There are several measures that attempt to assess tobacco dependence but the most appropriate measure to use is often unclear. Tobacco dependence was assessed, in Canadian adult smokers of black African descent, with three measures: the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV), the International Classification of Diseases (ICD-10) and the Fagerström Test for Nicotine Dependence (FTND). The different measures resulted in very different tobacco dependence diagnosis rates: 91% were dependent by DSM-IV, 48% were dependent by ICD-10 and 48% were dependent by FTND (score ≥3). Although ICD-10 and FTND had the same diagnosis rates, they did not identify the same individuals as dependent (i.e., 35% of those dependent by ICD-10 were not dependent by FTND). For exploratory purposes, the dichotomous measures, DSM-IV and ICD-10, were scored as continuous scale measures, DSMC and ICDC. ICDC had the strongest agreement with FTND (ICC=0.76), followed by DSMC with ICD (ICC=0.28) and DSMC with FTND (ICC=0.19). These exploratory analyses illustrate some limitations and strengths of the DSM-IV, ICD-10 and FTND. Moreover, we illustrate how measurement architecture and population specific variation may contribute to discordant diagnoses.

**Methods**

**Overview:** We conducted a nicotine pharmacokinetics, pharmacogenetics and smoking study in smokers and non-smokers in an adult population of black African descent. Participants were from a sample of unrelated healthy volunteers recruited by advertisements, radio announcements and posters that were targeted to individuals of African or black Caribbean heritage. Recruitment initially targeted non-smokers and smokers who averaged at least 10 CPD. However, this requirement was problematic and recruitment was subsequently opened to all smokers who smoked on at least 5 out of 7 days. Qualified subjects were men and non-pregnant women (aged 18–60 years); who (a) were either current smokers or non-smokers who had tried cigarettes, (b) had at least three grandparents of black African descent, (c) had no known contraindications to the administration of oral nicotine, (d) were not currently using any prescription or non-prescription medications thought to induce or inhibit hepatic enzymes, (e) had good general health and medical history, (f) had the capacity to give written informed consent and (g) were willing to abide by the rules of the study. Participants received 100 Canadian dollars in compensation for their time. Only smokers (≥100 cigarettes lifetime and currently smoking at least five days per week; n=77 males, n=60 females) were the subjects of this secondary analysis. The smokers reported consuming a median of eight cigarettes per day (range=0–35); overall, 74% smoked ≤10 cigarettes per day. The University of Toronto ethics board approved the protocol and the Institutional Review Board Services (Toronto, Canada) approved and monitored the study.

*Corresponding author: Rachel F. Tyndale, Rm 4326 Medical Sciences Building, 1 King’s College Circle, University of Toronto, Toronto, Ontario, Canada, M5S 1A8, Telephone: 416–978–6574; Fax: 416–978–6395; E-mail: rtyndale@utoronto.ca

