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Rural Opioid and Other Drug Use Disorder Diagnosis: Assessing Measurement Invariance and Latent Classification of DSM-IV Abuse and Dependence Criteria

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by

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ABSTRACT

Rural Opioid and Other Drug Use Disorder Diagnosis: Assessing Measurement Invariance and Latent Classification of DSM-IV Abuse and Dependence Criteria

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The rates of non-medical prescription drug use in the United States (U.S.) have increased dramatically in the last two decades, leading to a more than 300% increase in deaths from overdose, surpassing motor vehicle accidents as the leading cause of injury deaths. In rural areas, deaths from unintentional overdose have increased by more than 250% since 1999 while urban deaths have increased at a fraction of this rate. The objective of this research was to test the hypothesis that cultural, economic, and environmental factors prevalent in rural America affect the rate of substance use disorder (SUD) in that population, and that diagnosis of these disorders across rural and urban populations may not be generalizable due to these same effects. This study applies measurement invariance analysis and factor analysis techniques: item response theory (IRT), multiple indicators, multiple causes (MIMIC), and latent class analysis (LCA), to the DSM-IV abuse and dependency diagnosis instrument. The sample used for the study was a population of adult past-year illicit drug users living in a rural or urban area drawn from the 2011-2012 National Survey on Drug Use and Health data files (N = 3,369| analyses 1 and 2; N = 12,140| analysis 3). Results of the IRT and MIMIC analyses indicated no significant variance in DSM item function across rural and urban sub-groups; however, several socio-demographic variables including age, race, income, and gender were associated with bias in the instrument. Latent class structures differed across the sub-

groups in quality and number, with the rural sample fitting a 3-class structure and the urban fitting 6-class model. Overall the rural class structure exhibited less diversity and lower prevalence of SUD in multiple drug categories (e.g. cocaine, hallucinogens, and stimulants). This result suggests underlying elements affecting SUD patterns in the two populations. These findings inform the development of surveillance instruments, clinical services, and public health programming tailored to specific communities.

DEDICATION

I dedicate this work to my wife and kids: Jen, Ben, Fischer, Amelia, Shepherd, and Charlie, the six lights that guide my way.

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ACRONYMS AND ABREVIATIONS

ACEs – Adverse Childhood Experiences

BLRT – Parametric Bootstrap Likelihood Ratio Test

DEA – Drug Enforcement Agency

DIF – Differential Item Functioning

DSM-IV – Diagnostic and Statistical Manual of Mental Disorders, 4th Edition

ICC – Item Characteristic Curves

IRF – Item Response Function

IRT – Item Response Theory

ISU – Illicit Substance Use

LCA – Latent Class Analysis

MDE – Major Depressive Episode

MIMIC – Multiple Indicators, Multiple Causes

NESARC – National Epidemiologic Survey on Alcohol and Related Conditions

NMOU – Non-Medical Opioid Use

NMPDU – Non-Medical Prescription Drug Use

NSDUH – National Survey on Drug Use and Health

OPR – Opioid Pain Relievers

OUD – Opioid Use Disorder

PDMP – Prescription Drug Monitoring Program

PDUD – Prescription Drug Use Disorder

SES – Socio-Economic Status

SHEILD – Self-Help and Eliminating Life-threatening Diseases

SMI – Serious Mental Illness

SUD – Substance Use Disorder

TIC – Total Information Curves

US – United States

CHAPTER 1

INTRODUCTION

Problem Statement

The rates of non-medical prescription drug use (NMPDU) in the United States (U.S.) have increased dramatically in the last two decades, leading to a more than 300% increase in deaths from overdose, surpassing motor vehicle accidents as the leading cause of injury deaths (Centers for Disease Control and Prevention, 2014a; Substance Abuse and Mental Health Data Archive, 2014). One potential contributing factor to the epidemic is that there are more controlled substances prescribed in the US than ever in our history. Opioids alone, or opioid pain relievers (OPR), are dispensed today at a rate that is more than 2.76 times that seen in 1999 (National Institute on Drug Abuse, 2011). As a result OPRs are abused more than twice as frequently as stimulants, sedatives, or tranquilizers and account for nearly 75% of all prescription drug overdoses in the US (Centers for Disease Control and Prevention, 2013; Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Behavioral Health Statistics and Quality., 2012).

