



## Nicotine dependence and urge to smoke predict negative health symptoms in smokers

Ivan Berlin<sup>a,\*</sup>, Edward G. Singleton<sup>b</sup>

<sup>a</sup> Groupe Hospitalier Universitaire Pitié-Salpêtrière–Faculté de médecine, Université Pierre and Marie Curie Paris 6 – INSERM U 677, Paris, France

<sup>b</sup> The MayaTech Corporation, Silver Spring, MD, USA

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### ABSTRACT

**Objective.** To assess the predictive value of nicotine dependence or urge to smoke for negative health symptoms one year later.

**Methods.** Subjects were smokers ( $N=1519$ ) from the US, Canada, UK, France and Spain participating in the internet based ATTEMPT study between 2004 and 2006, a multi-national prospective cohort study. Nicotine dependence was assessed by the Fagerström Test for Nicotine Dependence (FTND) and urge to smoke by the 10-item version of the Questionnaire of Smoking Urges (QSU-10). Specific questions were used to assess presence of chest pain specified as angina pectoris, shortness of breath, depressive mood, feeling of anxiety and visit at a primary care physician, an index of global health and health care, one year after assessment of FTND and QSU-10.

**Results.** Smokers who reported angina pectoris, shortness of breath, low mood, anxiety or visit at a primary care physician 9 to 12 months after assessment have significantly higher FTND and QSU-10 scores than those who did not report these negative health symptoms or who did not visit a primary care physician.

**Conclusion.** Smokers with high level of nicotine dependence or urge to smoke are at higher risk of negative health symptoms than those who have low levels of nicotine dependence or urge to smoke.

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### Introduction

The global mortality attributable to smoking in 2000 has been estimated to be 4.83 million premature deaths; 2.41 million in developing countries and 2.43 million in industrialized countries (Ezzati and Lopez 2003) and the leading causes of death from smoking are cardiovascular diseases (1.69 million deaths), chronic obstructive pulmonary disease (0.97 million deaths) and lung cancer (0.85 million deaths) (Ezzati and Lopez 2003). Cessation at age 60, 50, 40, or 30 years leads to a gain of about 3, 6, 9 or 10 years of life expectancy among male British doctors followed up to 50 years (Doll et al., 2004).

Smoking is associated with highly increased risk of CHD. The INTERHEART study, realized in 52 countries, showed that current smoking was associated with a greater risk of non-fatal myocardial infarctions compared to never-smoking (OR: 2.95, 95% IC: 2.77–3.14) (Teo et al., 2006).

Smokers are not ignorant of the negative health effect of smoking. Continuing smoking may be motivated by several factors, among them are nicotine dependence and urge to smoke. Because smokers continue to smoke despite the awareness of its negative health effects, the question arises whether there is a relationship between these two core features of continuing smoking and specific health

outcomes. A positive answer to this question may signify that nicotine dependence or urge to smoke may have a causal but probably indirect relationship with smoking related negative health outcomes. We chose symptoms that may reflect the 3 main aspects of smoking related disorders: i) coronary heart disease: feeling of angina pectoris; ii) respiratory disorders: shortness of breath and iii) the most frequently evoked smoking related psychiatric disorders: depressive mood and anxiety. Visit at GP was used to provide an indication about the use of professional health care. To assess the relationship between nicotine dependence, urge to smoke, and selected health outcomes we analysed the ATTEMPT data set.

The ATTEMPT cohort is a multi-national, observational, internet-recruitment study. It is aimed to follow up the natural history of smoking and smoking cessation and assess smoking related health outcomes and medical resource utilisation. A previous paper (West et al., 2006) provided detailed description of the aims, collection methods, included measures and retention rate up to 12 months. We tested the following hypothesis: because it is widely accepted that the amount of cigarette consumption is insufficiently associated with health outcomes, we hypothesized that nicotine dependence or urge to smoke, core features of inability to quit, may predict smoking related negative health symptoms and visits at a health care professional. Thus, the objective of this study was to assess the predictive value of the largely used measure of nicotine dependence, the Fagerström Test for Nicotine Dependence (FTND) (Heatherton et al., 1991) and that of a measure of smoking urge, the Questionnaire of

\* Corresponding author. Groupe Hospitalier Universitaire Pitié-Salpêtrière, Service de Pharmacologie, 47, Boulevard de l'Hôpital, 75013 Paris, France. Fax: +33 1 42 16 16 88.  
E-mail address: [ivan.berlin@psl.aphp.fr](mailto:ivan.berlin@psl.aphp.fr) (I. Berlin).

Smoking Urges 10-item version (QSU-10) (Cox et al., 2001) on selected health outcomes among panellists who completed the baseline, the 3 months and the 15 months evaluations.

## Methods

To be eligible, panellists had to smoke at least 5 cigarettes per day, had to declare intent to quit during the next 3 months, had to be between 35 and 65 years old, not to anticipate to stop by an internet service within the next 30 days, and have no other household members participating in the ATTEMPT cohort. Eligible subjects were asked first to provide their consent online to participate. The ATTEMPT cohort provides assessments at every 3 months after baseline.

The FTND was completed at baseline, the QSU-10 at 3, 9 and 15 months after baseline. The FTND is widely used to assess nicotine dependence. It is the extensively studied revised version of the Fagerström Tolerance Questionnaire. It consists of 6 items and the total score varies from 0 to 10 (Heatherton et al., 1991). Higher score describes higher dependence. The FTND is an excellent predictor, according to a large number of studies, of the ability to quit.

