



# Measurement of multiple nicotine dependence domains among cigarette, non-cigarette and poly-tobacco users: Insights from item response theory

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## ABSTRACT

**Background:** Nicotine dependence (ND) is a key construct that organizes physiological and behavioral symptoms associated with persistent nicotine intake. Measurement of ND has focused primarily on cigarette smokers. Thus, validation of brief instruments that apply to a broad spectrum of tobacco product users is needed.

**Methods:** We examined multiple domains of ND in a longitudinal national study of the United States population, the United States National Epidemiological Survey of Alcohol and Related Conditions (NESARC). We used methods based in item response theory to identify and validate increasingly brief measures of ND that included symptoms to assess ND similarly among cigarette, cigar, smokeless, and poly tobacco users.

**Results:** Confirmatory factor analytic models supported a single, primary dimension underlying symptoms of ND across tobacco use groups. Differential Item Functioning (DIF) analysis generated little support for systematic differences in response to symptoms of ND across tobacco use groups. We established significant concurrent and predictive validity of brief 3- and 5-symptom indices for measuring ND.

**Conclusions:** Measuring ND across tobacco use groups with a common set of symptoms facilitates evaluation of tobacco use in an evolving marketplace of tobacco and nicotine products.

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## 1. Introduction

Nicotine dependence (ND) has been described as a combination of neurobiological symptoms and learned behaviors associated with repeated self-administration of nicotine (Collins and Marks, 1991; Edwards and Gross, 1976). For the past half century, knowledge about tobacco use and ND has come primarily from research conducted among cigarette users (United States Department of Health and Human Services (USDHHS), 2014). However, in recent years, tobacco products have diversified into new and

different forms, and poly-use of these products is becoming increasingly common (USDHHS, 2014). Tobacco products differ in nicotine content, route of administration, constituent ingredients and constituents, and behavioral patterns of persistent use and thus cigarette-focused instruments may not effectively reflect ND among non-cigarette product users (De Leon et al., 2014; Henningfield and Fant, 2000; National Cancer Institute, 2009). The extent that the occurrence and severity of symptoms of ND (e.g., tolerance, withdrawal) are similar or different across tobacco products (e.g., cigarettes versus non-combustible tobacco products) is currently unknown; therefore, there is an urgent need to examine the utility and validity of ND measures across users defined by different tobacco products.

In clinical practice and many research purposes, the diagnosis and treatment of ND relies on definitions in both the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American

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Psychiatric Association, 1994) and the International Classification of Diseases (Organization, 2008). Both classification systems use the 7 primary domains identified by Edwards and Gross (1976) and Collins and Marks (1991): (1) physiological tolerance, (2) evidence of characteristic withdrawal symptoms, (3) impaired control over tobacco use, (4) unsuccessful attempts to quit, (5) spending a great deal of time using tobacco, (6) prioritizing tobacco use over other activities, and (7) using tobacco despite physical or psychological health consequences. The DSM-IV and ICD-10 do not represent an exhaustive representation of domains of ND and efforts to expand definitions under the DSM-V (American Psychiatric Association, 2013) to include social consequences and craving or refine aspects of ND in self-report instruments continue to evolve (Piper et al., 2008). The NESARC developed 22 symptoms that fit into the seven DSM-IV domains and proposed additional symptoms that may also inform the ND construct. NESARC measured use of multiple tobacco-use products, making it well suited to investigate this set of ND domains across products.

The overarching aim of this project was to establish a parsimonious set of symptoms that efficiently and effectively measures ND across users of different tobacco products. We set out to identify a reduced set of questions that would make it easier for researchers and clinicians to assess ND for users of different types of tobacco products and poly-users. One such study that could benefit from identification of ND questions that are valid across different tobacco products is the Population Assessment of Tobacco and Health (PATH) Study, which is a nationally representative longitudinal cohort study of tobacco use and health outcomes within the United States population (National Institutes of Health and Food and Drug Administration, 2014) that includes a set of NESARC ND symptoms in its baseline survey. Using the entire set of questions from the NESARC study, we leverage the psychometric tools of item response theory to formalize commonalities and differences in symptom “signatures” among users of different tobacco products. A secondary goal was to identify and remove any symptom domains that were sensitive to product characteristics. Third, we examined whether the reduced set of symptoms would be a valid and efficient measure of ND to replicate in other national studies examining tobacco use.

## 2. Methods

### 2.1. Symptoms of nicotine dependence

We examined *Past Year* symptoms of ND in a US cohort using the NESARC study data. We utilized wave 1 (W1:  $n = 43,093$ ) conducted in 2001–2002 and wave 2 (W2:  $n = 34,653$ ) conducted in 2004–2005. We organized the 22 ND symptoms assessed by the NESARC Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS) into groups that either reflected specific DSM-IV criteria or had similar content. Initial groupings included Tolerance (2 symptoms), Withdrawal Syndrome (8 potential symptoms), Use for Withdrawal Relief (1 symptom), Use Upon Waking (1 symptom), Use After Temporary Abstinence (1 symptom), Used More Than Intended (1 symptom), Desire to Quit/Difficulty Quitting (2 symptoms), Loss of Control (1 symptom), Difficulty Refraining (1 symptom), Give Up Activity (2 symptoms), and Use Despite Health Consequences (2 symptoms). High symptom intercorrelations led us to collapse desire to quit/difficulty quitting symptoms (2 symptoms;  $r = 0.83$ ), and to collapse Give Up Activities symptoms (2 symptoms;  $r = 0.76$ ). We created a single symptom for the presence of the withdrawal syndrome using the DSM-IV criteria of endorsement of 4 of 8 symptoms and reporting impairment. The thirteen remaining symptoms were then organized into 8 multi-symptom domains: tolerance (2 symptoms); withdrawal (2 symptoms: Withdrawal Syndrome, Withdrawal Relief); use after temporary abstinence (2 symptoms); using more than intended (1 symptom); difficulty quitting (1 symptom); loss of control (2 symptoms – 1 Diff. Refrain, 1 Loss of Control); giving up activities due to use (1 symptom); and consequences of use (2 symptoms).

