

# **The bidirectional causality of anxiety and smoking cessation**

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Date: 11-04-2022

## Abstract

*Introduction:* Smokers with anxiety disorder are known to have worse smoking cessation outcomes. This is due to more severe withdrawal and anxiety symptoms and difficulty with treatment adherence. The aim of this study was to discover the predictability of anxiety on smoking cessation and whether smoking cessation is able to predict anxiety

*Methods:* A RCT with two types of treatment was offered to the participants. The first type of treatment was a blended smoking cessation treatment, which combined the good of both internet-based and face-to-face treatments and the second was a face-to-face treatment.

*Results:* Despite strong cross-sectional associations between anxiety and smoking cessation across all time points, only anxiety at 6 months showed a predictive effect on later smoking cessation. However, this was at the 9-month follow-up only (OR=1.1). Smoking cessation at 6 months also lead to lower anxiety over the duration of the intervention with large effect sizes at months 6 ( $p=.006$ ,  $\eta_p^2 = .067$ ), 9 ( $p=.020$ ,  $\eta_p^2 = .073$ ) and 15 ( $p=.017$ ,  $\eta_p^2 = .085$ ).

*Discussion:* All in all, a bidirectional causality between anxiety and smoking cessation was discovered with a stronger effect of smoking cessation on anxiety, albeit with some uncertainties as there was not a decrease in anxiety across all time-points. Anxiety was associated with smoking; however, baseline anxiety was not able to predict any sort of smoking cessation. This could be related to the high amount of drop-outs which could have led to some effects not being shown. Smoking cessation lead to lower anxiety levels across all time-points however at the 15-month mark anxiety did increase for the non-smoking group. The reason for this is not known and raises concerns about how much anxiety is able to predict as there are uncertainties for what may have caused this. Finally, for the difference in the types of treatment provided there was no conclusive evidence in this study whether a certain type of treatment could provide an increase in results.

**Keywords:** Anxiety, Smoking cessation, bidirectionality, causality, blended smoking cessation treatment, treatment as usual, adherence

## Contents

<b>Abstract</b> .....	2
<b>Introduction</b> .....	4
<b>Methods</b> .....	7
<b>Results</b> .....	11
<b>Anxiety as a predictor of smoking cessation</b> .....	12
<b>Successful smoking cessation effects on anxiety</b> .....	15
<b>Anxiety as a moderator on treatment outcome</b> .....	18
<b>Discussion</b> .....	19
<b>General discussion</b> .....	19
<b>Anxiety as a predictor of smoking cessation</b> .....	20
<b>Successful smoking cessation effects on anxiety</b> .....	21
<b>Limitations, strengths and recommendations</b> .....	22
<b>Conclusion</b> .....	24
<b>References</b> .....	25

## **Introduction**

### **An overview of tobacco use**

Smoking tobacco is one of the biggest public health risks in the general population. According to the World Health Organization (WHO) each year more than 8 million people die because of tobacco, of which more than 7 million of the deaths are caused by direct tobacco usage whereas 1.2 million people die due to being exposed to the smoke as second-hand smokers (WHO, 2020). Smoking is a risk factor due to the fact that it can cause various types of cancer almost anywhere in the human body. Lung cancer being the most common cause (U.S. Department of Health and Human Services, 2014), along with chronic obstructive pulmonary disease (COPD) and heart diseases (WHO, 2019). The burden of disease caused by smoking in the Netherlands was stated to be at least 9% according to Volksgezondheid Toekomst Verkenning (2018) making it one of the most important health risk factors and therefore requires an urgent need to develop and implement interventions which can facilitate health-promoting behaviour and smoking cessation.

### **Relationship of tobacco use and anxiety**

Mental health plays a big role in smoking and smoking cessation. It has a direct influence on smoking, as individuals with mental disorder seem to be smoking roughly twice as much as an adult without mental disorders (Cook, et al., 2014). Smoking rates seem to be consistent over time among individuals with a mental disorder, whereas there is a decline in smoking rates among individuals without indications of mental disorders (Szatkowski & Mcneill, 2014). Attempts to quit are also less successful among individuals with mental disorders compared to other groups (Aubin, Rollema, Svensson & Winterer, 2012; Glassman, et al., 1990). Anxiety in particular is an interesting mental health disorder topic to research as smokers can start smoking as a way of coping with their anxiety (McDermott, Marteau, Hollands, Hankins & Aveyard, 2013). Smokers with anxiety report worse smoking cessation outcomes and a higher anxiety sensitivity (Lewis, Jeffries, Zvolensky & Buckner, 2020). Anxiety sensitivity can lead to more severe withdrawal symptoms and a higher urge to smoke (Johnson, et al., 2018; Marshall, Johnson, Bergman, Gibson & Zvolensky, 2009). Smokers with anxiety sensitivity report that they find the idea of quitting difficult or threatening (Zvolensky, et al., 2007) either because of nicotine withdrawal symptoms or an increase in state anxiety (Marshall, et al., 2009; Zvolensky,

Feldner, Leen-Feldner & McLeish, 2005) which both can occur when abstinent (Mclaughlin, Dani & Biasi, 2015; Hughes, Higgins & Hatsukami, 1990). But on the other hand, smoking cessation does not seem to be associated with an increase in mental disorders (Cavozos-Rehg, et al., 2014) or specifically in anxiety (Bolam, West & Gunnell, 2011; Shabab, Andrew & West, 2013) but is also a cause for lowering anxiety among individuals (Taylor, et al., 2014; West & Hajek, 2006). Thus, there seems to be a relationship between anxiety, smoking and smoking cessation and a strong suggestion for anxiety leading to less successful smoking cessation, and successful smoking cessation leading to less anxiety. While there are only a few studies that have looked at the interaction between anxiety and smoking cessation over time, there have not been many that have looked at the bidirectional causality between anxiety and smoking cessation, which is what makes this study unique.