In 2010 it was estimated that 20 percent of the US population aged 12 years and older had engaged in some lifetime non-medical use of prescription drugs. In the same year, the prevalence of past-year non-medical use of Vicodin, a sedative, and Oxycontin, an OPR was reported to be 8.3% and 5%, respectively, among high school seniors (National Institute on Drug Abuse, 2011). Nearly half (45%) of individuals reporting past-year use of any illicit drug in 2012 indicated having misused pharmaceuticals (Substance Abuse and Mental Health Data Archive, 2014). The inevitable result of this trend in substance use is that half of all emergency department admissions for overdose are now attributed to NMPDU (Centers for Disease Control and Prevention, 2014a).

In rural areas, deaths from unintentional overdose have increased by more than 250% since 1999 while urban deaths have increased at a fraction of this rate (Keyes et al., 2014). Previous studies have explored the association between “rurality” and risk of substance abuse with mixed results (Havens et al., 2011; Havens et al., 2007; Wang et al., 2013). One study investigated adolescent prescription drug abuse and found that individuals in rural areas aged 12 to 17 years were more likely to report NMPDU than their counterparts in urban areas (Havens et al., 2011). Another study found rates of prescription opioid use to be much higher in rural populations of adult probationers (Havens et al., 2007). In a sample of non-institutionalized adults however, rates of NMPDU were found not to be significantly different between rural and urban areas (Havens et al., 2011).

Thanks to the studies cited above, we now have some idea of the prevalence of NMPDU in rural and urban areas. Unfortunately there remains a lack of research on the potential differences in prescription drug use disorder prevalence between these two populations. Prescription drug use disorder (PDUD) is a term used throughout this document indicating a diagnosis of substance abuse or dependency resulting from NMPDU. It is important to make the distinction between the prevalence of non-medical use and PDUD because we know that not every self-reporting illicit drug user meets the criteria for abuse or dependence. According to recent findings from the National Survey on Drug Use and Health (NSDUH), 24.6 million individuals in the US (9.4%) aged 12 years and older reported current Illicit Substance Use (ISU), while the same survey found that only 21.6 million people (8.2%) met the DSM-IV criteria for use disorder (Substance Abuse and Mental Health Services Administration, 2014). Not everyone reporting ISU is diagnosed with substance use disorder (SUD) defined as abuse or dependence, meaning they do not necessarily require treatment and are at lower risk for overdose.

The instruments used to diagnose SUD require thorough testing and re-testing in order to ensure validity of the underlying, or latent, construct so that public health policy can be based on reliable distributions of SUDs across groups. The need for consistency of diagnoses requires these instruments be generalizable to the population at risk, which in the case of SUDs is every individual in the US. It is this need for generalizability that creates potential for misdiagnosis due to sub-group differences that influence their response to instrument criteria. The instrument used to diagnose SUD, or abuse and dependency in clinical practice, the Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV) and now DSM-V, has been the subject of much study regarding the construct validity and dimensionality of the instrument (Blanco et al., 2013; Derringer et al., 2013; Gillespie et al., 2007; Kopak et al., 2014; Saha et al., 2012; Wu et al., 2008; Wu et al., 2009; Wu et al., 2011).

Of relevance to the proposed study is past research into measurement invariance of DSM-IV abuse and dependency criteria as assessed by differential item functioning (DIF) across sub-groups (Gillespie et al., 2007; Gizer et al., 2013;Wu et al., 2009a). The assessment of DIF can apply to one or all of three item response parameters, difficulty, discrimination and guessing, which apply to aspects or characteristics of the response probability curves associated with specific criteria in a test or survey instrument (Wu et al.; Ringwalt et al., 2009b). The third parameter, guessability, does not bear any relevance to the study of DSM-IV measurement invariance, as the instrument does not measure latent competency.