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Dependence Measures: Participants were interviewed using the Pharmacogenetics Drug History Questionnaire – a drug history questionnaire used to acquire information on demographics, ethnic admixture, drug use and tobacco dependence as assessed by the DSM-IV, ICD-10 and FTND [12]. Individuals were considered tobacco dependent by the DSM-IV if three of seven criteria were met in the same 12-month period [6]. For exploratory purposes and because it allowed better sensitivity in testing relationships, we expressed the DSM-IV as a scale measure and renamed it DSM continuous (DSMC). DSMC was scored as follows. In the DSM-IV, there are seven criteria and 21 questions. Each question has two choices (yes, no). If yes is selected then Q1=1, Q1b=1, Q2=1, Q2a=0.48, Q2b=0.24, Q2c=0.24, either Q3 or Q3a=1, Q3b=0.48, Q4=1, either Q5a or Q5b=1, Q5c=0.48, Q6=1, Q6a=0.48, Q6b=1, Q7=1, Q7a=0.24, Q7b=0.12, Q7c=0.12 and Q8=1. This scoring satisfies the condition that, if any 2 criteria other than Q8 are met, then the score is less than 3, but if any 3 criteria are met, then the score is at least 3. Thus, except for the additional simultaneity requirement of Q8, the dependence diagnosis is met if and only if, the sum is 3 or more. In some cases, when a negative response to one question was a precondition for asking another, both questions were scored identically. The ICD-10 dichotomous diagnosis of dependence is based on the method refined by O’Loughlin and colleagues, where individuals were considered tobacco dependent if three of six criteria are met [13]. The ICD-10 was also expressed as a scale measure and named ICD-10 continuous (ICDC). ICDC was scored as follows. The ICD-10 measure consists of 18 questions, divided into 3 groups of 4 questions and 3 groups of 2 questions. Each question has multiple response choices and is considered positive only if the most extreme positive choice is selected. Scoring for most criteria, where the original diagnostic scoring required at least one positive response, is as follows, 0=no questions positive, 1=1/2 or 1/4 question positive, 1.1=2/4 questions positive, 1.2=3/4 questions positive, 1.3=2/4 or 4/4 questions positive. However, for Criterion 3, where the original diagnostic scoring required two positive responses, the scoring is 0=no questions positive, 0.3=1/4 questions positive, 1=2/4 questions positive, 1.15=3/4 questions positive, 1.3=4/4 questions positive. This scoring satisfies the condition that, if any 2 criteria are met, then the score is less than 3, but if any 3 criteria are met, then the score is at least 3. Thus, the dependence diagnosis is met if and only if, the sum is 3 or more. FTND is a six-item continuous scale of dependence. Scores range from 0 to 10; a score of 0 to 2 indicated low/no dependence, 3 to 5 indicated moderate dependence and 6 to 10 denoted high dependence [8].

Statistical Analyses: The kappa statistic was used to assess agreement between dichotomous dependence measures. Intraclass correlation coefficients were used to assess the agreement between the continuous measures. Statistical analyses were carried out using SPSS software (SPSS for Macintosh, Release 11.0.4 2004. Chicago: SPSS Inc.).

Results

The Interesting Observation of Dependence Diagnosis Discordance: By DSM-IV, 91% of smokers were diagnosed as dependent, while only 48% were diagnosed as dependent by each of the ICD-10 and FTND (Figure 1A). The DSM-IV did not significantly agree (k=0.05, p=0.28) with either the ICD-10 or the FTND. Despite diagnosing the same overall proportion of participants as dependent, the agreement between the ICD-10 and FTND was only fair (k=0.33, p<0.001). (Figure 1B) illustrates the diagnostic discordance between measures.

Architectural Sources of Inter-Instrument Discordance: Five of the twenty DSM-IV questions (25%) are shared with ICD-10. Nine of the eighteen ICD-10 questions (50%) are shared with DSM-IV and two with FTND (11%). Two of the six FTND questions (33%) are shared with ICD-10 (Supplementary Table 2). All continuous dependence measures significantly agreed with each other. The best agreement, as assessed by intra class correlation coefficient (ICC), was between the ICD and FTND ICC=0.76 (substantial, p<0.001), followed by DSMC and ICDC ICC=0.28 (fair, p=0.001) and DSMC and FTND ICC=0.19 (poor, p=0.002).

Despite shared criteria and agreement in the assessment of the continuous dependence measures, the construction of the DSM-IV and ICD-10 based measures diverge in important ways. First, questions asked to assess the same criteria differ. For example, to assess tolerance, the DSM-IV and the ICD-10 both ask if more nicotine is required for the same psychoactive effect. The DSM-IV then uniquely asks if the same amount of tobacco results in less psychoactive effect, while the ICD-10 uniquely asks if more tobacco is required to feel negative effects such as nausea. Second, the measures diverge because slightly different wording is used to ask similar questions. For instance, of the 39% of smokers who indicated in DSM-IV that they had never had withdrawal symptoms (i.e. felt sick), 60% answered in ICD-10 that they rarely, sometimes, or often felt irritable or angry when in withdrawal (Figure 2A). Third, divergence between measures occurs at the level of question scoring, when one instrument’s graded response is forced to map to another instrument’s binary response. For example, both the ICD-10 and the FTND ask about smoking habits when sick. The FTND only allows a yes or no answer, whereas the ICD-10 allows for a range of answers and cutting down the amount smoked is the most highly endorsed answer. The individual does not stop smoking when sick, but neither does the individual smoke as usual, a subtlety that the FTND does not capture (Figure 2A). The design and construction (i.e. the dimensions of dependence assessed, criteria, questions, wording of questions and scoring of questions) all likely contribute to differences between measures.

