Dynamic Associations Between Anxiety, Depression, and Tobacco Use in Older Adults: Results From The Irish Longitudinal Study on Ageing

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Abstract

Evidence supports moderate-to-large reductions in anxiety, depression, and perceived stress after smoking cessation; however, much of the available evidence has focused on young adults. Therefore, this study quantified associations between smoking and smoking cessation on prevalent and incident generalised anxiety disorder (GAD) and major depression (MDD) in a nationally representative sample of Irish older adults. Participants (n=6,201) were community dwelling adults aged 50 years resident in Ireland. Smoking status and self-reported doctor diagnosis of anxiety or depression prior to baseline were assessed at baseline (i.e., Wave 2). At baseline and 2-, 4-, and 6-year follow-up (i.e., Waves 3–5), GAD and MDD were assessed by the Composite International Diagnostic Interview Short-Form. Logistic regression quantified cross-sectional and prospective associations (odds ratios (ORs) and 95% confidence intervals (95%CIs)) between smoking status and mental health. Prevalence and incidence of GAD was 9.1% (n=566) and 2.8% (n=148), respectively. Prevalence and incidence of depression was 11.1% (n=686) and 6.4% (n=342), respectively. Following full adjustment, current smokers had higher odds of prevalent

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GAD (OR=1.729, 1.332–2.449; $p<0.001$) and MDD (OR=1.967, 1.548–2.499; $p<0.001$) than non-smokers. Former smokers had higher odds of prevalent GAD than non-smokers (OR=1.276, 1.008–1.616; $p<0.001$). Current smokers did not have higher odds of incident MDD (OR=1.399, 0.984–1.990; $p=0.065$) or GAD than non-smokers (1.039, 0.624–1.730; $p=0.881$). Findings may have important implications for interventions designed to curb tobacco abuse, which tend to be less successful among those with anxiety and depression.

Keywords

Smoking; Smoking Cessation; Generalised Anxiety Disorder; Major Depression; Older Adults

Introduction

Tobacco use is the leading cause of preventable death worldwide (WHO, 2017) and a substantial economic burden through healthcare costs and lost productivity (USDHHS, 2014; Xu, 2014). Though tobacco use was initially promoted as a method for improving affect and coping with daily emotional stressors (Ikard, 1969), substantial evidence supports the paradoxical impact of chronic smoking on mental health (Baker, 2004). These effects have been associated with nicotine, the primary dependence-forming chemical compound in tobacco reinforces smoking behaviour (Di Chiara, 2000) and, with chronic administration, can have catastrophic consequences for nervous system function (Dani, 2011; Middlekauff, 2014). The pharmacological actions of nicotine map onto Clark and Watson's (1991) tripartite model of anxiety and depression to explain the associations between emotional psychopathologies and tobacco dependence. As an extension of this model, Leventhal and Zvolensky (2015) propose a transdiagnostic vulnerability framework around the central tenet that emotional vulnerabilities (i.e., anxiety sensitivity, distress tolerance, and anhedonia), which can be traced to dysfunction in the same midbrain circuits that are disrupted by nicotine, contribute to and are exacerbated by smoking behaviour. Analysing longitudinal data through the lens of this framework may help to tease out these complex associations and inform interventional strategies.

Epidemiological evidence collected in young adults supports this approach, and data from nearly 200 longitudinal studies have collectively informed novel and tailored approaches to promote successful cessation in young adult smokers with mental health disorders (Fluharty et al., 2017; Stockings, Metse, Taylor, 2021; Taylor, 2014). However, considering the dose-dependent effects of chronic nicotine administration, these interventions may not be as efficacious for older adults, many of whom started smoking as young adults and thus have been smoking for years or decades longer than young adult smokers (Cataldo, 2019). Few interventions have been designed with a gerontological focus (Doolan, 2008) to address the lower intention to, and different reasons for, quitting that are commonly exhibited by older smokers (Jordan et al., 2016; Kerr, 2006; Lugo, 2013). Thus, characterizing the cross-sectional and longitudinal relationships between mental health and smoking behaviours among older adults is a necessary first step to facilitating smoking cessation in this population.