### **Treatment as usual versus internet-based treatments for tobacco users with anxiety**

A wide variety of treatment options are available to provide support in smoking cessation, such as means of self-help, behaviour change techniques (BCTs), motivational interviewing and the use of medication among others (Lightfoot, Panagiotaki, & Nobes, 2020). The higher the level of support, the higher the chance is that someone is successful in smoking cessation (Black, et al., 2020). In conjunction with face-to-face treatments, the use of internet-based e-health interventions have also increased with the advancement of technology. Internet-based interventions have also shown to be effective in improving healthy behaviour (Lustria, et al., 2013). Compared to face-to-face treatments, an internet-based intervention is more widely accessible, especially for individuals who may have a disadvantage in terms of mobility or financial situation (Lustria, et al., 2013). Additionally, internet-based interventions can also be tailored to specific populations which may increase the effectiveness along with adherence (Lustria, et al., 2013). A study in the Netherlands had found that internet-based smoking cessation interventions in the Netherlands are both effective and cost-effective (Cheung, et al., 2017). A study in the Netherlands had found that internet-based smoking cessation interventions in the Netherlands are both effective and cost-effective (Cheung, et al., 2017). However, treatment as usual for individuals with anxiety may not be enough as individuals with anxiety also struggle more with treatment and medication adherence (Alcantara, et al., 2014; Santana & Fontenelle, 2011; Zvolensky, et al., 2007) For individuals with anxiety smoking cessation

programs should also offer resources for directly treating these emotional disorders that include evidence-based pharmacotherapy, CBT and other learning-based psychotherapies, such as bibliotherapy which can be either physically or online or provide use of a telephone hotline for smoking cessation and make use of follow-up contact with the clients. (Richards, Cohen, Morell, Watson & Low, 2013). Additionally, multifaceted combined therapies which take advantage of a multidisciplinary treatment approach seems to be justified as well. (Richards, et al., 2013). The use of internet-based treatment seems to be beneficial for individuals with mental health disorders, anxiety specifically and anxiety symptoms of smokers (Blankers, Saleminck & Wiers, 2016; Davoudi, Omid, Sehat & Sephrmanesh, 2017; Stjerneklar, Hougaard, Nielsen, Gaardsvig & Thastum, 2018). It is important, however, to not let go of face-to-face treatments altogether as solely online treatments seem to fall short when taking the therapeutic alliance into account as well, which could have implications on the effect of the treatment on the client. (Brech, et al., 2018; Kooistra, Ruwaard, Wiersma, Oppen & Riper, 2020) As both internet-based and face-to-face treatments have their benefits the next step would be to combine these to get the best out of both worlds and cover for weaknesses of each other.

A previous study had proposed that blended smoking cessation treatment (BSCT) was expected to improve the already existing smoking cessation treatments (Siemer, et al., 2016). A blended treatment is the combination of both internet-based and face-to-face treatments. In this manner, the weaknesses of face-to-face treatment such as therapist drift and participant no-show would be covered by internet-based interventions whereas face-to-face treatment would be able to cover for the lack of engagement which is present in internet-based interventions (Siemer, et al., 2016) this could also prove to be beneficial in smoking cessation for individuals with anxiety, but the question is whether a blended smoking cessation treatment is able to provide the same benefit treatment as usual is able to.

### **Aim of the study**

The aim of the study was to discover the predictability of anxiety on smoking cessation and whether smoking cessation is able to predict anxiety. This was studied through means of blended smoking cessation treatment and treatment as usual, taking the study by Siemer, et al. (2016) as a basis. The intervention consisted of both a blended and a face-to-face treatment. The research question of the study is whether *anxiety and smoking cessation have bidirectional causality*

*throughout the intervention.* The first research question was made because there is evidence of either side having an effect on one another, however the bidirectional, meaning simultaneous effect of anxiety and smoking cessation on each other has not been studied enough yet.

Along the research question of the study several hypotheses were made to get a better understanding of the treatment and findings. The first hypothesis 1. *Anxiety throughout the intervention is a predictor of smoking cessation* is stated in order to better understand the research question and is one part to answer the research question from the perspective of the interaction of anxiety with smoking cessation whereas the second hypothesis 2. *There are significant differences in anxiety between participants who were successful in smoking cessation compared to participants who were not* is stated as the second part to understanding the bidirectionality of the research question. It will be used to gain insights into how smoking cessation leads to lower anxiety levels. The third hypothesis 3. *Face-to-face treatment is more effective in successful smoking cessation among participants with anxiety at baseline level compared to blended smoking cessation treatment* is made so that the differences within the intervention can be taken into account and whether these had an effect on smoking cessation as well. The expectation here is that face-to-face performs better than the blended smoking cessation treatment. The final and fourth hypothesis 4. *Anxiety is a predictor of adherence, whereas adherence is a predictor of smoking cessation.* This hypothesis will be embedded within the first and second hypothesis due to its close relation to both of the hypotheses. Previous studies suggest that anxiety has an effect on whether the participant will be adherent to the study, whereas adherence also has an effect on whether the participant will realize the full effect of the treatment, which in this case is smoking cessation. Not finishing the treatment has an effect on successful smoking cessation as treatments are seen as the most effective way for smoking cessation.

## **Methods**

### **Study design**

This evaluation study was a single-centre randomized controlled non-inferiority trial with a parallel group design (Siemer, et al., 2016).

