Mediational pathways of tobacco use among adult daily smokers with psychiatric symptoms in the Population Assessment of Tobacco and Health (PATH) survey

Teresa DeAtley [*], Alexander W. Sokolovsky, Morgan L. Snell, Jennifer Tidey

Department of Behavioral and Social Sciences, Brown University School of Public Health, Providence, RI 02912, USA

A B S T R A C T

Introduction: Individuals with psychiatric conditions suffer disproportionately from tobacco-related morbidity and mortality, but the factors driving this relationship remain unclear. We used data from the Population Assessment of Tobacco and Health (PATH) to investigate whether associations between internalizing psychiatric symptoms and change in smoking heaviness (as measured by cigarettes per day (CPD) were mediated by self-reported respiratory symptoms, smoking risk perceptions, and cigarette dependence.

Methods: This study used data from PATH Waves 1 through 4 (2013–2017, n = 4,152). Psychiatric symptoms were indexed with the internalizing sub-scale of the Global Appraisal of Individual Needs-Short Screener (GAIN-SS) among daily smokers. We fit auto-regressive structural equation models (SEM) to data from Wave 1–3 and 2–4 to determine the direct and indirect associations between internalizing symptom scores and CPD through each mediator.

Results: The association between internalizing symptoms and CPD was mediated by cigarette dependence (indirect: B = 0.004, SE = 0.041, p = 0.023) and respiratory symptom severity (indirect: B = 0.018, SE = 0.097, p < 0.001). Internalizing symptoms predicted higher harm perceptions (B = 0.056, SE = 0.035, p < 0.001) but the indirect relationship with CPD was non-significant. Findings from Waves 2–4 replicated these results.

Conclusion: Our results indicate that cigarette dependence and respiratory symptom severity partially mediate the relationship between internalizing symptoms and CPD but risk perceptions were not significant predictors in our models. This suggests that efforts to reduce smoking among people with internalizing disorders should focus on decreasing nicotine dependence and increasing awareness of respiratory symptoms to encourage a quit attempt or switch to a less harmful source of nicotine.

1. Introduction

Individuals with psychiatric disorders suffer disproportionately from tobacco-related morbidity and mortality, (De Hert et al., 2011; Walker et al., 2015) due to persistent high smoking rates and low cessation success (Callaghan et al., 2014; Goodwin et al., 2012). Smoking remains prevalent among those with psychiatric conditions, with 35% of people with affective disorders (such as anxiety and depression), (Smith et al., 2014) 64% of people with schizophrenia, and 44% of people with bipolar disorder reporting current smoking (Dickerson et al., 2013). In addition to causing medical comorbidities, smoking can exacerbate a number of chronic disease conditions such as chronic obstructive pulmonary disease and asthma (U.S. Department of Health & Human Services, 2014).

Reviews of the literature to date indicate that transdiagnostic factors underly the comorbidity of smoking and mental health (Tidey & Miller, 2015). Smoking to alleviate psychiatric symptoms such as anhedonia (lack of pleasure from everyday activities) and negative affect is one mechanism underlying smoking rates among individuals with mental health conditions (Leventhal & Zvolensky, 2015). In addition, individuals with mental health conditions may smoke to improve cognitive performance (Sacco et al., 2004) or to reduce side effects of antipsychotic drugs (Morisano et al., 2009). Exploration of the mechanisms that underlie persistent tobacco use in smokers with psychiatric

conditions may provide insight as to how regulatory authorities, clinicians and mental health professionals could better support individuals with psychiatric conditions who smoke.

We recently compared biological, behavioral, and subjective measures associated with tobacco use in smokers with serious mental illness (n = 58) and controls (n = 83), among participants enrolled in one of two clinical trials investigating six-week use of low nicotine content cigarettes (Donny et al., 2015; Tidey et al., 2019). Consistent with previous findings, we found that smokers with serious mental illness reported higher craving, nicotine withdrawal symptoms and motivation to smoke for cognitive enhancement than a group of smokers without psychiatric disorders that smoked a similar number of cigarettes per day (DeAtley et al., 2020). In addition, the group with serious mental illness (SMI) also reported higher cigarette dependence, higher respiratory symptoms, and lower health risk perceptions than the control group matched on cigarettes per day (DeAtley et al., 2020). The relationship between cigarette dependence and smoking persistence is well established (Baker et al., 2007). Respiratory symptom severity is associated with intention to quit among smokers, (Melzer et al., 2016) but the relationship between respiratory symptom severity and actual quitting is unclear. Predictive relationships between smoking risk perceptions and quitting have also been reported (Borrelli et al., 2010). Moreover, the extent to which these factors mediate relationships between psychiatric symptom severity and change in heaviness of smoking among daily smokers is unknown.

To better understand the contributions of nicotine dependence, adverse health symptoms, and smoking risk perceptions to persistent smoking among individuals with varying degrees of psychiatric symptoms, we tested mediational pathways between psychiatric symptoms and change in smoking heaviness among adult daily smokers with internalizing disorders using the Population Assessment in Tobacco and Health (PATH) survey. There are four waves of the PATH study available. We tested our mediators longitudinally between Waves 1–3 and Waves 2–4. We hypothesized that cigarette dependence, risk perceptions and respiratory symptoms would mediate the relationship between internalizing symptoms at Wave 1 and cigarettes per day at Wave 3 among individuals who smoke daily. Specifically, based on the studies described above, we hypothesized that higher symptom severity at Wave 1 would be associated with higher cigarette dependence, lower risk perceptions, and higher respiratory symptoms at Wave 2, and that these would be associated with higher cigarettes per day at Wave 3.