Anxiety and depression are the most common psychiatric diagnoses in older adults (Beaudreau & O'Hara, 2008), they are more prevalent in older adult smokers than non-smokers (An & Xiang, 2015; Bonnet et al., 2005) and can have profound effects on physical health (Lever-van Milligen et al., 2016; Penninx et al., 2000). Little is known about the risks of smoking on future mental health outcomes because of a lack of longitudinal studies. In two studies of older US adults, nicotine dependence was associated with a greater risk of developing anxiety but not future major depression (Chou, 2011; Sachs-Ericsson, 2011). However, both studies represent relatively small proportions of the ageing population, a bias which left uncorrected limits the generalizability of their findings to understand the effects of smoking on anxiety in depression in larger, non-US populations of older adult smokers. Lacking prospective data also contributes to a lack of knowledge about the effects of cessation on mental health outcomes in this population.

What we do know about cessation in older adults comes exclusively from cross-sectional comparisons of current and former smokers without prospective comparisons to help discern whether smoking likely contributed to psychiatric symptoms or vis versa. For example, current and past heavy smokers were 40 and 60% more likely to be clinically depressed than never or past light smokers, respectively, yet the reduction in risk between former and current smokers was statistically significant (Almeida & Pfaff, 2005; Lam, 2004). Similar reductions in relative risk for anxiety (24%) and depression (28%) were observed more recently in a small sample of older Chinese-American men (Li et al., 2019). There are also a handful of studies in which these the benefits of cessation for former smokers are not as large or statistically significant (e.g., Bazargan et al., 2020; Jing et al., 2020), though the lack of null-findings is probably due in part to a file-drawer effect. Ultimately, the cross-sectional nature of these studies means that the extent to which smoking cessation is prospectively associated with rates of anxiety and depression in older adults remains unclear.

A preliminary report from The Irish Longitudinal Study on Ageing (TILDA), a large ongoing cohort study that assesses the social, economic, and health circumstances of community dwelling adults aged 50 years resident in Ireland (Barrett et al., 2011), revealed that anxiety is more common than depression in Irish older adults, with 10% and 13% of participants reporting clinically significant depressive and anxiety symptoms, respectively (Barrett, 2011). Ancillary analyses showed relationships between tobacco use and ageing perceptions (Villiers-Tuthill, 2016) and cross-sectional associations between smoking status, smoking-related disease burden, and "mental health difficulties" among Wave 1 TILDA participants (Burns et al., 2017). However, cross-sectional and prospective associations between smoking status and individual mental health conditions were not investigated. Thus, to address the limitations of existing literature, we used data from TILDA Waves 2–5 to quantify associations of smoking and smoking cessation with prevalent and incident generalised anxiety disorder (GAD) and depression (MDD) in a representative sample of Irish older adults.

Methods

This study used STROBE recommendations to guide reporting (von Elm et al., 2008).

Ethics

The Irish Longitudinal Study on Ageing (TILDA) was approved by the Faculty of Health Sciences Research Ethics Committee at Trinity College Dublin. All experimental procedures adhered to the Declaration of Helsinki. All participants gave written informed consent and assessments were carried out by trained research nurses.

Study design

This is a cross-sectional and prospective study examining the association of smoking with GAD and MDD. This study is embedded within TILDA, a large population-based study of a nationally representative sample of over 8000 community dwelling older adults aged 50 years. Details of the methodology employed by TILDA are fully described elsewhere (Kearney et al., 2011; Kenny et al., 2010; Whelan and Savva, 2013). Data were analysed from Wave 2 (i.e., baseline) through Wave 5 of TILDA. Participants were considered for cross-sectional analyses if they were aged 50 years at Wave 1, reported that they had never been told by a doctor that they had dementia, had data on smoking, GAD, and depression at baseline, and had follow-up data on either GAD or depression (n=6274). As physical activity was planned as a key covariate, physical activity data were processed consistent with standard guidelines/procedures for the International Physical Activity Questionnaire, such that unreasonable values of 16 hours of moderate and/or vigorous physical activity were excluded (Craig et al., 2003). Thus, participants with missing covariate data or who reported 16 hours of physical activity per day were then excluded (n=73; 1.2% of total), leaving a final sample of 6201 for cross-sectional analyses. Participants were included in prospective analyses if they were also free from GAD or MDD at baseline and reported having never been told by a doctor that they had anxiety or depression (n=5309).