## **Participants**

The participants were recruited from the patients that had signed up for smoking cessation treatment at the outpatient smoking cessation clinic. The participants (n=344) were patients of an outpatient smoking cessation clinic at the Medisch Spectrum Twente in Enschede, the Netherlands. The participants were filtered with the use of inclusion criteria: in order to participate the participants had to be admitted to the cessation clinic, at least 18 years old, smoke daily, be proficient in Dutch and be able to access the websites and communicate via email. The possibility to access the websites and communicate by email were verified during the intake.

The participants were randomly assigned to either blended smoking cessation treatment or treatment as usual, which refers to a face-to-face treatment. Randomization was performed at an individual level using QMinim Online Minimization. The minimization was stratified according to 3 criteria: level of internet skills, level of nicotine dependence and quitting strategy favored by the patient (Siemer, et al., 2016)

## **Study intervention**

Described by Siemer, et al. (2016) the blended smoking cessation treatment consisted of a combination of 5 face-to-face smoking cessation counselling sessions and 5 internet-based sessions which participants could access through the website [www.rokendebaas.nl](http://www.rokendebaas.nl) which was developed by Tactus, which are specialized in addiction treatment. The treatment as usual was personalized to the participant's needs and contained flexibility in quitting strategies. As a means of comparability this flexibility was also provided and integrated in the blended smoking cessation treatment. The flexibility consisted of three quitting strategies which the participant was asked to favor one: stopping at once, gradual change and scheduled reduced smoking.

Both the blended smoking cessation treatment and treatment as usual consisted of ten sessions with comparable content spread over the 6 months of treatment with a gradual decrease in session frequency over time. The participants received 6 sessions within the first 3 months, followed up by 4 sessions within the final 3 months. The favored quitting strategy only affects the content of the treatment marginally and the quitting strategy does not affect the amount nor order of sessions in the treatment.

The sessions in treatment as usual all take place at the outpatient smoking cessation clinic whereas the blended smoking cessation treatment alternates between face-to-face and online.



Both treatments consisted of counselor-dependent and counselor-independent components and made sure that both content and intensity is equivalent to each other.

Both treatments provided behavioural change techniques used in smoking cessation as well as techniques which have proven to be associated with better cessation outcomes (Siemer, et al., 2016)

## **Measurements**

The follow-up measurements were conducted at standard time-points of 3 months after treatment start, 6 months after treatment start and end also the end of treatment, 9 months after treatment start, which is 3 months after treatment end and finally 15 months after treatment start which is 9 months after the end of treatment.

## **Materials**

### ***Depression, Anxiety and Stress Scale (DASS-21)***

The DASS-21 was used as a questionnaire for presence of depressive, anxiety or stress disorders among with the participants as these mental illness indications are common co-morbid disorders in substance use disorder patients. The self-report questionnaire consists of 4-point severity and frequency scales which they can use to report their state over the past week. The Dutch translation of the DASS-21 was used in order to conduct this questionnaire among a Dutch speaking participants. The DASS-21 is a reliable and valid questionnaire with good psychometric properties, the cut-off scores for anxiety can be seen in table 1. (Antony, Bieling, Cox, Enns & Swinson, 1998; Lovibond & Lovibond, 1995) The Cronbach's alpha scores of DASS-21 for subscales depression, anxiety and stress are 0.81, 0.89 and 0.78 respectively (Coker, Coker, & Sanni, 2018).

Table 1.

#### *DASS-21 anxiety cut-off scores*

Severity label	Anxiety cut-off scores
Normal	0-7
Mild	8-9

Moderate	10-14
Severe	15-19
Extremely severe	20+

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### **Smoking cessation**

The smoking cessation of participants are composed through means of self-reports of quit attempts that lasted longer than 24 hours, number of relapses or the amount of daily tobacco consumption. These variables were based on a standardized questionnaire for Dutch tobacco research. (Siemer, et al., 2016)

A self-reported measure for the completion of treatment was used, a variable was created called “flow\_2” and was provided after the 6 month period which indicated the end of treatment, which had 3 answer possibilities: 1 = yes, 2 = did not finish treatment but finished a number of steps and 3 = did not start treatment after registration. Afterwards this variable was recoded into a “finished” variable which had 2 answer possibilities: 1 = yes, 2 = no.

The data-set consisted of missing data from users who had quit the intervention half-way through. Imputation was not used to account for the missing data and instead only the data of the participants who had finished the treatment were used.

### **Analysis plan**

SPSS 26.0 was used to analyze the data in this study. For the research question and the hypotheses, the following test were conducted:

Initially an overview of descriptive and frequency analysis was made to get an overview of the data followed up by the statistical analyses. In order to get a better understanding of the bidirectionality of anxiety and smoking cessation 3 different analyses were conducted. A binary logistic regression was used in order to account for the high amount of degrees of freedom of the anxiety variables which would make it unfit for an ANOVA. The binary logistic regression was used in order to get a better understanding of the predictive capabilities of anxiety on adherence and smoking cessation along with a repeated measure ANOVA in order to answer hypothesis 1 and 4. As for the relation of smoking cessation on anxiety and adherence on cessation a one-way ANOVA was conducted in order to see whether there were within-subject and between-subject