2. Methods

2.1. Data Source:

This analysis was conducted using participant data from the Public-Use Files (PUF) of the Population Assessment in Tobacco and Health (PATH) Study (U.S Department of Health and Human Services., 2014). The PATH Study is a nationally representative longitudinal cohort study funded by the National Institutes of Health (NIH), the Food and Drug Administration (FDA) and FDA's Center for Tobacco Products (CTP). Data collection for the PATH study started in October 2013 (Wave 1) and has been collected every subsequent year, with Wave 4 data collection ending in October 2018. A total of 45,971 U.S. youth and adults participated in this survey. Participants were recruited using a multistage area-probability sampling approach. The methods and sampling design of the PATH study are reported elsewhere (Hyland et al., 2017). The weighted response rate among adults eligible to participate in all four waves was 74% (U.S. Department of Health & Human Services, 2014). The weighted response rate refers to the estimated proportion of the survey population for which there is useable information available for all four waves.

2.2. Population:

This analysis was restricted to U.S. adults who were ages 18 and older during Wave 1 data collection, participated in all four waves of data collection, and self-identified as daily cigarette users at every wave. A daily cigarette user was defined in the PATH Study as anyone who has smoked at least 100 cigarettes in their lifetime and now smokes every day. All measurement models and structural equation models were run using complete case analysis. Among 5,782 eligible individuals at Wave 1 there was complete data available across all four waves for 4,152 individuals. We report our main findings based on this sample. We also undertook a detailed missing data analysis to assess any systematic patterns of missing data associated with our exposure variable, mediators and outcome and identify any potential sources of bias due to our complete case restriction.

Our findings focused on daily cigarette users due to our interest in understanding potential mediators of smoking heaviness among those who are persistent cigarette users, which interpreted as people who demonstrate consistent and committed use of cigarettes. Persistent cigarette use among this population is well documented in the literature people with psychiatric disorders are at an increased risk of incurring smoking-related health harms.

2.3. Measures:

2.3.1. Tobacco use outcome

Our outcome was change in smoking heaviness. Smoking heaviness was measured by participant's self-reported cigarettes per day (CPD) at each wave. CPD values beyond three standard deviations of the mean in Wave 1 were removed from the dataset. We modeled changes in smoking behavior between Waves 1–4.

2.3.2. Psychiatric Symptoms:

Our exposure of interest was elevated symptoms of internalizing disorders such as depression, anxiety, somatic disorder and traumatic distress, based on DSM criteria (Dennis et al., 2006). These symptoms were assessed using the internalizing subscale of the Global Appraisal of Individual Needs–Short Screener (GAIN-SS), which asks about symptoms of depression, insomnia feeling nervous/anxious and feeling distressed about things in the past (Cohn et al., 2018; Conway et al., 2017; Dennis, Feeney, Titus, 2008). When responding to the internalizing scale, participants indicated how recently they experienced internalizing symptoms using the following rating: "Never," "1 + years ago," "2 to 12 months ago," and "Past month." Rather than collapse internalizing scale scores into a binary measure representing low severity versus high severity of symptoms, we modeled internalizing symptoms based on the original scores to better understand the association between mediators and the degree of internalizing symptom severity.

2.3.3. Mediators:

In order to better understand how the constructs of general harm perceptions of cigarettes, self-reported cigarette dependence, and respiratory symptoms are associated with heaviness of smoking among people internalizing disorders more broadly, three mediation variables were selected a-priori using questions from the PATH dataset: "How harmful do you think cigarettes are to health"; " Usually want to smoke/use cigarettes right after waking up"; and experiences of 5 different respiratory symptoms in the last 12 months. These measures are described in detail below.

2.3.4. Cigarette risk Perception:

In order to assess self-perceived cigarette risk perception, we used a stand-alone question that asked cigarette users about their general perception of cigarette harm, "How harmful do you think cigarettes are to health". Response options ranged from 1 (not at all harmful) to 5 (extremely harmful). Selection of this measure was used based on its

availability in all four waves of the PATH study and that the construct (perception of risk) closely matched the measure we used in our secondary analysis focused on biopsychosocial mechanisms associated with tobacco use among people with and without serious mental illness.

2.3.5. Respiratory Symptoms:

Respiratory symptom severity was treated as a latent variable indicated by five questions from the PATH study that ask participants about the number of 1) wheezing attacks 2) sleep disruptions, 3) instances of limited speech due to wheezing, 4) instances of chest wheezing after exercise, and 5) instances of experiencing a dry cough at night not associated with a cold of chest infection in the past 12 months. For number of wheezing attacks, response options ranged from 1 (never) to 4 (more than 12 times). For number of sleep disruptions, response options ranged from 1 (never) to 4 (one or more nights per week). For the remaining three respiratory symptom questions, response options ranged from 1 to 2, with 1 being yes and 2 being no. We also adjusted for unique covariance between two questions, sleep disruptions due to wheezing and chest wheezing during or after exercise

2.3.6. Cigarette Dependence:

Time to first cigarette is commonly used as a phenotype measure of nicotine dependence (Fagerström, 2003). Participants were asked their level of agreement with the following statement "Usually want to smoke/use [tobacco products / specific product] right after waking up". Response options ranged from 1 to 5 with 1 being "not true for me" and 5 being "extremely true for me".