Smoking

Participants were asked whether they had ever smoked 'cigarettes, cigars, cigarillos or a pipe daily for a period of at least one year.' Those who answered 'No' were categorised as 'Never' smokers. Those who answered 'Yes' were asked if they smoked at the present time, including the past three months. If they answered 'No' they were categorised as 'Former' smokers, and if they answered 'Yes' they were categorised as 'Current' smokers.

GAD and MDD

The Composite International Diagnostic Interview Short-Form (CIDI-SF) was used by trained interviewers at Wave 2 through Wave 5 to determine fulfilment of criteria for GAD and a major depressive episode in the last twelve months (Kessler et al., 1998). Participants were categorised as having GAD if they reported: 1) a period of worry lasting at least five months, 2) severe worry, 3) difficult to control worry, and 4) three of seven additional physiological symptoms. Compared to the full CIDI in the US National Comorbidity Survey, the CIDI-SF has demonstrated sensitivity of 96.6%, specificity of 99.8%, positive predictive value of 96.8%, negative predictive value of 99.8%, and total classification accuracy of 99.6% for GAD. Participants were categorised as having had MDD if they reported: 1) feeling depressed or a loss of interest in most activities at least almost every day for at least most of the day in the past 12 months as well as three or more additional depression

symptoms out of six assessed, or 2) loss of interest in most activities almost every day at least most of the day for two weeks or more in a row in the past 12 months as well as three or more additional depression symptoms out of six assessed. Compared to the full CIDI in the US National Comorbidity Survey, the CIDI-SF has demonstrated sensitivity of 89.6%, specificity of 93.9%, positive predictive value of 75.7%, negative predictive value of 86.9%, and total classification accuracy of 93.2% (Kessler et al., 1998).

Participants were also asked if they had ever been told by a doctor that they had anxiety or depression at, or prior to, Wave 2. Participants were classified as having prevalent anxiety or depression if they answered yes or if they screened positive for GAD or an MDD in the Wave 2 CIDI-SF assessment. These participants were excluded from prospective analyses. Incidence of anxiety or depression was defined as screening positive for GAD or MDD in any of the Waves 3, 4, or 5 CIDI-SF assessments.

Covariates

Covariates were selected based on logical, theoretical, and/or prior empirical associations with smoking, depression, and/or anxiety and were measured at baseline. They included socio-demographic information, including age (years), sex (male, female), education level (primary/none, secondary level, third level or higher), and marital status (married/living together as if married, not married, separated/divorced, widowed). Physical activity was measured using the short-form International Physical Activity Questionnaire (Craig et al., 2003). Participants were classified according to meeting WHO PA guidelines (i.e., 150 minutes weekly of MVPA or 75 minutes weekly of vigorous PA, or an equivalent combination; WHO, 2010). Chronic conditions included lung disease, asthma, arthritis, osteoporosis, cancer, Parkinson disease, stomach ulcer, varicose ulcer, liver disease, thyroid disease, or kidney disease. Cardiovascular conditions included hypertension, stroke, angina, heart attack, heart murmur, or abnormal heart rhythm. Participants were classified as having none, one or two, or 3 chronic conditions, and none, one or two, or 3 cardiovascular conditions. Number of physical limitations was determined by asking about, and subsequently summing the number of, difficulties with walking, running, sitting, sit-to-stand, stair climbing, reaching overhead, stooping, kneeling, crouching, lifting heavy weights, pushing or pulling large objects and picking small coins from a table.

Statistical analyses

Data were analysed in Stata version 14.2 (StataCorp for Windows). Participant characteristics were described by means and standard deviations for continuous variables and frequencies for categorical variables. Binary logistic regression quantified crude and adjusted associations (i.e., odds ratios (ORs) and associated 95% confidence intervals (95%CIs)) between smoking and prevalent and incident GAD and depression. Data were weighted with an inverse probability weight using the *svy* command in STATA to be representative of the population of adults aged 50 in Ireland.