Potential Sources of Inter-Population Variability: On a similar but separate note, the scoring of questions is not always appropriate for the population under investigation. For example, 70% of participants scored zero on FTND-Q4 because they smoked fewer than ten CPD (Figure 3A). We rescored the question to be more reflective of the smoking levels in the population so that cigarette consumption scores formed a quasi-normal distribution (Figure 3A). (Figure 3B) shows the change in the dependence diagnosis with the new scoring is as follows: 31% were highly dependent compared with the original 15%; 38% were moderately dependent compared with the original 34%; and 31% were nondependent compared with the original 52%.

Figure 1: Differential diagnosis of dependence by DSM-IV, ICD-10 and FTND. A The number of smokers dependent by the DSM-IV, ICD-10 and FTND. As DSM-IV and ICD-10 only diagnose the presence or absence of dependence, the ‘High’ (66 score) and ‘Moderate’ (3-5 score) descriptors apply only to the FTND. B Venn diagram showing the number of smokers diagnosed as dependent by at least one measure in circles (n=131). The number of smokers diagnosed as nondependent by all measures is outside the circles (n=6).
Although the new continuous scoring has not been validated, the DSMC and ICDC continuous scores were defined such that scores exceeding a threshold (3 of 7 for DSMC and 3 of 6 ICDC) satisfied the original binary definitions of dependence. Thus, the rankings of dependent individuals were not substantially modified but refined with the conversion of the dichotomous outcome to a continuous score. The DSMC and ICDC may be excellent tools for researchers interested in assessing the continuous nature of dependence.

**DSM-IV Dependence:** In the DSM-IV, criteria for dependence diagnosis are identical across substances (e.g. alcohol, marijuana, cocaine, tobacco) [6]. A moderate correlation between DSMC and ICDC has also been seen in a study of moderate smokers [14]. The relationship is likely due to similar generic definitions of dependence and content overlap. However, our findings suggest that the specific questions, the wording of questions and the scoring of questions are key sources of discordance between measures even if they are based on similar generic constructs of dependence. As in several other studies [9,14,15], we found that the DSMC and Fagerström measure were weakly related. The DSM-IV and the FTND had no obvious criterion/question overlap; consistent with the DSM-IV identifying tobacco dependence as a psychological disorder [6], while the FTND focuses on physical tobacco dependence [8]. Despite this, the two measures still have a level of agreement, possibly reflecting a higher-order construct of dependence. Nonetheless, the categorical DSM-IV may lack sensitivity as the large majority of the current study's smokers, despite smoking a median of eight cigarettes per day, were diagnosed as tobacco dependent.

**ICD-10 Dependence:** The ICD-10 uses “a cluster of behavioral, cognitive and physiological phenomena that develop after repeated substance use” to diagnose a generic dependence syndrome [7]. The ICD-based measure uses questions and concepts from both the DSM-IV and FTND as well as capturing the additional dimensions of craving/compulsion [13]. Mathematically, the ICDC and FTND scores were the most strongly related. This finding differs from a study of heavier smokers, where the measures were not significantly correlated (r=0.32, p>0.05) [14]. The discrepancy may be due to: (a) distinct architecture of measures as Hughes and colleagues developed a different continuous score for the ICD-10 based on the number of criteria endorsed [14]; (b) cigarette consumption because the relationship between tobacco dependence and cigarette consumption seems to be stronger in light smokers compared to heavier smokers [16]; or (c) ethnicity since African American smokers score higher than European American smokers compared to heavier smokers [16]; or (c) ethnicity since African American smokers scored higher than European American smokers on similar generic constructs of dependence. As in several other studies [9,14,15], we found that the DSMC and Fagerström measure are in some cases discordant, perhaps more so than the underlying construct.