2.3.7. Demographic covariates:

All analyses accounted for relevant covariates associated with variation in cigarette use including socioeconomic status (attainment, average household income, and employment), age, race, and Latino ethnicity (U.S. Department of Health & Human Services, 2014).

2.3.8. Confounders:

In order to maximize our ability to identify longitudinal changes in the mediator and their impact on smoking, we conditioned each mediator on its own score from the previous wave (this was done in both the Waves 1–3 and Waves 2–4 models). In addition, we controlled for cigarettes per day in the previous wave to adjust for baseline differences. Sex was also treated as potential confounder since women are found to have a higher mean level of internalizing symptoms (Eaton et al., 2012) and higher prevalence of affective disorders than men (Tibubos et al., 2019).

2.4. Statistical Analyses:

Selected sample characteristics were described using Fay's variant (Westat, 2021) of balanced repeated replication weights survey to provide estimates generalizable to the non– institutionalized, U.S. adult population and to account for potential bias due to non-response. Structural equation models (SEM) were fit across two sets of participant data, spanning Waves 1–3 and 2–4, to determine the direct and indirect associations between internalizing symptoms (W1 or W2, respectively), all three mediators (W2 or W3, respectively) and CPD (W3 or W4, respectively). Models were based on a complete case analysis and restricted to daily smokers. We included auto-regressive effects for the mediator at the respective baseline wave in the mediator path and for CPD at the respective baseline wave in the outcome path to account for potentially confounding baseline differences. Conditioning each mediator on its prior score using an autoregressive SEM approach, allows us to maximize the measurement of change that happens over time between our exposure, mediators, and outcome. Models were fit with bootstrapped standard errors (SE) and accounted for sociodemographic covariates in all paths.

Confirmatory Factor Analysis (CFA) was used to develop the latent

variable measurement model for respiratory symptoms noted previously. Variables included in our CFA measurement model met univariate and regression assumptions in the context of an appropriately sized sample. As indicators of respiratory symptoms were non-multivariate normal (Henze-Zirkler < 0.001) which could bias estimates when using maximum likelihood estimation, bootstrapping was used in the computation of standard errors (Fouladi, 1998; Hancock & Nevitt, 1999; Nevitt & Hancock, 2001). We also observed residual covariance across two items (i.e., sleep disruption due to wheezing and chest wheezing during or after exercise) in our respiratory symptoms measure. We accounted for this unique covariance between items and allowed them to correlate in our final model. We estimated standardized coefficients across latent measurement models. All analyses were run using R statistical programming software (R Core Team, 2018).

3. Results

A total of N = 4,152 individuals were included in this analysis. At Wave 1, the sample was 52.7% male and 47.3% female. Approximately 55.7% participants were between the ages of 18–44 years and the majority of the sample was white, (80%) and non-Latino (92%). Approximately 58.42% had a high school education or less, 46.6% worked at least 35 h a week, and 77.02% reported annual household income at or below \$50,000 (Table 1).

We created one latent variable for respiratory symptoms. Modification indices suggested unaccounted-for covariance between two items (sleep disruptions due to wheezing and exercise disruptions due to wheezing).

Table 1

Weighted Descriptive Characteristics of Sample Participants at Wave 1 of the Population Assessment of Tobacco and Health (PATH) Study.

Variables	Total Sample n = 4,152 N[1] = 32,514,300 % (SE)
Male	52.7 (0.75)
Female	47.3 (0.75)
18 to 44 years old	55.7 (0.94)
45 to 64 years old	38.3 (0.85)
65 years old or older	6.0 (0.47)
White	80 (0.75)
Black	13.5 (0.60)
Other	6.5 (0.40)
Latino Ethnicity	8.00 (0.46)
Non-Latino Ethnicity	92.00 (0.46)
High School or Less	58.42 (0.98)
Some college / Associates degree	33.57 (0.87)
Bachelors or higher	8.01 (0.50)
<50,000 (Mean \$/year)	77.02 (1.00)
More than 50,000 (Mean \$/year)	22.98 (1.00)
Don't currently work for pay	38.1 (1.02)
Work part time<15 h per week	4.4 (0.3)
Work part-time 15–24 h per week	10.9 (0.57)
Work full time at least 35 h per week	46.6 (1.04)
Cigarettes Per Day Mean (95% CI)[†]	16.6 (16.2 – 16.9)
Cigarette Dependence Mean (95% CI)[2]	2.7 (2.7–2.8)
Cigarette Risk Perception Mean (95% CI)[3]	3.0 (3.0 – 3.1)
Respiratory Symptoms Mean (95% CI)[4]	1.5 (1.5 – 1.6)

†Structured in line with our analysis, means are shown for Wave 3 outcome (CPD) and Wave 2 mediators

[1] N represents the US population to which the sample generalizes.