effect along with a repeated measures ANOVA and multiple general linear model (GLM) repeated measures. However, not all assumptions were met to use the GLM repeated measures as the normal distribution assumption was the only violated assumption. Three specific models were made which tested the following specific time-points: the first model tested baseline anxiety and anxiety at 6 months with smoking cessation at 6 months. The second model tested baseline anxiety, anxiety at 6 months and anxiety at 9 months with smoking cessation at 9 months. The third and final model tested anxiety across all time-points with smoking cessation at 15 months. These analyses were used in order to answer hypothesis 2. As for hypothesis 3 moderation analyses were conducted through the usage of Hayes' process macro in SPSS. A moderation analysis was necessary in order to find out whether the treatment types have a different smoking cessation outcome and whether anxiety plays a moderating role in this. Anxiety could be affecting the specific treatment type leading to a different smoking cessation outcome within the two treatments in the RCT. The reason for using Hayes' process macro is due to it being a suitable choice for research when working with directly measured data for estimating direct and indirect effects in single and multiple mediator or moderator models along with its state-of-the-art approach while also producing bootstrap confidence intervals for parameters without having to use additional manners of analysis. Model 1 was used since this represents a moderation analysis. (Hayes, 2012)

## **Results**

### **General overview**

From the total amount of participants (n=344) 75 had finished the treatment of which 43 had their treatment face-to-face and 32 participated in the blended treatment. See table 2 for a general sociodemographic overview.

Table 2.

*Sociodemographic characteristics of participants*

Characteristics	Blended smoking cessation treatment		Face-to-face treatment		Full sample	
	n	%	n	%	n	%
<b>Gender</b>						
Male	25	56.8%	47	66.2%	163	49.8%
Female	19	43.2%	24	33.8%	164	50.2%
<b>Marital status</b>						
Single	19	43.2%	20	28.2%	120	36.8%
Married/partnered	25	56.8%	51	71.8%	206	63.2%
<b>Education</b>						
Higher education <sup>a</sup>	30	68.2%	47	68.1%	191	59.1%
Lower education <sup>b</sup>	12	27.3%	20	30.0%	118	36.5%
Other	2	4.5%	2	2.9%	14	4.3%

*Note.*  $N = 344$  for the entire data-set of participants. Participants were on average 46.9 years old ( $SD = 12.9$ ). Per treatment type the average age was 47.5 ( $SD = 12.5$ ) for blended smoking cessation treatment and 50.8 ( $SD = 12.6$ ) for face-to-face treatment.

<sup>a</sup> Higher education = mbo, hbo or wo. <sup>b</sup> Lower education = lbo, mavo, vmbo or havo/vwo

**Anxiety as a predictor of smoking cessation**

The first hypothesis was tested by means of a binary logistic regression analysis and a repeated measures ANOVA. The results of the binary logistic regression analysis (see Table 3) show that anxiety at 6 months was predictive of smoking at 9 months ( $p=.045$ ) and the estimated odds ratio favored an increase in smoking. Anxiety at 6 months was not predictive of smoking at 15 months. However, when taking a closer look at the significance and effects of anxiety on smoking cessation at later time-points it would seem that reason for smoking cessation at 15 months ( $p=.070$  and  $p=.095$ ) to not be statistically significant could confirm predictive effect on

smoking cessation at 9 months. This could mean that the desired effect was already reached at 9 months and that at 15 months there was no additional benefit recorded.

Table 3.

*Binary logistic regression analysis of anxiety on smoking cessation across time-points*

Effect	Estimate	SE	OR	95% CI		p
				LL	LL	
Anxiety T0 <sup>a</sup>						
Smoking cessation T1 <sup>b</sup>	.054	.034	1.056	.989	1.128	.105
Smoking cessation T2 <sup>c</sup>	.017	.038	1.017	.945	1.095	.648
Smoking cessation T3 <sup>d</sup>	.028	.051	1.028	.931	1.135	.582
Anxiety T1						
Smoking cessation T1	.120	.045	1.127	1.032	1.232	.008*
Smoking cessation T2	.114	.057	1.121	1.002	1.253	.045*
Smoking cessation T3	.134	.074	1.143	.989	1.322	.070
Anxiety T2						
Smoking cessation T2	.252	.091	1.287	1.077	1.537	.005*
Smoking cessation T3	.136	.082	1.146	.976	1.346	.095

### Anxiety T3

Smoking cessation T3	.308	.097	1.361	1.126	1.645	.001*
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<sup>a</sup>T0 = baseline. <sup>b</sup>T1 = at 6 months. <sup>c</sup>T2 = at 9 months. <sup>d</sup>T3 = at 15 months. \*  $p \leq .005$

The follow-up and results of the repeated measures ANOVA show different results across time-points and were conducted to account whether an increase of anxiety can lead to relapse on future smoking cessation time-points. As the effect of anxiety on smoking cessation is of importance different sets of analysis was used to underline the effect. To account for multiple points in time anxiety was taken as a predictor at a single point in time and the change in anxiety between two time-points and its effect on smoking cessation at a later time-point. Through these analyses it will become clear which changes have an effect.

#### *Difference between baseline anxiety and anxiety at 6 months on smoking cessation at 9 months*

The results of within-subject effects tests reveal that the interaction of time and smoking cessation at 9 months was significant  $F(1, 79)=6.569, p=.012, \eta_p^2=.077$ . This result suggests that an increase in anxiety between baseline and at 6 months predicts higher likelihood of relapse at 9 months. The between-subject effect test does not reveal a main effect  $F(1, 40)=1.837, p=.179, \eta_p^2=.023$ .

#### *Difference between anxiety at 6 months and anxiety at 9 months on smoking cessation at 15 months*

The results of within-subject effects tests reveal that the interaction of time and smoking cessation at 15 months was non-significant  $F(1, 40)=.838, p=.365, \eta_p^2=.021$ . The between-subject effect test does not reveal a main effect  $F(1,40)=2.631, p=.113, \eta_p^2=.062$  either.