Results

Participant characteristics

Characteristics of the analytic sample are presented in Table 1. Briefly, participants (n=6201) were predominantly female (55%) and aged 64 years. Overall, 45% (n=2794) never smoked, 41% (n=2483) were former smokers, and 15% (n=924) were current smokers. Prevalence and incidence of GAD was 9.1% (n=566) and 2.8% (n=148), respectively. Prevalence and incidence of depression was 11.1% (n=686) and 6.4% (n=342), respectively.

GAD

Table 2 presents ORs for the associations between smoking and prevalent and incident GAD. Briefly, fully adjusted cross-sectional and prospective results are as follows. Compared to non-smoking, prior smoking (OR=1.276, 95%CI=1.008–1.616; p=0.043) and current smoking (1.729, 1.332–2.449; p<0.001) were associated with prevalent GAD. Prior smoking (1.041, 0.672–1.614; p=0.856) and current smoking (1.039, 0.624–1.730; p=0.881) were not associated with developing GAD.

MDD

Table 2 presents ORs for the associations between smoking and prevalent and incident MDD. Briefly, fully adjusted cross-sectional and prospective results are as follows. Compared to non-smoking, prior smoking (1.191, 0.958–1.482; p=0.116) was not associated with prevalent depression, but current smoking was (1.967, 1.548–2.499; p<0.001). Former (1.183, 0.889–1.573; p=0.248) and current (1.399, 0.984–1.990; p=0.061) smokers did not have higher odds developing depression than non-smokers, respectively.

Discussion

Leventhal's and Zvolensky's (2015) integrative model proposes that the reward associated with smoking is enhanced by emotional vulnerabilities which ultimately potentiate smoking behaviour: anhedonia amplifies the pleasure-enhancing effects of smoking, anxiety sensitivity amplifies smoking's anxiolytic effects, and poor distress tolerance amplifies the distress terminating effects of smoking. Within the context of this model, we report three noteworthy associations between mental health outcomes and smoking status from cross-sectional and prospective observations of a representative sample of ageing Irish adults.

First, current smokers were nearly twice as likely to report prevalent MDD (i.e. past or current MDD) compared to non-smokers. These patterns support the conclusions of a recent systematic review and qualitative synthesis of 297 studies that chronic smoking perpetuates negative affect and anhedonia, which may collectively act to stymie attempts at cessation (Mathew, 2016). Since this association was purely cross-sectional, it is possible that this pattern emerges from MDD as a risk factor for initiation of smoking behaviour. On one hand, former smokers exhibited no greater odds of MDD than non-smokers, suggesting that this alternative explanation is less likely. On the other hand, it might be that MDD makes quitting more difficult, meaning that smokers with MDD were at lower odds of becoming former smokers. Also notable for the interpretation of this pattern is the lack of

a greater prospective risk for current smokers to develop MDD. Thus, it is possible that the neurobiological effects of nicotine administration that perpetuate anhedonia occur proximal to when smoking is initiated, do not change over the course of maintenance, and then abate relatively quickly if administration ceases (Leventhal et al., 2009).

Second, current smokers had 73% higher odds of prevalent GAD, a pattern consistent with a review of 47 population-based epidemiological studies (Moylan et al., 2012), and former smokers were 27% more likely to report prevalent GAD compared to non-smokers. This pattern is also consistent with a proposed role of anxiety as a risk factor for nicotine dependence: elevated negative affect during abstinence, appraisal of these symptoms as harmful (i.e., anxiety sensitivity), and expectancy that smoking will reduce negative affect underpin associations between smoking and prevalent GAD (Piper et al., 2011; Zvolensky et al., 2004; Tidey and Miller, 2015). This interpretation is supported by previous reports that adult smokers with GAD report more severe nicotine dependence (Piper et al., 2010) and higher negative affect, even before cessation, (Piper et al., 2011) compared to smokers without GAD. These associations may also represent the deleterious effects of chronic smoking behaviour on structure (Fritz, 2014; Zorlu, 2017) and function (Claus, 2020; Pariyadath, 2014) in emotional control brain networks, features which have also been reported to predict cessation success (Addicott, 2015; Froeliger, 2015; Li, 2017). The time-course of these changes in the human brain likely aggregate over time and are unlikely to abate immediately upon cessation (Karama, 2015; McClernon, 2015), thus explaining why former smokers exhibited an elevated risk of anxiety at initial assessment, but not at follow-up.