[2] Response options ranged from 1 to 5 with 1 being "not true for me" and 5 being "extremely true for me"

[3] Response options ranged from 1 to 5 with 1 being "not at all harmful" and 5 being "extremely harmful"

[4] Response options for wheeze attacks and sleep disruptions ranged from 1 to 4 with 1 being "never" and 4 being "more than 12 times" and "one or more nights per week", response options for the other three respiratory symptom questions ranged from 1 to 2, with 1 being "yes" and 2 being "no".

Results from the Confirmatory Factor Analysis suggested excellent fit for the respiratory symptoms measurement model, Root Mean Squared Error Approximation (RMSEA) = 0.035; Comparative Fit Index (CFI) = 0.946; Tucker-Lewis Index (TLI) = 0.930; Standardized Root Mean Square Residual (SRMR) = 0.036. We also achieved excellent fit for the cigarette dependence measurement model (RMSEA = 0.046; CFI = 0.936; TLI = 0.902; SRMR = 0.044) and the risk perceptions of cigarettes measurement model (RMSEA = 0.045; CFI = 0.937; TLI = 0.904; SRMR = 0.042). We replicated these measurement models at Wave 3 and achieved similar results for the measurement model for respiratory symptoms (RMSEA = 0.034; CFI = 0.952; TLI = 0.938; SRMR = 0.035). At Wave 3, the measurement model for cigarette dependence was (RMSEA = 0.044; CFI = 0.945; TLI = 0.916; SRMR = 0.044) and fit for the measurement model for perceived harmfulness of cigarettes was (RMSEA = 0.043; CFI = 0.944; TLI = 0.914; SRMR = 0.041) and for cigarette dependence.

Higher internalizing symptoms at Wave 1 were associated with lower CPD at Wave 3 (B = -0.030, SE = 0.313, p = 0.021) (Fig. 1). In addition, higher internalizing symptoms at Wave 1 were associated with higher respiratory symptoms at Wave 2 (B = 0.270, SE = 0.037, p < 0.001), higher cigarette dependence at Wave 2 (B = 0.033, SE = 0.055, p = 0.019) and higher cigarette risk perceptions at Wave 2 (B = 0.56, SE = 0.035, p < 0.001).

Our mediators were associated with our outcome in the following ways; higher respiratory symptoms at Wave 2 predicted higher cigarettes per day at Wave 3 (B = 0.067, SE = 0.169, p < 0.001), higher cigarette dependence at Wave 2 predicted higher cigarettes per day at Wave 3 (B = 0.117, SE = 0.074, p < 0.001) and higher cigarette risk perceptions at Wave 2 predicted lower CPD at Wave 3 (B = -0.009, SE = 0.114, p = 0.404).

In the structural equation models, the relationship between internalizing symptoms and CPD was mediated by cigarette dependence (indirect: B = 0.004, SE = 0.041, p = 0.023). Similarly, respiratory symptom severity mediated the relationship between internalizing symptoms and CPD (indirect: B = 0.018, SE = 0.097, p < 0.001). Internalizing symptoms predicted higher risk perceptions (B = 0.056, SE = 0.035, p < 0.001) but the indirect relationship with CPD was non-significant. Findings from Waves 2–4 replicated these results (Fig. 1) with two exceptions, the b path between cigarette risk perceptions at Wave 2 and cigarettes per day at Wave 4 became significant (B = -0.028, SE = 0.128, p = 0.042). This did not change the indirect relationship between respiratory symptoms severity, internalizing symptoms and smoking heaviness because the relationship between internalizing symptoms at Waves 2 and cigarettes per day at Wave 4 became non-significant (B = -0.28, SE = 0.365, p = 0.73)

4. Discussion

The main objective of this study was to explore the longitudinal associations between elevated psychiatric symptoms and persistent smoking among daily cigarette users with three mediators that were selected *a priori* based on our previous work (DeAtley et al., 2020): cigarette dependence, risk perceptions, and respiratory symptoms. Consistent with our hypothesis, we found that higher internalizing symptom severity at Wave 1 was associated with higher cigarette dependence severity and higher respiratory symptom severity at Wave 2, which in turn predicted more cigarettes per day at Wave 3. These relationships were replicated in Waves 2–4. Contrary to our hypothesis, internalizing symptom severity at Wave 1 was associated with higher risk perceptions about cigarettes at Wave 2 and was associated with lower smoking heaviness at Wave 3. In addition, the relationship between risk perceptions at Wave 2 and smoking heaviness at Wave 3 was not significant. While the relationship between risk perceptions at Wave 3 and smoking heaviness at Wave 4 was significant, this did not change the indirect results for the overall relationship between these variables in Waves 2–4.

Our novel findings demonstrated that cigarette dependence mediates the relationship between internalizing symptoms and smoking heaviness over time. Nicotine dependence has been studied as a key process underlying persistent tobacco use both in the general population (Donny et al., 2008) and among individuals with psychiatric conditions (Tidey & Miller, 2015). Furthermore, symptoms of nicotine dependence such as craving and withdrawal appear to be key factors driving smoking relapse among psychiatric (Tidey & Miller, 2015) and non-psychiatric samples (Allen et al., 2008). Our findings were consistent with a recent PATH study analysis that found that adults with internalizing symptoms and high nicotine dependence had higher cigarette consumption compared to adults with internalizing symptoms alone (Snell et al., 2021). This study also found that adults with psychiatric conditions who were not highly dependent were more likely to attempt to quit smoking and to be successful. Taken together, these findings suggest that while adults with psychiatric conditions are at increased risk of smoking, this risk is driven in part by increased vulnerability for nicotine dependence rather than directly by psychiatric symptomatology alone. Our findings also lend support to evidence from clinical trials that reducing cigarette dependence by lowering the reinforcing efficacy of cigarettes (i.e. through reducing nicotine content) may be an effective strategy to reduce the significant public health burden of smoking among both the general population of adults who smoke, and those with psychiatric conditions (Higgins et al., 2020) including adults with serious mental illness (Tidey et al., 2019).