The difficulty parameter is an indicator of how high on the severity scale of a latent construct, in this case SUD, an individual has to be before their probability of endorsing a survey item crosses 50%. This is also referred to as the threshold in factor analysis terminology. Discrimination is the ability of a particular item to differentiate between an individual at a higher latent variable severity from one at a lower level, essentially the slope of the logistic response curve. The correlative parameter for discrimination in factor analysis terms is the factor loading. The study of DIF is conducted through several approaches including Item response theory (IRT) likelihood ratio analysis, mantel-haenszel chi-square difference tests, as well as mixed factor analysis and regression methods. Research into the DSM-IV abuse and dependency criteria has generated results indicating DIF across gender, racial groups and drug class (Agrawal & Lynskey, 2007; Gillespie et al., 2007; Gizer et al., 2013; Wu et al., 2009a).

Another approach to examining potential heterogeneity across sub-groups with regard to general SUD is through latent class analysis (LCA), which applies modeling techniques to identify categorical levels within the latent construct SUD (Collins LM, 2010). LCA has been applied to the identification of both substance use behavior and SUD class structures (Agrawal et al., 2007; Chung & Martin, 2005; Grant et al., 2006; Lynskey et al., 2006). The goal of applying LCA to SUD classification in rural and urban populations is to identify qualitative differences across the populations presumed to be the result of cultural factors. This approaches also allows for exploration of the predictive nature of variables such as gender, race, and other socio-demographic characteristics with regard to class membership. Information gained from LCA can be used to inform treatment modalities targeted at specific groups, as well as trend analyses of the ecological effects of prevention methods on classes of use disorders.

Aims of the Study

The hypothesis tested herein is that cultural, economic, and environmental factors prevalent in rural America affect the rate of SUD in that population, and that diagnosis of these disorders across rural and urban populations may not be generalizable due to these same effects. The first two studies discussed below apply measurement invariance analysis techniques, specifically IRT descriptive assessment and Multiple Indicators, Multiple Causes (MIMIC) modeling, to DSM-IV diagnoses of opioid use disorder (OUD) using rural vs. urban as the main grouping variable. The sample population for both of these analyses was adult (age 18+) past-year non-medical users of opioid pain relievers. In the first study a descriptive IRT analysis was conducted in order to assess any differences in the difficulty and discrimination parameters across rural and urban populations. The MIMIC model was then applied to the data in order to statistically test for differences in the difficulty parameter. Once the variance in difficulty was controlled for across the sub-groups by including significant effects between covariates and indicators in the model, regression methods were applied to estimate the association of predictors with OUD in rural and urban areas.

In order to assess for differences in multiple substance use disorder groupings in the two populations, a multiple-groups LCA with covariates was conducted on a sample of adult past-year users of nine drug categories. The resultant class structures were then used to assess effect of covariates on class membership probability.

Objectives

Objective 1: To describe the functioning of the DSM-IV OUD criteria across rural and urban populations using IRT methods of assessment. The target population for this analysis was adult past-year non-medical users of prescription pain relievers. These individuals report using a prescription painkiller in the past year for purposes other than for which it was prescribed or for the feeling it generated. Potential measurement invariance between the groups was assessed through the comparison of item characteristic curves, total information curves, and conditional standard errors of measurement.

Objective 2: To assess measurement invariance of DSM-IV OUD criteria across rural and urban populations, searching for potential DIF within the instrument. MIMIC modeling was applied to identify DIF in the measurement items in relation to a set of covariates. MIMIC is a form of structural equation modeling (SEM) that employs factor analysis and regression to test the effect of sub-group categories (e.g., gender, race, rural vs. urban, etc.) on the probability of endorsing a measurement item. In addition to identifying potential differences in item function across sub-groups, effects of covariates on OUD factor scores were calculated controlling for DIF found in MIMIC analysis.

Objective 3: To apply multiple-groups LCA with covariates to examine potential differences in latent classifications of multiple drug SUD between rural and urban populations. Nine different drug categories including cannabis, stimulants, hallucinogens, opiates, cocaine, sedatives, inhalants, heroin, and tranquilizers were used to identify latent classes of SUD based on the groupings of different illicit and prescription drugs. Once the class structure was established for each sample population (i.e. rural and urban), the second step was then to apply multinomial regression methods to assess for any association between a set of socio-demographic covariates and class membership. This study attempts to illuminate differences in the type and number of use disorders classes across rural and urban populations.