Additionally, another analysis was conducted on whether anxiety is predictive of adherence. The binary logistic regression which was conducted shows that baseline anxiety seems to be predictive of finishing the treatment  $b=-.073, SE=.027, p=.006$ . The estimated odds ratio favors non-adherence  $OR=.929, 95\% CI [.882-.979]$ . This suggests that participants with high baseline anxiety predict a lower likelihood of adherence compared to participants with low baseline

anxiety. Anxiety at 6 months does not seem predictive of finishing the treatment ( $b=-.057$ ,  $SE=.037$ ,  $p=.116$ ,  $OR=.944$ , 95% CI [.879-1.014])

### **Successful smoking cessation effects on anxiety**

The second hypothesis was tested by means of one-way and repeated measures ANOVA analyses, each difference between time-points were analyzed through these tests. Additionally, adherence was also analyzed as to whether it had an effect on the differences on smoking cessation over time-points.

#### *Difference in anxiety at 6, 9 and 15 months following smoking cessation at 6 months.*

There were no significant differences between groups for anxiety at 9 months  $F(1,54)=.769$ ,  $p=.385$  and anxiety at 15 months  $F(1,60)=3.277$ ,  $p=.075$ .

#### *Differences in anxiety at 9 and 15 months following smoking cessation at 9 months.*

There was a significant effect of smoking cessation at 9 months on anxiety at 15 months  $F(1,60)=4.128$ ,  $p=.047$ , which means that the differences in anxiety scores were statistically significant in anxiety at 15 months following smoking cessation at 9 months.

In order to see whether smoking cessation leads to a decrease in anxiety another set of repeated measures ANOVA were conducted and an additional analysis was conducted to correct for anxiety at 9 months on the effect of smoking cessation at 15 months.

#### *Difference between anxiety at 6 months and anxiety at 15 months through means of smoking cessation at 6 months*

The results of within-subject effects tests reveal that the interaction of time and smoking cessation at 6 months was non-significant  $F(1, 54)=1.833$ ,  $p=.181$ . This result suggests that the differences between anxiety at 6 months and anxiety at 15 months were not caused as a result of smoking cessation at 6 months. The between-subject effect test reveals that smoking cessation at 6 months does have a main effect  $F(1, 54)=5.042$ ,  $p=.029$ .

#### *Difference between anxiety at 9 months and anxiety at 15 months through means of smoking cessation at 9 months*

The results of within-subject effects tests reveal that the interaction of time and smoking cessation at 6 months was non-significant  $F(1, 45)=1.211, p=.277$ . This result suggests that the differences between anxiety at 9 months and anxiety at 15 months were not caused as a result of smoking cessation at 9 months. The between-subject effect test reveals that smoking cessation at 6 months does have a main effect  $F(1, 45)=4.712, p=.035$ .

### **Cross-sectional analysis of the effects of anxiety and smoking cessation on each other**

To explore the effects at the present time of these variables cross-sectional analyses were ran for both sides of the variables anxiety and smoking cessation as an addition to the predictor analysis across multiple time-points

#### *Anxiety on smoking cessation*

There were significant effects of anxiety at 6, 9 and 15 months on their respective smoking at 6, 9 and 15 months ( $p=.008, p=.005, p=.001$  respectively) and each of the estimated odds ratio favored an increase in smoking.

#### *Successful smoking cessation on anxiety*

Whereas for smoking cessation there were significant effects of smoking cessation at 6, 9 and 15 months on their respective anxiety at 6, 9 and 15 months ( $p=.003, p=.002, p=.000$  respectively)

These results were followed up by GLM repeated measures analyses. The GLM repeated measures was conducted in order to get a better view of the changes of anxiety over time comparing the groups that have quit smoking and are still smoking (see figure 1). The analyses were conducted on 3 separate moments, namely at 6 months, 9 months and 15 months and each subsequent model is a separate model in itself. None of the time-points violated Mauchly's test of Sphericity nor violated Levene's variance test of homogeneity.



