance that a person will start-smoking, making the direction of association difficult to establish' (p.7278). Hahad *et al* also remind us that psychiatric disorders, 'have strong link with chronic stress, which represents one of the most prominent risk factors for their onset' (p.7279), and that chronic stress is also featured in several chronic conditions (eg,cardiac and metabolic conditions) and can, therefore intuitively increase the risk of psychiatric disorders.

Our synthesis of findings suggests that tobacco may not predict psychosis, which was notable because numerous studies (n=12) examined this relationship. Of the six studies that found a positive effect direction, only one of these was a high-quality study,[30] though several other moderate quality studies also found a positive effect direction. Tobacco use may have failed to predict psychosis because other confounders play a true causal role in the young person's experience of psychosis (eg, other substance use; Ward *et al*).[31] Alternatively, it has been hypothesised that nicotine could actually decrease negative psychotic symptoms, mediated by an increase in dopamine.[32] Our sign test showed an overall lack of effect of tobacco on bipolar, which contradicts past research that does propose a causal effect.[33] However, only two included studies examined the effect of tobacco on bipolar, indicating that more longitudinal research is needed on this topic.

A similar pattern of results was found when investigating reverse causation. The presence of both depression and anxiety predicted future tobacco use, potentially because people who experience depression and anxiety may have a greater probability of using tobacco to self-medicate (ie, to try to reduce adverse symptoms; Swendsen *et al*).[34] However, as with the effect of tobacco on depression, these relationships may only exist until familial and genetic confounders are controlled for.[25 26] Presence of psychosis may have failed to predict tobacco use due to certain confounders (eg, cannabis use) that better explain the variance in tobacco use,[35] but the number of studies that examined this relationship was minimal (n=4). Similarly, according to the sign test, presence of bipolar did not have an overall effect on tobacco use. However, only three studies examined this relationship, and one of these studies was high quality and did find an effect. Hence, more longitudinal research is needed on this question.

There were several limitations to this review. First, the included studies were very heterogeneous, particularly

with regards to sample size, sample nature (ie, clinical vs non-clinical), number and type of confounders, follow-up period, number of waves and type of statistics used. Due to this heterogeneity, we were unable to meta-analyse the results and capture effect sizes. However, despite these constraints, we were still able to synthesise the quantitative data using vote counting based on effect direction, which is current best practice when meta-analysis is not possible, according to recent recommendations by Cochrane.[18] A second limitation is consideration of causation itself. For example, where tobacco use precedes and predicts depression, it is conceivable that tobacco use is having an 'effect' on depression, but it is also plausible that some other common factor/s may be causing both disorders, and the temporal sequence is somewhat arbitrary. Further research is needed, investigating to potential interplay of genetics and environmental factors that may act as confounders. A third limitation was the way in which we classified psychological disorder categories. For example, under the category of 'anxiety', we grouped various disorders including panic, social anxiety, generalised anxiety and agoraphobia. However, it is possible that young people's experiences of these disorders differ in how they relate to tobacco use. For example, tobacco might have a greater effect on panic compared with social anxiety because tobacco can cause impaired respiration, which is more associated with panic symptoms than social anxiety symptoms.[36] Also, we included mania under the bipolar category; however, mania could be unipolar as well without depressive symptoms.[37] As more research accumulates on tobacco and mental health, future reviews should distinguish between subtypes of psychological disorder categories.

Given the gap in the literature, future research should examine the reciprocal longitudinal relationship between tobacco use and BPD. Additionally, more studies should be conducted that investigate the relationship between tobacco, psychosis and bipolar. Although there are numerous studies on tobacco and both depression and anxiety, future research should continue to examine confounders such as familial and genetic factors in order to strengthen causal inferences.

The mechanisms underlying smoking and mental illnesses are complex and yet to be thoroughly investigated and understood. In the meantime, a number of clinical implications are apparent for addressing the health and socioeconomic burdens of tobacco use, which are disproportionately high among people living with mental disorders. Addressing the uptake of tobacco use by young people must remain a high priority as part of public health measures targeting prevention and early intervention. This should include promoting greater awareness of the links between smoking and the onset of neuropsychiatric disorders among youth, their families, health and welfare professionals (particularly those working with at-risk individuals and families), school systems and the community. More concerted treatment and smoking cessation support for young people must also be developed, made available and accessible, with health messaging that is better matched to their help-seeking behaviours, peer networks and motivations for addressing smoking behaviours. Coupled with this, and in order to prevent the longer term harms of smoking, health professionals must be supported to gain more skills and confidence to ask, advise and actively help young people with emerging and existing psychological disorders who smoke to address their smoking.

CONCLUSION

We found support for reciprocal relationships between tobacco and both depression and anxiety for youth, though questions remain around whether these relationships are causal. In contrast, we did not find overall evidence for a causal relationship between tobacco and psychosis for this population, perhaps because nicotine has conflicting effects on the person's experience of psychosis. For the other relationships examined (tobacco >bipolar; bipolar tobacco; psychosis >tobacco), evidence was weak because of low numbers of studies. Further studies that examine the complexities of interactions between tobacco and mental health for different diagnostic groups are needed to inform prevention, early intervention, treatment and smoking cessation support for youth with comorbid psychological conditions and tobacco use.

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