Significance of Study

The results of the first two studies have implications for rural area clinicians and treatment facilities that base their clinical care of OUD on DSM-IV diagnostic criteria. These studies explore the validity of applying the DSM-IV to rural populations. In addition, surveillance of OUD prevalence distributions in the US and abroad is in question as many of the statistics are generated through administering the DSM-IV instrument to a nationally representative sample. Currently our understanding of the prevalence of OUD is driven by the inclusion of DSM abuse and dependency criteria in nationally representative population-based surveys such as the NSDUH and the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). These surveys and others like them are our best and only source for estimating OUD in the population. It is essential to the external validity of these data that we are confident in the function of measurement criteria across sub-groups.

Identifying differences in the latent class structure of SUD between rural and urban areas can further illustrate the socio-demographic idiosyncrasies that exist in these groups. Levels of cultural diversity, economic viability, and access to services are just a few variables that could influence the types of drugs being abused in a community as well as the variety of disorder classes that may exist. Exploring these class structures and the elements that predict membership can help inform a more efficient public health system in both rural and urban areas.

Public health policy can increase access to treatment and recovery services, initiate diversion control efforts, and stimulate economic growth to reduce poverty and increase educational attainment. Without effective measures of the distribution of OUD in the US our policies will not prove to be successful in bringing the appropriate resources to bear on the populations or geographic regions that need them. This study will contribute to the understanding of those data already gathered and inform the collection of more valid and reliable data in the future. Our public health system is under funded and over burdened, making the efficient use of available funds to serve the communities in need our top priority.

Dissertation Framework

As mentioned above, OPRs are abused more than twice as frequently as stimulants, sedatives, or tranquilizers and account for nearly 75% of all prescription drug overdoses in the US (Centers for Disease Control and Prevention, 2013). Due to this overwhelming burden on the health care system caused specifically by OPR use, the first two analyses in this study are limited to adults reporting past-year non-medical opioid use (NMOU). The third analysis includes adults reporting past-year use of nine drug categories (i.e. cannabis, stimulants, hallucinogens, opiates, cocaine, sedatives, inhalants, heroin, and tranquilizers) in a latent class model that explores the relationship between OUD and other drug use disorders.

Chapter one describes the current research findings on OUD prevalence, correlates and distribution. The prevalence of risk factors in rural populations is discussed in order to explain the increased NMOU seen in this population. This discussion is framed around the economic, social, and cultural characteristics of rural America and their probable role in the prevalence of OUD in the population. The resultant matrix of factors is then built upon to motivate the development of a theoretical model of the problem.

Due to the fact that all three analyses herein are studies of the DSM-IV SUD a discussion has been included concerning the historical development of the DSM leading to its present incarnation, the DSM-V, with an emphasis on the validity and dimensional study of the abuse and dependency criteria.

Chapters two, three, and four address each analysis individually (i.e. IRT, MIMIC, LCA respectively). Each chapter includes background, methods, results, and discussion of the analyses. An overall discussion and conclusion is presented in chapter five.

Prevalence and Incidence of OUD

The 2010 US Census estimated that 19.3% of the population lived in areas designated as rural, which is down from 21% in 2000 (US Census Bureau, 2013). Most of this shift in percent population is accounted for by the increase in individuals living in urbanized areas. Despite the decline, rural communities represent a significant portion of the population that has seen a more than 248% increase in unintentional drug poisoning from narcotics (i.e., heroin, cocaine, and analgesics) between 1999 and 2004, whereas urban populations only experienced a 16% increase during the same time period (Paulozzi & Xi, 2008). This means unintentional narcotic overdose deaths in rural, non-metropolitan, populations increased a rate 15.5 times that seen in urban, large metropolitan, areas in five years.

In 2011 Havens, Young and Havens used data from the National Survey on Drug Use and Health (NSDUH) to examine the moderation effect of being in a rural, non-metro area on adolescent risk of lifetime NMOU (Havens, et al., 2011). The public use data file of the NSDUH survey classifies sample zip codes into large metro (at least 1,000,000 residents), small metro (less than 1,000,000 residents but inside metro statistical area (MSA), and non-metro (less than 1,000,000 residents and lying outside of an MSA). Non-metro designations are here after referred to as rural.