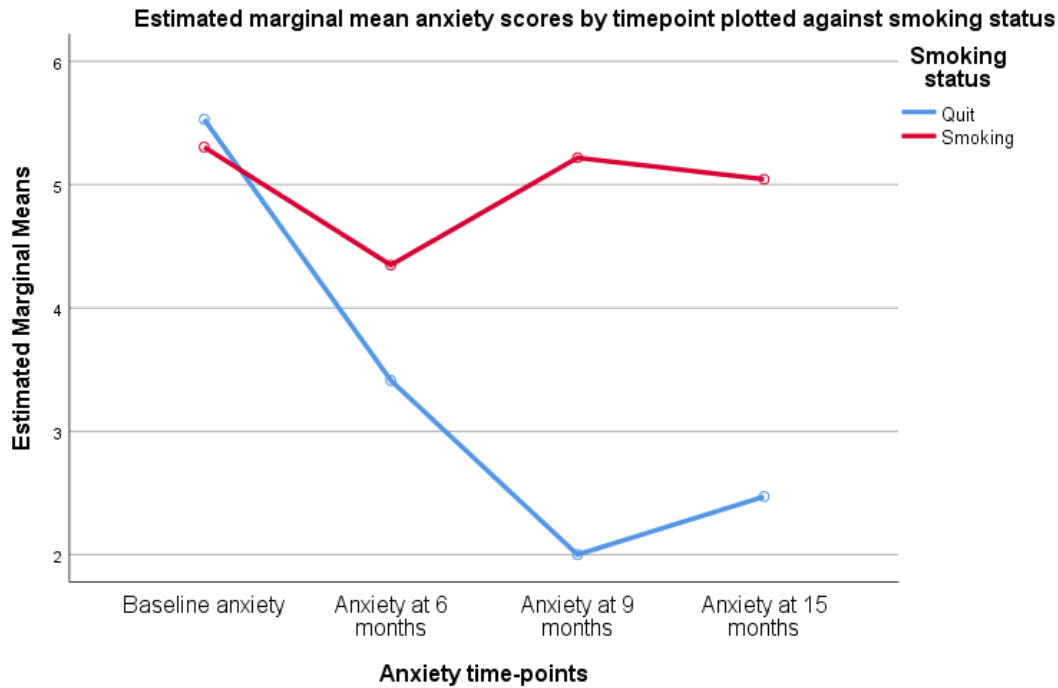


Figure 1. *Estimated mean anxiety score per time-point plotted against smoking cessation of the final model (N = 40)*

#### *At 6 months*

The results of within-subject effects tests reveal that there was a significant main effect of time  $F(1, 112)= 7.868, p=.006, \eta_p^2 = .067$ , this means that there was a decrease in anxiety for the whole sample from baseline anxiety to anxiety at 6 months and that the effect size is large. In contrast there the interaction of time with smoking cessation at 6 months was found to be non-significant  $F(1, 112)=1.431, p=.234$ .

#### *At 9 months*

Similar to the 6 month results, the results of within-subject effects tests reveal that at the 9 months follow-up there was as significant main effect of time  $F(2, 54)= 4.078, p=.020, \eta_p^2 = .073$ , which means that there was a decrease in anxiety for the whole sample from anxiety at 6 months to anxiety at 9 months and that the effect size is large. The interaction of time with smoking cessation at 9 months was found to be significant too  $F(2, 54)=3.810, p=.025$ .

#### *At 15 months*

Finally, at 15 months the results of within-subject effect tests reveal that there was a statistically significant main effect of time  $F(3, 40)= 3.519, p=.017, \eta_p^2 = .085$ , which also means that there was a decrease in anxiety for the whole sample from anxiety at 9 months to anxiety at 15 months and that the effect size is large. The interaction of time with smoking cessation at 15 months was found to be significant too  $F(3, 40)= 3.036, p=.032$ .

As for adherence, interestingly, there was a statistically significant effect of adherence on smoking cessation at 6 months  $F(1,125)=52.584, p=.000$ , at 9 months  $F(1,101)=9.307, p=.003$  and at 15 months  $F(1,71)=5.183, p=.026$ . These results suggest that adherence to the treatment has a statistically significant effect on difference in smoking cessation.

### **Anxiety as a moderator on treatment outcome**

The RCT had 2 treatment consisting of face-to-face treatment as well as a blended treatment as depicted in figure 2. In order to discover whether face-to-face had less effect in smoking cessation at 15 months among participants with anxiety a moderation analysis was conducted using Hayes' model 1.

The interaction term of baseline anxiety was not statistically significant ( $b=0.0024, SE=0.724, p=.9738, 95\% CI [-.1395-.1443]$ ) as a moderator on the treatment on smoking cessation.

In order to discover whether the two different treatment methods developed a different impact on anxiety two additional moderation tests were conducted using Hayes' model 1.

Face-to-face treatment was not a statistically significant predictor ( $b=.0160, SE=.0687, p=.8163, 95\% CI [-.1187-.1506]$ ), nor was blended treatment ( $b=.0134, SE=.0711, p=.8503, 95\% CI [-.1260-.1528]$ ).

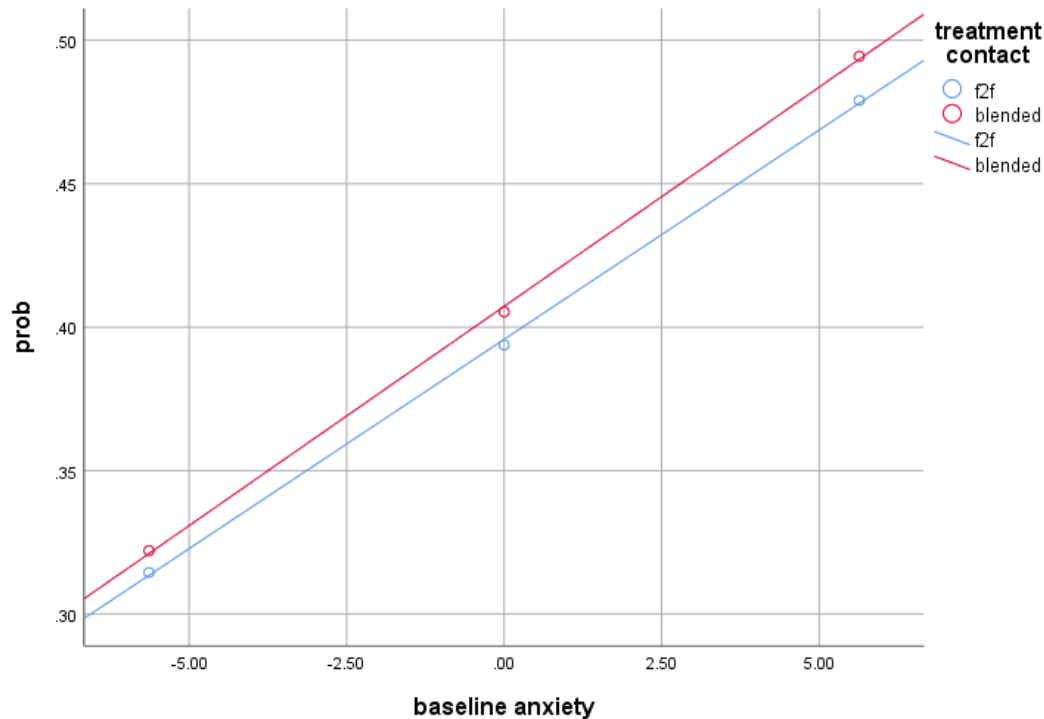


Figure 2. *Baseline anxiety probability plotted against treatment contact forms f2f (blue) and blended (red)*