### 2.2. Overview of data analytic plan

We established four mutually exclusive past year tobacco-user groups: cigarette only users ( $n = 9305$ ), cigarette and cigar users ( $n = 581$ ), cigar only users ( $n = 538$ ), and smokeless tobacco users with or without other forms of tobacco ( $n = 615$ ). W2 included 8289 tobacco users of whom 356 were successful quitters (i.e. no tobacco

use for  $\geq 12$ -months). Item response models (IRM) were used to detail symptom responses among the four tobacco use groups. Prior to fitting IRM we evaluated model assumptions that symptoms measured a single common construct of ND. When covariation among symptoms arises from inclusion of multiple symptoms to assess the same domain of the ND construct (i.e. 2 tolerance or 2 withdrawal symptoms), the estimated relationships of symptoms with the primary single common construct of ND can be affected. Understanding any significant covariation within multi-symptom domains is important in selecting an IRM that can accommodate violations of this local independence assumption. To evaluate the significance of covariation within multi-symptom domains, we used a series of bifactor models to organize covariance of all symptom responses using a primary factor to reflect a single dimension of nicotine dependence while also allowing secondary factors to account for additional covariation within multi-symptom domains. We used full information maximum likelihood confirmatory factor analysis (Cai, 2010) and the Metropolis-Hastings Robbins-Monro (MH-RM) algorithm implemented in the ‘mirt’ package (Chalmers, 2012). Fit to a single primary factor of ND was compared to fit to a series of bifactor models of ND that added covariation within multi-symptom domains. We evaluated increasingly complex bifactor models that accounted for either a minimum of three multi-symptom domains (Tolerance, Withdrawal, Use After Temporary Abstinence) or a maximum of five-multi-symptom domains (three multi-symptom domains plus either loss of control and/or consequences). We used model-fit indices including AIC, BIC, and  $-2\log$  likelihood to guide evaluations. We selected an IRM model based in Testlet Response Theory (Wainer et al., 2007). In this context, all symptoms are believed to measure a single primary dimension of ND and the ‘testlets’ are the groupings of symptoms within multi-symptom domains. This IRM allows comparison of symptom endorsements and evaluation of brief symptom indices for use across tobacco use groups. To evaluate validity we compared observed W1 ND symptom counts with concurrent quantity of product use, and also assessed predictive validity of W1 ND assessment on quit success by W2. We then used symptom characteristics from these analyses to select reduced sets of symptoms that could be used to assess ND equitable across all tobacco-use groups.

### 2.3. Bayesian item response model

We fit an IRM that accommodated non-normal distributions of ND and included testlets to account for variability within multi-symptom domains. Although confirmatory bifactor models supported assumptions that all symptoms reflect a single primary dimension of ND, the models also suggested that additional variability remained within multi-symptom domains. We selected an IRM that included testlets, or groupings of symptoms that belong to these multi-symptom domains. Each testlet is modeled with a random effect term to adjust for this additional source of covariation that would otherwise violate local independence assumptions of other IRM models. By adding random effects to reflect significant variability within multi-symptom domains, IRM with testlets were used to evaluate the measurement equality of ND symptom reports from each tobacco use group. We evaluated (1) the relative strength of association (i.e., discrimination) between each symptom and levels of ND; (2) the ability to map each symptom within identified levels of ND (i.e., severity threshold). Finally, a series of models isolated and compared each ND symptom report from each tobacco use group in Differential Item Functioning (DIF) analyses. Using methods described by Wang and colleagues (2008) and SCORIGHT software (Wang et al., 2005), we obtained Markov Chain Monte Carlo (MCMC) generated samples from the posterior distribution of each of the model parameters separately for each symptom and each tobacco use group. Significant DIF in the discrimination (‘a’ parameter) and/or severity (‘b’ parameter) was interpreted when differences between pairs of posterior values sampled from each group were  $>0$  in 95% of 10,000 draws.

## 3. Results

### 3.1. Descriptive analyses

The analytical sample of adults who used tobacco within the last 12 months was identified at W1. Demographic characteristics of the W1 sample and the rate of W2 re-interviews are detailed by each demographic subgroup in Table 1. At W2, the percentage of re-interviews was lower among (1) those 18–25 and 65+ relative to other age groups, (2) Asian relative to other racial groups, and (3) those with less than high school education relative to other levels of education attainment. Importantly, rates of re-interview were similar among the tobacco-use groups.

### 3.2. Domains of nicotine dependence symptoms among tobacco use groups

All 13 symptoms were expected to be related to a single underlying dimension of ND. Five of the eight domains included

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