Third, we also observed that current smokers exhibited no practical increase in odds of incident GAD (3.9%), but moderately, albeit statistically non-significant, greater odds of incident MDD (39%) when compared to non-smokers. A moderate-to-large and statistically significant greater odds of developing MDD was also observed in current smokers relative to former smokers prior to statistical adjustment. Although speculative, this might mean that the effects of smoking on depression may not be due to the pharmacological effects of smoking per se, but also might be attributed to mediating or moderating intermediate variables, such as sex or physical activity, that have known prospective associations with MDD and were controlled for in this study. Greater variability (i.e., large confidence intervals) was also observed in prevalent and incident MDD and GAD among current smokers compared to former smokers. Although this may simply be a function of a smaller sample of current smokers, it is also possible that this variability is biologically meaningful and represents moderating genetic, biological, or cognitive factors (Kendler et al., 1993, Qiao et al., 2020).

As in all epidemiological cohort studies it is possible that any of these unmeasured variables might also explain the cross-sectional associations we observed. For example, there is evidence that high neuroticism or extraversion, as personality types that tend to be associated with high anxiety, may also increase the risk of smoking (Hu et al., 2000; McCrae, Costa, and Bosse, 1978;). However, a strength of the current study was the adjustment of the statistical models for demographic, medical, and behavioural covariates. This means that a third variable would need to be largely independent of these covariates in order to

meaningfully explain the observed patterns. Although personality was not controlled for, the relationships between personality, anxiety, and smoking may be different for male and female smokers (Spielberger & Jacobs, 1982), thus adjustment of the current models for sex would have greatly reduced the influence of personality on the observed patterns.

These findings may have implications for interventions designed to curb tobacco abuse, which tend to be less successful among those with anxiety and depression (Haller, 2014; Watson, 2012), thus explaining the disproportionate rates of tobacco-related mortality in these populations (Prochaska et al., 2017). For example, in a recent sample of 1,162 English adults who reported currently smoking or having stopped within the past 12 months, despite smokers who reported depression/anxiety recalling a greater offer of support to stop smoking by their General Practitioner, this did not translate into use of a cessation aid or successful cessation (McGowan et al., 2018). One interpretation of the patterns reported herein is that, while anhedonia keeps ageing adults smoking (and abates after successful cessation), anxiety sensitivity lingers longer after attempted abstinence and may promote relapse among older smokers. This conceptualization is supported by the broad use of anti-depressants (e.g., buprorion) that attenuate cravings via altered neurotransmission in midbrain emotional control circuits (Culbertson et al., 2011; Simon et al., 2004) and tend to work better when combined with behavioural therapies (Secades-Villa, 2017; Das, 2017). We speculate that it may be useful to target anxiety sensitivity, as a trait that is exacerbated by smoking but not wholly targeted by these drugs, through behavioural therapies with demonstrated anxiolytic properties.

Exercise is one such therapy with demonstrated anxiolytic effects that has been demonstrated as an effective adjuvant for traditional cessation therapies. The associations reported here were corrected for individual differences in physical activity at baseline, meaning that the cross-sectional associations with GAD and MDD cannot be attributed to variability in physical activity. However, physical activity is also dynamic and thus it possible that prospective effects of smoking (or lack thereof) might be due partly to changes in physical activity. Higher physical activity levels are associated with lower incident anxiety, depression, and GAD (McDowell et al., 2018a, 2018b, 2019), less smoking behaviour (Taylor et al., 2005), and a greater likelihood of a successful quit attempt (Marcus, 1999; Zvolensky, 2018). A single bout of even low-to-moderate intensity exercise may curb cravings and improve mood and affect (Roberts, 2012) by acting on emotional and cognitive control brain circuits (Monroe, 2020; Van Rensburg, 2009). Therefore, a physical activity intervention initiated prior to cessation may be effective as a prophylactic to curb both anhedonia and anxiety sensitivity (Ussher, 2014; Rollo, 2019). A recent well-designed randomized control trial suggested that vigorous-intensity exercise may improve the odds of successful quitting in young adults with high anxiety sensitivity (Smits, 2016). However, even in smokers that do not ultimately quit, we speculate exercise may modify act through different mechanisms to reduce the risk of GAD and MDD.