While respiratory symptoms severity did mediate the relationships between internalizing symptoms and smoking heaviness, the direction of these relationship between our mediator and outcome suggests that there may be a disconnect between people with internalizing symptoms experiencing high respiratory symptoms and wanting to quit. As shown in our models, higher respiratory symptoms lead to more cigarettes per day in our sample rather than less, suggesting that interventions to
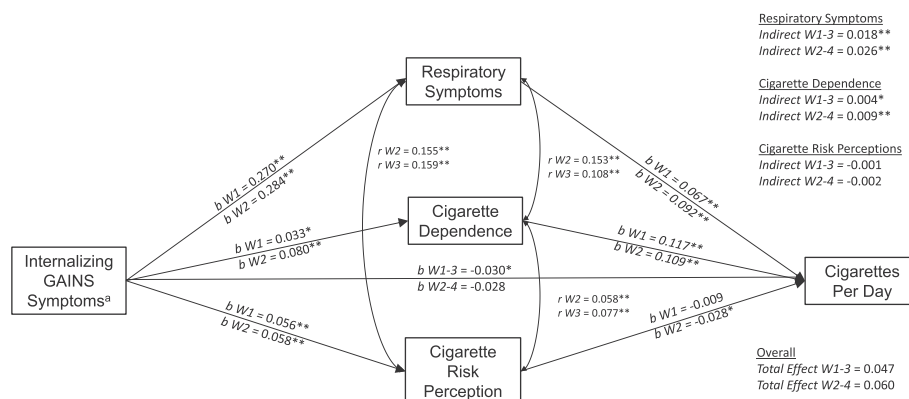

Fig. 1. Auto Regressive SEM analysis of W1 internalizing symptoms W2 mediators (respiratory symptoms, cigarette dependence and cigarette risk perception) predicting W3 cigarettes per day & W2 internalizing symptoms W3 mediators (respiratory symptoms, cigarette dependence and cigarette risk perception) predicting W4 cigarettes per day. Standardized coefficients signified with an asterisk are significant. * p < 0.05, ** p < 0.01. a) Controlling for CPD at Wave 1, for analysis of Waves 1–3 and controlling for CPD at Wave 2 for analysis of Waves 2–4.

encourage quitting if respiratory symptoms are high is needed.

One relationship that did not align with our hypothesis was that internalizing symptoms were positively associated with smoking risk perceptions. While we hypothesized that internalizing symptoms would be associated with lower risk perceptions based on our previous study people with serious mental illness who smoke, (DeAtley et al., 2020) other studies have found positive associations between psychiatric disorders and cigarette risk perceptions. For example, frequent depression emerged as a predictor of fatalistic cancer beliefs and increased perceptions of cancer risk among a sample of individuals who identified as never, current and former cigarette users, in an online cancer questionnaire (Cunningham et al., 2019). In a separate study, associations between risk perceptions of lung cancer and depressive symptoms were explored among two different samples of individuals who smoke: 1) college students and 2) the Health Information National Trends Survey (HINTS) (Floyd et al., 2009). In that study, women with more depressive affect who were heavier cigarette users perceived a greater risk of developing lung cancer in the future than those with lower depressive affect (Floyd et al., 2009).

A possible explanation for why risk perceptions may not have mediated the relationship between internalizing symptoms and smoking heaviness is because of the complexity of the behavior change (Costello et al., 2012). Although health behavior change models such as the Health Belief Model, (Janz & Becker, 1984) Protection Motivation Theory, (Rogers, 1975) and the Theory of Reasoned Action (Fishbein & Ajzen, 1977) highlight the importance of perceived health risks in predicting behavior change, perceived risk and other motivational factors appears to play a larger role in predicting less complex behaviors like making plans to quit or making a quit attempt than more complex behaviors such as maintaining cessation (Borland et al., 2010). Our finding that internalizing symptom severity is positively associated with smoking risk perceptions but that this does not predict changes in smoking behavior is consistent with the suggestion that smoking persistence among people with psychiatric symptoms is not due to low motivation to quit but may instead be due to factors such as lack of access to effective cessation interventions (Siru et al., 2009).

It should be noted that our findings are limited to daily cigarette users. Patterns of missingness were explored for our outcome (CPD) as well as two of our mediators, cigarette dependence and cigarette risk perception. Our exposure variable, internalizing symptoms and mediator respiratory symptoms had over a 95% response rate. From our missing data analysis, participants were more likely to not report CPD at Wave 3 if they had a high-risk perception of cigarettes at Wave 2. This pattern of missing data was observed between Waves 2–4. The overall mean of cigarette risk perception for this sample was 3 out of 4, meaning that most people in this sample thought cigarettes were relatively harmful. We did not observe a significant association between the cigarette risk perception and CPD pathway in our multiple mediator model at Waves 1-3. While this relationship became significant at Waves 2-4,the relationship between internalizing symptoms and CPD at Waves 2- 4 became non-significant, therefore there are no additional considerations for our interpretation due to this pattern of missingness.