The following health outcome measures were analyzed: chest pain specified as angina pectoris, shortness of breath, depression, anxiety and visit at primary care physician during the 3 months prior to the baseline and at 15 months. This schedule allowed analyses of the occurrence of symptoms during a period of one year after the initial QSU-10 assessment and 15 months after the assessment of FTND.

Answers to the following questions were analyzed:

“Did you experience angina also called angina pectoris in the past 3 months?”

“Did you experience shortness of breath in the past 3 months?”

“Did you experience depression in the past 3 months?”

“Did you experience anxiety in the past 3 months?”

“Did you visit a general practitioner, family physician or a primary care physician in the past 3 months for a health problem?”

Angina pectoris is a well known symptom even among those who have not yet experienced it. Its specificity is high for coronary heart disease. In men reporting angina specificity is 90% but sensitivity only 29% for coronary heart disease (Bulpitt et al., 1990). Men reporting angina are at increased risk of a major ischemic heart disease event (Lampe et al., 1998).

Smoking is strongly associated with respiratory symptoms and smoking cessation leads to remitting of these symptoms (Eagan et al., 2004). The symptom “shortness of breath” was chosen because its level of understanding by lay people may be high, reporting error may be low and it generalizes wheezing, dyspnoea, and attacks of dyspnoea of whatever origin.

There is a multifaceted but not fully understood relationship between depression and smoking (West and Jarvis 2005, Hughes 2007). Smokers with previous history of major depression (Covey, 1999) or depressive mood (Berlin and Covey 2006) are less likely to quit and there may be an association between depressed mood after cessation and relapse (Glassman et al., 2001). Depressive mood is also considered a withdrawal symptom (APA, 1994) and abstinence may increase mood disturbance compared to the precessation level (Hughes, 2006). The incidence of postcessation major depressive disorder (MDD) ranges from 0 to 14% and is higher in smokers with previous history of MDD but definitive conclusions cannot be made (Hughes, 2007).

Smokers may report that smoking decreases symptoms of anxiety but this may reflect relief from withdrawal symptoms such as anxiety, irritability, restlessness or insomnia (West and Jarvis, 2005).

Visit at a primary care physician was chosen because it may reflect an overall health problem independent or not from the 4 previous symptoms and may be a proxy measure of health care utilisation.

The 10-item Brief Questionnaire of Smoking Urges (QSU-Brief (Cox et al., 2001)) is derived from the multi-dimensional Questionnaire of Smoking Urges (Tiffany and Drobes, 1991). Factor analysis of the QSU-Brief has yielded two factors or manifestations of urges to smoke cigarettes: Factor 1 reflects a strong desire and intention to smoke, with smoking perceived as rewarding for active smokers, while Factor 2 represents an anticipation of relief from negative affect with an urgent desire to smoke (Cox et al., 2001). The QSU-Brief has been validated in treatment seekers (Toll et al., 2006), in a laboratory setting and in an outpatient smoking cessation clinic in both urge and no urge conditions (Cox et al., 2001), and in clinical trials (Cappelleri et al., 2007). Participants responded to each statement using a 1–7 scale ranging from strongly disagree to strongly agree. The total score ranges from 10 to 70 and the subscores for each factor range from 5 to 35. In this paper the denomination QSU-10 is used for QSU-Brief to avoid confusion with the five-item QSU-Brief proposed by Toll et al. (Toll et al., 2006).

## Data analysis

One-way analysis of variance (ANOVA) was used to compare groups. In case of multiple comparisons, the alpha level of each individual test was adjusted downwards (Bonferroni method) to ensure that the overall (experiment wise) risk for a number of tests remained  $P \leq 0.05$ . Univariate ANOVAs (adjusted for cumulative smoking free days over the previous 3 months, baseline reported presence of the disorder, and all covariates having a significant effect on FTND or QSU-10) were used to compare health outcomes. Correlations were tested using Pearson's  $r$ . A  $P$  value of  $\leq 0.05$  was considered as significant.

## Results

The demographic characteristics of the 1519 panellists whose baseline, 3 and 15 months' data were available are shown in Table 1.

Bonferroni corrected  $P$ -values in Table 2 show that females had significantly higher QSU-10 scores than males while there was no difference in the FTND score. French panellists had significantly lower FTND than USA, UK or Spanish panellists and QSU-10 total score than USA or UK panellists. White respondents had significantly higher FTND score than those of other ethnicities but not Black. The QSU-10 was significantly lower in Black than in White respondents. Marital status significantly influenced FTND ( $P=0.03$ ), divorced smokers had higher FTND than any other categories. Neither age nor educational level affected either the QSU-10 or FTND.

Table 3 shows the mean adjusted FTND and QSU-10 scores in smokers who reported angina pectoris, shortness of breath, depression, anxiety or a visit at a primary care physician during the previous 3 months of the 15 months assessment (i.e., one year later). The mean adjusted FTND scores were significantly and considerably higher in those smokers who reported angina pectoris, shortness of breath, depression, anxiety or a visit at a primary care physician. Similarly, total QSU-10 scores were significantly higher in smokers having reported shortness of breath, depression, anxiety or visit at a primary care physician. Difference in QSU-10 total scores for angina pectoris did not quite reach statistical significance. QSU-10 Factor 1 scores, reflecting a strong desire and intention to smoke with smoking perceived as rewarding, were also significantly higher in smokers reporting the 4 symptoms or having had a visit at a primary care physician. QSU-10 Factor 2 scores (anticipation of relief from negative affect with an urgent desire to smoke) were also significantly higher except for the comparisons for angina pectoris. Pearson's coefficients showed that there was a significant correlation between FTND and QSU-10

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