**Continuous Scoring:** Our aim in rescoring the DSM-IV and ICD-10 was to take advantage of the underlying construct of tobacco dependence. Each measure’s outcome is artificially dichotomized to dependent and not dependent; this limits the sensitivity in assessing relationships. Our analysis demonstrated that agreement scores between measures improved when the continuous scores were used.
fewer cigarettes. However, there is a modified Fagerstrom questionnaire for adolescents [20] and modifying the FTND so that it has the capacity to discriminate between levels of dependence in lighter smokers (e.g. splitting the lowest category of <10 CPD into two) may be a valuable addition to the measure. The need for sensitivity to differential levels of nicotine dependence among light smokers has been suggested by others [18].

Caveats: Our ability to generalize these results is tempered by several caveats. First, these are secondary analyses of a nicotine pharmacokinetic and smoking pharmacogenetic study. As such, it has potential selection bias as participants were not sampled randomly but were selected according to eligibility criteria specific to the parent study. Moreover, participating in a full day research study may have introduced self-selection. In addition to the analyses being secondary, the numbers of study participants is small relative to the number of questions in the measures (i.e. 137 participants and 45 questions); thus, our findings must be considered hypothesis generating. Finally, because the study participants are relatively light smokers and are of black African descent, we cannot determine if the discordance between measures is influenced by ethnic specific factors. From the literature, it seems that African Americans score differently on some dimensions of dependence [3], thus ethnicity may be a variable that contributes to the magnitude of discordance we see between measures. Moreover, in a general heaviest/lightest smokers the ICD-10 and DSM-IV are highly correlated [14], perhaps suggesting that the discordance between the DSM-IV and the ICD-10 may be due to daily cigarette consumption.

Implications for future tobacco research and practice: There is no gold standard for assessing of tobacco dependence but both the ICD-10 and the DSM-IV are based on similar generic constructs of dependence. The APA has defined dependence as “a maladaptive pattern of substance abuse, leading to clinically significant impairment or distress, as manifested by three (or more) specified criteria, occurring at any time in the same 12-month”. A limitation of this definition is it classifies dependence as a dichotomous trait. Complex human traits are influenced by both environmental and genetic factors; consequently, they exhibit phenotypes along a continuum. A strength of the dichotomous DSM-IV and ICD-10 is that they possess content validity because they are based on a definition that recognizes multiple facets of the dependence construct. However, if dependence is a maladaptive harmful pattern of use, then the ability of a continuous measure to predict cessation of may be the most relevant test of validity.

Tobacco dependence questionnaires are often used to identify individuals suitable for inclusion in smoking cessation trials, to distinguish cases in epidemiological investigations, or as an outcome variable. Study participants classified by tobacco dependence using different measures results in practical problems comparing finding across studies and with subpopulation selection. The findings of the present study illustrate some limitations and strengths of the DSM-IV, ICD-10 and FTND in an adult population of black African descent. More generally, it highlights the importance of (a) the type, wording and scoring of the questions in tobacco dependence measures and (b) population specific factors that may confound tobacco dependence assessment. Finally, we have developed continuous scoring methods for the DSM-IV and ICD-10 that can discern ranges of tobacco dependence rather that dichotomous categorization.

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Competing Interests

Dr. RF Tyndale holds shares in Nicogen Research Inc., a company focused on novel smoking cessation treatment approaches. None of the data contained in this manuscript alters or improves any commercial aspect of Nicogen and no Nicogen funds were used in this work.

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