## Discussion

### General discussion

The aim of this study was to take a better look into the bidirectional causality between anxiety and smoking cessation through means of blended smoking cessation treatment and treatment as usual. The research by Siemer, et al. (2016) was taken as a basis for this study. Interestingly, what was found regarding anxiety was that it co-varies with smoking. However, smoking cessation also lead to lower levels of anxiety for participants who were successful compared to participants who were still smoking. Additionally, baseline anxiety was found to be predictive of treatment adherence which is also in line with previous research (Zvolensky, et al., 2007). Subsequently, adherence was also predictive of smoking cessation; this means that finishing treatment has had an effect on successful smoking cessation. The results of the different

treatment types did not seem to differ from each other on a significant level nor was there any result indicating that anxiety worked as a moderator on the treatment types. Thus, there is a clear evidence that there is a bidirectional causality between anxiety and smoking cessation as there is an interaction with anxiety leading to (more) smoking whereas smoking cessation leads to lower anxiety, however the effect of smoking cessation on anxiety does seem to be stronger in this relationship. All in all, with multiple significant effects and predictions between anxiety and smoking cessation it can be said that there is a potential bidirectional relationship between these variables. This is in line with

### **Anxiety as a predictor of smoking cessation**

Anxiety at 6, 9 and 15 months was associated with smoking in each other of their corresponding smoking cessation time-points. Meaning that the anxiety levels at these time-points were able to indicate whether the participant was more inclined to smoke or whether they were more inclined to stop. This was in line with previous studies which had indeed found that individuals can start smoking as a way to cope with anxiety (McDermott, et al., 2013) and that anxiety lead to worse smoking cessation outcomes and higher anxiety sensitivity which could also lead to difficulty quitting (Lewis, et al., 2020; Zvolensky, et al., 2007). Interestingly baseline anxiety was not associated with any of the smoking cessation time-points while the participants had scored the highest on anxiety at baseline. This can mean that an effect which was expected to be seen here was not present due to drop-outs, as individuals with anxiety struggle more with adherence (Zvolensky, et al., 2007). Interestingly, high baseline anxiety was also associated with low adherence which ties the findings of Zvolensky, et al. (2007). The follow-up repeated measures analysis resulted in a difference between baseline anxiety and anxiety at 6 months which lead to a change on a follow-up time-point on smoking cessation at 9 months. This suggests that an increase between these two time-points can also indicate a possibility that a relapse may occur at the following time-point, or between 6 and 9 months. Another interesting point is that smoking participants realize an increase in anxiety at 9 months and a decrease in anxiety at 15 months whereas participants who had quit realize a decrease in anxiety at 9 months but an increase at 15 months. The exact reason for this cannot be said with certainty as we do not know for sure whether the participants had relapsed at 15 months or whether another factor was in play. This also causes uncertainty in the relationship between anxiety and smoking cessation as a result.

While the hypothesis can be accepted as there is evidence that anxiety can be associated with smoking, the effect is not large enough and there are some remaining uncertainties.

### **Successful smoking cessation effects on anxiety**

Just like baseline anxiety, smoking status at 6, 9 and 15 months seems to have an effect on the anxiety levels at the corresponding time-points while additionally smoking status at 9 months seems to have an effect on anxiety at 15 months as well. The follow-up repeated measures analysis also reveals that smoking cessation seems to cause significant differences in anxiety levels. Most importantly, there seem to be decreases in anxiety over the course of the treatment from baseline until at 15 months which seems to be in line with previous studies (Taylor, et al., 2014; West & Hajek, 2006). However, the minor increase in anxiety in the non-smoker group at 15 months, seems to not be in line with previous research as they had stated that abstinence did not lead to an increase in anxiety (Bolam, West & Gunnell, 2011; Shabab, Andrew & West, 2013). There is no clear explanation for this increase in anxiety, it could be speculated that the participants had relapsed, or had other life circumstances which had led to reporting higher anxiety levels. However, this was not something that was researchable in this study, therefore leading to careful interpretation of the results as not everything could be accounted for. Across the study there was however a clear reduction in anxiety levels at 6 months and 9 months which account for the effect of the treatment being effective. The increase in anxiety at 15 months does raise questions about the cause of this increase and should be kept in mind in future research as a point of interest in order to delve into the cause of this increase. With the current results the hypothesis cannot be rejected, however the increase at 15 months should be kept in mind for future research.

Finishing the treatment proved to have an effect on smoking status at 6, 9 and 15 months meaning that finishing the treatment or not plays a role in successful smoking cessation. Given that the treatment had made use of previously found effective methods in treating smoking cessation these results do provide support that the selection of treatment methods was adequate in providing successful smoking cessation treatment. All in all, this hypothesis can be accepted as there is clear evidence that smoking cessation does lead to lower anxiety levels.