Participants were more likely to miss the CPD question at Wave 3 if they reported lower cigarette dependence at Wave 2. Given that higher cigarette dependence at Wave 2 is associated with increases in cigarettes per day at Wave 3, our estimate may be underestimating the strength of this association, for example, individuals with low dependence are likely to have low CPD per known associations as well as cross-sectional observations. Omitting these observations may attenuate the relationship between dependence and CPD, which may plateau at high levels of dependence. However, given that small proportion of missing data, such biases are unlikely.

Lastly, participants were more likely to not answer the smoking dependence question at Wave 3 if they reported high risk perceptions at Wave 3. Given that the sample overall thought that cigarettes were harmful to health, participants may be less willing to report their

dependence due to shame or perceived stigma given that they reported a high awareness of cigarette risk perception. We did not study variation in smoking behavior for individuals who were dual users of cigarette and electronic cigarettes nor those who may have used cessation aids over the course of the four-wave study. Future studies should investigate how these mediators interact with use of cessation aids or reduced risk products among daily cigarette users. However, our findings are important in that they describe the associations between smoking, cigarette harm perceptions, respiratory symptoms, and cigarette dependence among a sample of individuals with elevated symptoms of anxiety and depression; a population that suffers from persistently high rates of tobacco use and related disease. Our analysis utilized a large, nationally representative data set, and because we analyzed cigarette users with elevated internalizing symptoms, our results may be more generalizable than results from studies that focus on people with a specific psychiatric diagnosis. The availability of four waves of data among a cohort of adults allowed for a rigorous examination of several mediational pathways over time that may guide intervention future intervention development.

5. Conclusion

Our results indicate that cigarette dependence and respiratory symptom severity mediate the relationship between internalizing symptoms and CPD. While higher amount of internalizing symptoms were associated with higher smoking risk perceptions, higher risk perceptions were not associated with higher amount of CPD. These findings suggest that efforts to reduce smoking among people with internalizing disorders should focus on reducing cigarette or nicotine dependence and increasing awareness of respiratory symptoms to encourage a quit attempt or switching to less harmful sources of nicotine rather than focusing on smoking risks.

CRediT authorship contribution statement

Teresa DeAtley: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Visualization, Writing – original draft. **Alexander W. Sokolovsky:** Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – review & editing. **Morgan L. Snell:** Data curation, Investigation, Methodology, Software, Supervision, Visualization, Writing – review & editing. **Jennifer Tidey:** Conceptualization, Formal analysis, Funding acquisition, Investigation, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Allen, S. S., Bade, T., Hatsukami, D., & Center, B. (2008). Craving, withdrawal, and smoking urges on days immediately prior to smoking relapse. *Nicotine & Tobacco Research, 10*(1), 35–45. https://doi.org/10.1080/14622200701705076

Baker, T. B., Piper, M. E., McCarthy, D. E., Bolt, D. M., Smith, S. S., Kim, S. Y., … Toll, B. A. (2007). Time to first cigarette in the morning as an index of ability to quit smoking: Implications for nicotine dependence. *Nicotine & Tobacco Research, 9*(Suppl 4), S555–570. https://doi.org/10.1080/14622200701673480

Borland, R., Yong, H. H., Balmford, J., Cooper, J., Cummings, K. M., O'Connor, R. J., … Fong, G. T. (2010). Motivational factors predict quit attempts but not maintenance of smoking cessation: Findings from the International Tobacco Control Four country project. *Nicotine & Tobacco Research, 12*(Suppl 1), S4–11. https://doi.org/10.1093/ntr/ntq050

Borrelli, B., Hayes, R. B., Dunsiger, S., & Fava, J. L. (2010). Risk perception and smoking behavior in medically ill smokers: A prospective study. *Addiction, 105*(6), 1100–1108. https://doi.org/10.1111/j.1360-0443.2010.02900.x

Callaghan, R. C., Veldhuizen, S., Jeysingh, T., Orlan, C., Graham, C., Kakouris, G., Remington, G., & Gatley, J. (2014Patterns of tobacco-related mortality among individuals diagnosed with schizophrenia, bipolar disorder, or depression. *Journal of Psychiatric Research, 48*(1), 102-110. 10.1016/j.jpsychires.2013.09.014.

Cohn, A. M., Johnson, A. L., Rose, S. W., Pearson, J. L., Villanti, A. C., & Stanton, C. (2018). Population-level patterns and mental health and substance use correlates of alcohol, marijuana, and tobacco use and co-use in US young adults and adults: Results from the population assessment for tobacco and health. *The Americal Journal of Addictions, 27*(6), 491–500. https://doi.org/10.1111/ajad.12766

Conway, K. P., Green, V. R., Kasza, K. A., Silveira, M. L., Borek, N., Kimmel, H. L., … Compton, W. M. (2017). Co-occurrence of tobacco product use, substance use, and mental health problems among adults: Findings from Wave 1 (2013–2014) of the Population Assessment of Tobacco and Health (PATH) Study. *Drug and Alcohol Dependence, 177*, 104–111. https://doi.org/10.1016/j.drugalcdep.2017.03.032