Their study was limited to individuals aged 12 to 17 years (N=17872), 82.9% of whom lived in either a large or small metro region. Lifetime NMOU was measured by a positive response to the question, "Have you ever, even once, used any type of opioid pain reliever that was not prescribed to you or that you took only for the experience or feeling caused?" The results from their study indicated that a significantly higher percentage of adolescents in rural areas reported lifetime NMOU compared to urban adolescent populations (Rural:11.5%; 95% CI 10.1-12.9; Urban: 8.6%; 95% CI 7.76-9.47) (Havens et al., 2011).

When they included their covariates (i.e., race, lifetime illicit substance use, self-reported health, gender, age, and income) rural adolescents were 26% more likely to report NMOU compared to urban adolescents (95% CI: 1.01-1.57). In addition, age was highly predictive of NMOU in rural adolescent populations, with 17 year olds nearly 4 times as likely to report lifetime NMOU as compared to 12 year olds. This trend of increased risk in lifetime NMOU during adolescence was seen for both rural and urban populations in their sample, indicating significant NMOU risk for this age group (Havens et al., 2011).

In 2008, another study of adolescent NMOU was published which utilized the same age group, 12-17 (N=18,678), from the 2005 NSDUH public use data file (Wu et al., 2008). The objective of the research was not to look specifically at "rurality" as a predictor but it was included as a covariate in the model. Consistent with findings from the Havens et al. study, the Wu et al. study found that the unadjusted prevalence of NMOU was higher among non-metro populations compared to large metro groups (11% and 8.6% respectively; p-value < 0.001). The adjusted odds ratios did not prove significant in the final model with all covariates included (Wu et al., 2008).

Another study conducted between 2000 and 2004 drew a sample from populations of adult felony probationers in urban Delaware and rural Kentucky (Havens et al., 2007). One thousand five hundred twenty-five participants were recruited through an HIV study; the Kentucky cohort (n=782) was recruited between 2001 and 2004 and the Delaware cohort (n=743) was recruited between 2000 and 2003. Study participants were asked about their lifetime and past 3-month NMOU as well as treatment, criminal involvement, and demographic information.

Multiple logistic regression was utilized to test the association of the "rurality" predictor along with covariates; age, race, gender, marital status, income, education, sexual orientation, and other drug use including injection. Results of this analysis indicated that rural probationers were nearly five times as likely to report NMOU than urban probationers (OR: 4.92; 95% CI: 2.70-8.97) (Havens et al., 2007). In this study of institutionalized adults, 36.6% of rural participants reported NMOU compared to just 9.5% of urban participants (Havens et al., 2007). This study is limited in its generalizability due to the lack of geographic randomization, participant population characteristics, and inclusion of a single rural county and urban county in its sampling frame.

A study published in 2013 used data from the 2008-2009 NSDUH to model the effect of "rurality" in the US adult population (Wang et al., 2013). The sample included individuals 18 and older who responded to the survey in 2008 or 2009 (N=75,964). Results of multiple logistic modeling indicated no significant difference in prevalence of NMOU between rural and urban populations (Wang et al., 2013). This suggests the non-institutionalized, adult population in rural areas does not differ in their likelihood of NMOU compared to urban areas. There remains the question of contributing factors to the meteoric rise in overdose deaths in these areas over the last two decades. In addition, we still have little to no understanding regarding the nature of SUD in rural populations.

Results from studies of ISU in rural America have been mixed and at times contradictive. Rural substance users admitted to treatment centers vary in the types of drugs they most commonly abuse, not only when compared with urban populations, but also with individuals from very rural settings (Schoeneberger et al., 2006). Based on results from the Schoeneberger et al. study, very rural populations have significantly lower prevalence of reported use of opiates, cocaine, cannabis, and multiple drugs compared to rural areas. In addition, the mean age of first drug use is higher in very rural areas compared to rural (Schoeneberger et al., 2006). This suggests a dose effect of the protective factor; "rurality" within communities identified as more rural according to rural-urban continuum codes (Schoeneberger et al., 2006; United States Department of Agriculture, 2013).