Limitations

Firstly, the smoking measure was somewhat crude, and this study would benefit from a more finite measure of nicotine exposure or dependence. Secondly, as with all observational

studies, there is the potential for residual confounding. Nonetheless, we controlled for key factors in analyses, including other lifestyle behaviours, such as physical activity, physical health, and prior mental health problems in prospective analyses. Finally, these findings are only representative of those aged 50 years in Ireland; it is plausible that age-related, geographic, and cultural differences exist.

Conclusion

Smoking is associated with increased odds of prevalent GAD and MDD. Even smokers who have quit exhibited greater odds of prevalent GAD relative to older adults who have never smoked. These findings may have important implications for interventions designed to curb tobacco abuse among older adults, which tend to be less effective for those with anxiety and depression.

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Table 1.

Participant characteristics at baseline (n=6201)

Variable	
Smoking	
Never	2794 (45.1)
Former	2483 (41.0)
Current	924 (14.9)
GAD	566 (9.1)
Depression	686 (11.1)
Age	64.4 ±9.1
Sex	
Female	3404 (54.9)
Male	2797 (45.1)
Education	
Primary	1584 (25.5)
Secondary	2492 (40.2)
Tertiary	2125 (34.3)
Marital status	
Married	4403 (71.0)
Separated/divorced	451 (7.3)
Widowed	813 (13.1)
Never married	534 (8.6)
Physical activity	
Sufficient	3086 (49.8)
Insufficient	3115 (50.2)
Alcohol	
Non-problem drinker	4444 (71.7)
Problem drinker	700 (11.3)
Not reported	1057 (17.1)
Chronic conditions	
0	3062 (49.4)
1–2	2849 (45.9)
3+	290 (4.7)
Cardiovascular conditions	
0	5331 (86.0)
1–2	836 (13.5)
3+	34 (0.5)
Number of physical limitations	2.1±2.2

Numbers are N (%) or mean±standard deviation

Table 2.

Odds ratios (OR) and 95% confidence intervals (CI) derived from binominal logistic regression analyses as indicators of cross-sectional and prospective associations between smoking and generalised anxiety disorder (GAD) and major depression (MDD).

		Cross-sectional			Prospective		
		Cases/persons at risk	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Cases/persons at risk	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
GAD	Non-smoker	210/2794	**REF**	**REF**	65/2463	**REF**	**REF**
	Former smoker	219/2483	1.261 (1.010 to 1.576)[*]	1.276 (1.008 to 1.616)[*]	57/2139	1.012 (0.665 to 1.542)	1.041 (0.672 to 1.614)
	Current smoker	137/924	2.120 (1.655 to 2.716)[**]	1.729 (1.332 to 2.449)[**]	26/707	1.413 (0.869 to 2.296)	1.039 (0.624 to 1.730)
MDD	Non-smoker	244/2794	**REF**	**REF**	135/2463	**REF**	**REF**
	Former smoker	263/2483	1.198 (0.975 to 1.472)	1.191 (0.958 to 1.482)	140/2139	1.077 (0.815 to 1.424)	1.183 (0.889 to 1.573)
	Current smoker	179/924	2.346 (1.862 to 2.955)[***]	1.967 (1.548 to 2.499)[***]	67/707	1.645 (1.175 to 2.303)[**]	1.399 (0.984 to 1.990)

Adjusted model includes adjustment for age, sex, education, marital status, physical activity, chronic conditions, cardiovascular conditions, and number of physical limitations

[*] p 0.05;

[**] p 0.001