Costello, M. J., Logel, C., Fong, G. T., Zanna, M. P., & McDonald, P. W. (2012). Perceived risk and quitting behaviors: Results from the ITC 4-country survey. *American Journal of Health Behavior, 36*(5), 681–692. https://doi.org/10.5993/ajhb.36.5.10

Cunningham, S. A., Yu, R., Shih, T., Giordano, S., McNeill, L. H., Rechis, R., … Shete, S. (2019). Cancer-Related Risk Perceptions and Beliefs in Texas: Findings from a 2018 Population-Level Survey. *Cancer Epidemiology Biomarkers & Prevention, 28*(3), 486–494. https://doi.org/10.1158/1055-9965.Epi-18-0846

De Hert, M., Correll, C. U., Bobes, J., Cetkovich-Bakmas, M., Cohen, D., Asai, I., Detraux, J., Gautam, S., Möller, H.-J., Ndetei, D. M., Newcomer, J. W., Uwakwe, R., & Leucht, S. (2011). Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World psychiatry: official journal of the World Psychiatric Association (WPA), 10*(1), 52-77. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3048500/.

DeAtley, Teresa, Denlinger-Apte, Rachel, Cioe, Patricia, Colby, Suzanne, Cassidy, Rachel N, Clark, Melissa A, … Tidey, Jennifer W (2020). Biopsychosocial mechanisms associated with tobacco use in smokers with and without serious mental illness. *Preventive Medicine, 140*, Article 106190. https://doi.org/10.1016/j.ypmed.2020.106190

Dennis, M. L., Chan, Y. F., & Funk, R. R. (2006). Development and validation of the GAIN Short Screener (GSS) for internalizing, externalizing and substance use disorders and crime/violence problems among adolescents and adults. *The American Journal on Addictions, 15*(Suppl 1), 80–91. https://doi.org/10.1080/10550490601006055

Dennis M., Feeney T., Titus J. (2008). version. 2.0.3. Global Appraisal of Individual Needs-Short Screener (GAIN-SS): Administration and scoring manual, Version 3. 2008. (Accessed 19 Jan 2022).

Dickerson, F., Stallings, C. R., Origoni, A. E., Vaughan, C., Khushalani, S., Schroeder, J., & Yolken, R. H. (2013). Cigarette smoking among persons with schizophrenia or bipolar disorder in routine clinical settings, 1999–2011. *Psychiatric Services, 64*(1), 44–50.

Donny, E. C., Denlinger, R. L., Tidey, J. W., Koopmeiners, J. S., Benowitz, N. L., Vandrey, R. G., al'Absi, M., Carmella, S. G., Cinciripini, P. M., Dermody, S. S., Drobes, D. J., Hecht, S. S., Jensen, J., Lane, T., Le, C. T., McClernon, F. J., Montoya, I. D., Murphy, S. E., Robinson, J. D., Stitzer, M. L., Strasser, A. A., Tindle, H., & Hatsukami, D. K. (2015). Randomized Trial of Reduced-Nicotine Standards for Cigarettes. *New England Journal of Medicine, 373*(14), 1340-1349. 10.1056/NEJMsa1502403.

Donny, E. C., Griffin, K. M., Shiffman, S., & Sayette, M. A. (2008). The relationship between cigarette use, nicotine dependence, and craving in laboratory volunteers. *Nicotine & Tobacco Research, 10*(5), 934–942. https://doi.org/10.1080/14622200802133681

Eaton, N. R., Keyes, K. M., Krueger, R. F., Balsis, S., Skodol, A. E., Markon, K. E., … Hasin, D. S. (2012). An invariant dimensional liability model of gender differences in mental disorder prevalence: Evidence from a national sample. *Journal of Abnormal Psychology, 121*(1), 282–288. https://doi.org/10.1037/a0024780

Fagerström, K. (2003). Time to first cigarette; the best single indicator of tobacco dependence? *Monaldi Archives for Chest Disease, 59*(1), 91–94. PMID: 14533289.

Fishbein, M., & Ajzen, I. (1977). Belief, attitude, intention, and behavior: An introduction to theory and research.

Floyd, A. H., Westmaas, J. L., Targhetta, V., & Moyer, A. (2009). Depressive symptoms and smokers' perceptions of lung cancer risk: Moderating effects of tobacco dependence. *Addictitive Behaviors, 34*(2), 154–163. https://doi.org/10.1016/j.addbeh.2008.10.006

Fouladi, R. T. (1998). Covariance Structure Analysis Techniques under Conditions of Multivariate Normality and Nonnormality-Modified and Bootstrap Based Test Statistics.

Goodwin, R. D., Lavoie, K. L., Lemeshow, A. R., Jenkins, E., Brown, E. S., & Fedoronko, D. A. (2012). Depression, Anxiety, and COPD: The Unexamined Role of Nicotine Dependence. *Nicotine & Tobacco Research, 14*(2), 176–183. https://doi.org/10.1093/ntr/ntr165

Hancock, G. R., & Nevitt, J. (1999). Bootstrapping and the identification of exogenous latent variables within structural equation models. *Structural Equation Modeling: A Multidisciplinary Journal, 6*(4), 394–399.