### **Anxiety as a moderator on treatment outcome**

As the study consisted of two types of treatment, namely blended treatment and face-to-face treatment it was important to know whether blended treatment could on par or better than face-to-face treatment due to the proposed benefits of blended smoking cessation treatment in Siemer et al. (2016) and whether anxiety played a moderating role in the treatment outcomes. In order to research this baseline anxiety was taken as the moderator as it is not affected by other variables before the start of the treatment. No difference in treatment types was observed when baseline anxiety was taken as the moderating variable and both treatments performed comparatively to another, thus indicating anxiety did not have moderating effect on either treatment type. This does not seem to be in line with similar studies as a study by Powers, Larowe, Garey, Zvolensky & Ditre (2020) seem to have found moderator effect on pain-related anxiety whereas Reuven, et al. (2021) had similar success recognizing anxiety sensitivity as a moderator and in both cases lead to possibilities of increased smoking cessation. However, given the scope of both of these studies being larger on focusing largely on one type of treatment the possibilities of other variables which were not taken into account in this study that may have played a role in the results cannot be ruled out and thus would also be a suggestion for future studies to have a broader scope of variables in order to rule out variables and their moderating effects. Since the results were not statistically significant the hypothesis can be rejected.

### **Limitations, strengths and recommendations**

A strength of this study is that there is currently no standard to compare the results of the study with yet as blended smoking cessation treatment is a relatively new and upcoming research topic within the widely researched topic of smoking cessation treatments. Therefore, the outcomes of this study could serve as one of the first results to be used as comparison to future studies in the same field.

The first limitation might be that negative affect as a whole might have played a bigger role in smoking cessation whereas anxiety might have just been a part of a bigger factor at play. As anxiety is not the only negative influence on abstinence after successful cessation. (McLaughlin, Dani & Biasi, 2015). This could make the multitude of negative factors stemming from cessation symptoms play a bigger role than just anxiety and also play a role in causing relapse. (Baker, Piper, McCarthy, Majeskie & Fiore, 2004). Additionally, the function of

smoking might play a role in successful cessation too. If smoking is used as a coping mechanism against negative affect, or in this case anxiety, it may be more difficult to successfully abstain (McDermott, Marteau, Hollands, Hankins & Aveyard, 2013). Therefore, accounting for negative affect as a whole in addition to anxiety might prove to play a role in the discovery of underlying factors which may affect smoking cessation.

A second limitation is that, anxiety in this study was taken at a full scale instead of looking at the effects per severity. As previously mentioned, participants with a higher baseline anxiety might have benefitted more from the treatment than participants with a lower baseline anxiety. However, monitoring this per severity and the changes overtime could reveal a difference in non-clinical and clinical anxiety levels and their effect on smoking cessation and additionally it could also which variables are really affected by anxiety as right now normal to moderate severities of anxiety could be dictating the majority of the effects, but severe to extremely severe could just as well be the cause.

A third limitation is the decision to not work with imputation. The decision was made to only make use of data of participants that have finished the study. This can however lead to biased analysis as a treatment effect is provided which would occur under optimal conditions. Whereas, with an intention-to-treat analysis the last value would be carried forward. This was done with the intention to reduce potential bias in treatment effects which could occur due to missing data. (Re, Maisel, Blodgett & Finney, 2013; Shah, 2011). As a lot of participants had dropped out in this study, the question was whether the majority of these drop-outs were participants with high severity of anxiety or low severity of anxiety. A high severity of anxiety means that their adherence rate would be lower as well as anxiety has an effect on treatment adherence. It also has implications on the results. If the drop-outs had high severity of anxiety it could mean that that we are not seeing the results you would normally see, or inversely, we are seeing results you should normally not see. This could have influenced the results of anxiety across all time-points comparatively to smoking status as a sample with a lot lower severity could be more successful in smoking cessation whereas if the drop-outs were of high severity it could skew the data and result in less favorable outcomes for the RCT. Therefore, imputation techniques as well as an intention-to-treat approach might lead to different results.

A fourth limitation is that this study is a sub-set of a previously made study by Siemer, et al. (2016) and was based on their RCT with blended smoking cessation and treatment as usual.

This intervention did not focus on anxiety specifically. Anxiety was a secondary addition in the vast amount of variables which were included in the intervention. This meant that the previously mentioned resources which should be provided to individuals with anxiety who are about to partake in a smoking cessation treatment were not provided. This may lead to different results compared to a study which has taken anxiety as one of its primary targets to treat together with tobacco use and would therefore be a recommendation for future studies to keep in mind and make use of these resources as they may lead to an increase in successful smoking cessation.

A final limitation is that not all assumptions for the GLM repeated measures was met as the dependent variables were not normally distributed. This may have caused certain results to not be valid as the analysis assumed a normally distributed dependent variable. A recommendation for future studies would be to make use of non-parametric tests for data comparison.

## **Conclusion**

The results were able to answer the research question along with most of the hypotheses, falling short on the third hypothesis regarding anxiety as a moderator on the two different treatment types within the RCT of the study. The aim of the study was successfully researched however. Evidence for a bidirectional causality between anxiety and smoking cessation was discovered with a bigger effect of smoking cessation on anxiety. Additionally, high baseline anxiety predicted low adherence whereas adherence predicted successful smoking cessation. This also adds to the bidirectionality of anxiety and smoking cessation as they both influence and are influenced by adherence too. Anxiety was associated with smoking and an increase in anxiety between baseline and 6-month time-points were able to predict a relapse in smoking cessation at 9 months. Smoking cessation lead to a statistically significant decrease in anxiety over the duration of the intervention however some concerns were raised as non-smokers reported an increase in anxiety at 15 months. Because we do not know what the reason for this could be it does create some uncertainty in the predictabilities of anxiety on smoking cessation. All in all, a bidirectional causality between anxiety and smoking cessation was discovered with a stronger effect of smoking cessation on anxiety.



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