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Is the Fagerström test for nicotine dependence invariant across secular trends in smoking? A question for cross-birth cohort analysis of nicotine dependence

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ABSTRACT

Background: The Fagerström Test for Nicotine Dependence (FTND), a derivation of the Fagerström Tolerance Questionnaire, was first published in 1991. The FTND remains one of the most widely used measures of nicotine dependence for studying genetic and epidemiological risk factors and the likelihood of smoking cessation. However, it is unclear whether secular trends in patterns of smoking alter the psychometric properties of the FTND and its interpretation.

Methods: We examined measurement invariance in the lifetime and current FTND scores across birth cohorts using participants drawn from six study samples (N = 13,775).

Results: We found significant ($p < 0.05$) measurement non-invariance in means and factor loadings of most FTND items by birth cohort, but effect sizes, ranging from $r^2 = 0.0001$ to $r^2 = 0.0035$, indicated that less than 0.5% of the model variance was explained by the measurement non-invariance for each factor loading. To assess its impact, we regressed the lifetime FTND latent variable on well-established factors associated with nicotine dependence (quitting smoking and the nicotinic acetylcholine receptor gene [*CHRNA5*] variant rs16969968, separately), and we observed that the regression coefficients were unchanged between models with and without adjustment for measurement non-invariance.

Conclusions: These findings suggest that possible FTND non-invariance that occurs across study samples of various birth years has a negligible impact on study results.

1. Introduction

Nicotine dependence studies are increasingly combining samples of participants to increase statistical power and make comparisons across groups of diverse age, race/ethnicity, and sex (Belsky et al., 2013; Bierut et al., 2007; Fagerstrom and Furberg, 2008; John et al., 2003). In studies that compare an underlying latent trait, like nicotine dependence, it is assumed that the instrument is measuring the trait on a consistent scale (i.e., it is invariant, measuring the trait similarly across groups) (Widaman and Reise, 1997). Measurement non-invariance is a type of measurement error that can bias study results toward or away from the null hypothesis, thereby leading to incorrect results in statistical comparisons and increasing the chances of both Type 1 and Type 2 errors. A non-invariant measure of nicotine dependence might incorrectly suggest that groups differ in their dependence levels (Schroeder and Moolchan, 2007) or the relation between dependence

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and other key variables (e.g., estimating the association between nicotine dependence and cessation, in which cessation is correlated with group membership like age (Johnson et al., 2008)). Measurement invariance may also obscure true associations, making them appear non-significant. Moreover, if a non-invariant measure is used as an inclusion criterion across groups, it might allow recruitment of groups that unintentionally differ on trait dependence because the same score may be differently related across groups to the underlying latent dependence (Robinson et al., 2006).

The Fagerström Test for Nicotine Dependence (FTND; also called the Fagerström Test for Cigarette Dependence (Fagerstrom, 2012)) is perhaps the most widely used measure for studying genetic and epidemiological risk factors of nicotine dependence and likelihood of smoking cessation (Haddock et al., 1999; Heatherton et al., 1991). It focuses on core dependence criteria, including heavy use/tolerance and withdrawal (Baker et al., 2012), and remains an especially strong predictor of smoking cessation (Fagerstrom et al., 2012; Fidler et al., 2011). Its use across diverse studies with varying participant characteristics makes measurement invariance a vital psychometric issue to support the accuracy of analytic findings across a variety of studies.

Secular trends in smoking might produce measurement non-invariance in longitudinal studies and studies that incorporate cross-sectional data collected at different times across multiple samples if the salience of dependence symptoms were affected across different birth cohorts. Smoking prevalence was relatively low in the U.S. before 1939 but increased up until the 1960s, when almost half of adults smoked. The 1964 Surgeon General's report (U.S. Surgeon General's Advisory Committee on Smoking and Health, 1964) marked another turning point, and smoking prevalence has fallen since (Fig. S1) (U.S. Department of Health Human Services, 2014). A concomitant evolution in the social stigma and legal context of smoking have also affected smoking behaviors that are key indicators of dependence in the FTND (e.g., more difficulty refraining from smoking, fewer cigarettes per day [CPD] because smoking is forbidden in many public places), potentially making them more salient indicators of nicotine dependence.

Our study assessed measurement invariance in FTND by birth cohort and quantified the magnitude of significant effects. This address whether FTND scores have the same meaning when collected in different individuals studied at different times and whether results of studies using FTND across multiple birth cohorts are likely to be biased by this measurement error.