Higgins, S. T., Tidey, J. W., Sigmon, S. C., Heil, S. H., Gaalema, D. E., Lee, D., … Harfmann, R. F. (2020). Changes in Cigarette Consumption With Reduced Nicotine Content Cigarettes Among Smokers With Psychiatric Conditions or Socioeconomic Disadvantage: 3 Randomized Clinical Trials. *JAMA Network Open, 3*(10), e2019311. https://doi.org/10.1001/jamanetworkopen.2020.19311

Hyland, A., Ambrose, B. K., Conway, K. P., Borek, N., Lambert, E., Carusi, C., … Compton, W. M. (2017). Design and methods of the Population Assessment of Tobacco and Health (PATH) Study. *Tobacco Control, 26*(4), 371. https://doi.org/10.1136/tobaccocontrol-2016-052934

Janz, N. K., & Becker, M. H. (1984). The health belief model: A decade later. *Health education quarterly, 11*(1), 1–47.

Leventhal, A. M., & Zvolensky, M. J. (2015). Anxiety, Depression, and Cigarette Smoking: A Transdiagnostic Vulnerability Framework to Understanding Emotion-Smoking Comorbidity [Article]. *Psychological Bulletin, 141*(1), 176–212. https://doi.org/10.1037/bul0000003

Melzer, A. C., Feemster, L. C., Crothers, K., Carson, S. S., Gillespie, S. E., Henderson, A. G., … Au, D. H. (2016). Respiratory and Bronchitic Symptoms Predict Intention to Quit Smoking among Current Smokers with, and at Risk for, Chronic Obstructive Pulmonary Disease. *Annals of the American Thoracic Society, 13*(9), 1490–1496. https://doi.org/10.1513/AnnalsATS.201601-075OC

Morisano, D., Bacher, I., Audrain-McGovern, J., & George, T. P. (2009). Mechanisms underlying the comorbidity of tobacco use in mental health and addictive disorders. *The Canadian Journal of Psychiatry, 54*(6), 356–367. https://doi.org/10.1177/070674370905400603

Nevitt, J., & Hancock, G. R. (2001). Performance of bootstrapping approaches to model test statistics and parameter standard error estimation in structural equation modeling. *Structural equation modeling, 8*(3), 353–377.

R Core Team. (2018). *R: A language and environment for statistical computing.* In R Foundation for Statistical Computing. Retrieved from: http://www.R-project.org/.

Rogers, R. W. (1975). A protection motivation theory of fear appeals and attitude change1. *The journal of psychology, 91*(1), 93–114.

Sacco, K. A., Bannon, K. L., & George, T. P. (2004). Nicotinic receptor mechanisms and cognition in normal states and neuropsychiatric disorders. *Journal of Psychopharmacology, 18*(4), 457–474. https://doi.org/10.1177/0269881104018004003

Siru, R., Hulse, G. K., & Tait, R. J. (2009). Assessing motivation to quit smoking in people with mental illness: A review. *Addiction, 104*(5), 719–733. https://doi.org/10.1111/j.1360-0443.2009.02545.x

Smith, P. H., Mazure, C. M., & McKee, S. A. (2014). Smoking and mental illness in the US population. *Tobacco Control, 23*(e2), Article e147. http://tobaccocontrol.bmj.com/content/23/e2/e147.abstract.

Snell, Morgan, Harless, David, Shin, Sunny, Cunningham, Peter, Barnes, Andrew, et al. (2021). A longitudinal assessment of nicotine dependence, mental health, and attempts to quit Smoking: Evidence from waves 1–4 of the Population Assessment of Tobacco and Health (PATH) study. *Addictive Behaviors, 115*, Article 106787. https://doi.org/10.1016/j.addbeh.2020.106787

Tibubos, A. N., Brähler, E., Ernst, M., Baumgarten, C., Wiltink, J., Burghardt, J., … Beutel, M. (2019). Course of depressive symptoms in men and women: Differential effects of social, psychological, behavioral and somatic predictors. *Scientific Reports, 9*, 18929. https://doi.org/10.1038/s41598-019-55342-0

U.S Department of Health and Human Services. (2014). The health consequences of smoking—50 years of progress: a report of the Surgeon General. *Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 17*. Reference to a website: https://www.ncbi.nlm.nih.gov/books/NBK179276/.

Tidey, Jennifer W., Colby, Suzanne M., Denlinger-Apte, Rachel L., Goodwin, Christine, Cioe, Patricia, Cassidy, Rachel N., … Donny, Eric C. (2019). Effects of 6-Week Use of Very Low Nicotine Content Cigarettes in Smokers With Serious Mental Illness. *Nicotine & Tobacco Research, 21*(1), S38–S45. https://doi.org/10.1093/ntr/ntz133

Tidey, J. W, & Miller, M. E (2015). Smoking cessation and reduction in people with chronic mental illness. *British Medical Journal (Clinical research ed.), (351)*, h4065. https://doi.org/10.1136/bmj.h4065

Walker, E. R., McGee, R. E., & Druss, B. G. (2015). Mortality in mental disorders and global disease burden implications: A systematic review and meta-analysis. *JAMA Psychiatry, 72*(4), 334–341. https://doi.org/10.1001/jamapsychiatry.2014.2502

Westat. (2021). PATH Study Public Use Files User Guide. The National Addiction & HIV Data Archive Program. Retrieved from:https://www.icpsr.umich.edu/files/NAHDAP/documentation/ug36498-all.pdf.