2. Methods

2.1. Study samples

We used five study samples that collected FTND data from 1989 to 2013: African American Nicotine Dependence (AAND), Collaborative Genetic Study of Nicotine Dependence (COGEND), Center for Oral Health Research in Appalachia (COHRA1), Chronic Obstructive Pulmonary Disease Gene (COPDGene®), and University of Wisconsin Transdisciplinary Tobacco Use Research Center (UW-TTURC). See Supplementary Material and Table S1 for detailed sample descriptions. All protocols received Institutional Review Board approval at their respective sites. All study participants provided informed consent.

2.2. Measures

2.2.1. Exposure

Birth cohort was categorized into three groups (Figure S1) (U.S. Department of Health Human Services, 2014): (1) those born before 1945, a period of low but increasing cigarette consumption; (2) those born 1945–1975, the period of highest per capita cigarette consumption that peaked around the 1964 report (U.S. Surgeon General's Advisory Committee on Smoking and Health, 1964); and (3) those born after 1975, when cigarette consumption steadily declined.

2.2.2. Outcomes

The FTND is a six-item questionnaire with scores ranging from 0 (no dependence) to 10 (highest dependence level). Our study focused on FTND scores based on habits among current smokers (current FTND) and compared them with results from when they reported smoking the most (lifetime FTND).

To evaluate the impact of any measurement non-invariance, we examined the relationship of lifetime FTND on quitting smoking. Quitting smoking was defined among lifetime smokers as either a self-reported status of "quit" or a frequency of 0 cigarettes smoked in the past month (depending on which measure was available).

Finally, we conducted analyses to evaluate the impact of any measurement non-invariance on rs16969968, the functional coding single nucleotide polymorphism (SNP) in the nicotinic acetylcholine receptor gene *CHRNA5*, that is robustly associated with nicotine dependence (Hancock et al., In-press). Rs16969968 was either genotyped or imputed with high quality (IMPUTE2 "info" quality metric = 0.99–1) in each of the five study samples and additively coded (ranging from 0 to 2 for the number of G alleles carried) for analysis, as previously described (Hancock et al., 2017).

2.3. Statistical analyses

2.3.1. Measurement invariance

We tested item-level measurement invariance for birth cohort by using multiple-indicator, multiple-cause (MIMIC) models with a weighted least squares parameter estimates with standard errors and a mean- and variance-adjusted chi-square test statistic that used a full weight matrix (an estimator appropriate for use with categorical data) (Johnson et al., 2008; Kline, 2010). MIMIC models are structural equation models that can examine group-specific effects on item responses relative to a reference group, without mediation through a latent variable (i.e., nicotine dependence). Fig. 1 provides an example of a MIMIC model testing an item-level difference in FTND item 5 (smoke more frequently during the first hours after waking than during the rest of the day) by birth cohort, with those born < 1945 as the reference. Each FTND item was tested this way. Modeling the direct paths from each birth cohort, adjusting for nicotine dependence level, results in estimates of response differences attributable to measurement non-invariance. Models including direct paths from each birth cohort to each FTND item were compared to nested models, where direct paths were fixed to zero using Mplus difftest to determine the statistical significance of non-invariance (Muthén and Muthén, 1998). Separate models were run with different reference groups to examine all pairwise differences (e.g., birth cohorts 2 and 3 vs. 1; birth cohorts 1 and 3 vs. 2).

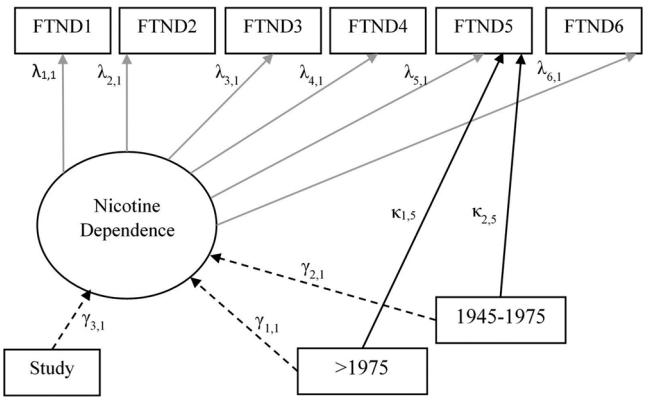

Fig. 1. Example MIMIC Model Testing for Item-level Differences in FTND Item 5 (Smoke More Frequently During the First Hours After Waking than During the Rest of the Day) by Birth Cohort Using < 1945 as the Reference Group.
Note: Study sample is dummy coded into indicator variables but has been simplified in this figure for illustrative purposes.