The underlying causes of this “rurality” effect are not yet clear. A handful of studies have examined the association between “rurality” and ISU prevalence, but nearly all have been limited either in the generalizability or their inclusion of socio-demographic factors. One study that was conducted by Young et al., showed increased risk of ISU in rural populations despite the inclusion of income and education factors into multiple regression models (Young et al., 2012). When these potential confounders were included in the models, odds ratios remained stable and indicative of an increased likelihood of reporting illicit use. This suggests there is an underlying predictive construct for substance abuse at play in rural populations beyond socio-demographics; however, again there are major limitations in this study including sample size and frame (Young et al., 2012).

The studies above indicate an increased risk for NMOU in rural at risk populations. Adolescents are at risk for substance abuse independent of regional sub-group identifiers and probationers have a host of risk factors for SUD including but not limited to mental health disorders and low socio-economic status (SES). While these results are compelling when considered in conjunction with upward trending rural overdose deaths, it is important to understand the risk profile of non-institutionalized adult populations in these areas.

Theoretical Framework

The following section includes a discussion of the risk factors for ISU, NMPDU, and OUD. First, determinants of ISU as supported by the literature are enumerated, then those associated with NMPDU are described along with how these factors may be playing out in rural populations. In their systematic review of social determinants of substance use, Galea et al. identify key studies of the risk factors for substance abuse conducted up to that point (Galea et al., 2004). Figure 1 summarizes the findings of this review in the form of a social-ecological model of ISU.

<u>Illicit Substance Use</u>

In the US it is reported that 20% of kids try alcohol by the time they turn 13 years old, while 40% of high school students report trying marijuana at least once (Office of Adolescent Health (OAH), 2013). Classic risk factors for adolescent substance abuse include the lack of parental supervision, poverty, drug availability, and parental substance use (National Institute on Drug Abuse (NIDA), 2003). Other individual factors such as race, gender, SES, and education have been well established with regard to their effect on ISU risk (Galea et al., 2004). As expected, those adults with lower educational attainment and SES are at higher risk for ISU. Additionally, marital status, housing, and adverse childhood experiences (ACEs) can predict ISU in adulthood (Galea et al., 2004).

Findings from many studies support the effect of socio-demographics on risk of ISU. Interactive or moderating effects have been observed between many of these factors and social, neighborhood, and environmental-level characteristics. The interactive effect of race in particular has been found significant when modeling the effect of SES and school experiences on ISU consequences and age of initiation (Galea et al., 2004).

At the institutional level, research suggests that adolescent perception of school and family connectedness can impact the risk of substance use, violent behavior, and early engagement in sexual activity (Christiansen et al., 2014; Luthar & Zigler, 1991; Resnick et al., 1993). As mentioned above, other studies have found that the school experience can moderate the classical influence of race on ISU risk, with results indicating a more predictive effect for whites compared to black students (Galea et al., 2004).

Finally, neighborhood characteristics can have a powerful effect on health behavior. This idea is not new, yet is still in need of further scrutiny. Research into this phenomenon has uncovered striking results that suggest that community-level factors (e.g., average income, unemployment rates, neighborhood disadvantage, etc.) can sometimes be even more predictive of ISU than individual-level characteristics (Boardman et al., 2001; Carpiano et al., 2011; Galea et al., 2004; Schroeder et al., 2001; Sellstrom et al., 2011).

With all this in mind, researchers have begun to examine the role of social-emotional resiliency in determining individual risk of substance abuse (Luthar & Zigler, 1991; Luthar et al., 2000). An individual's resiliency is a measure of their ability to resist pressures to engage in risky behavior. It is the outcome of social environmental influences' interaction with predisposed emotional and social competency. Resiliency can be impacted by factors at the family, institutional, social, and community levels; and may be a moderator for all other ISU risk factors.

Social Ecological Theory

Social Ecological theory has broad application in community and behavioral health, assuming a framework of bidirectional influence between the environment, inter and intra personal relations, and behavior (McLeroy et al., 1988). Individual ISU risk is determined in this model by influences at multiple levels including personal, institutional, community and public policy (McLeroy et al., 1988). This idea of multiple levels of influence interacting to determine health behavior is widely accepted.

Figure 1 displays ISU predictors in the social ecological framework. This figure illustrates the three spheres of influence on ISU risk proposed; individual, socio-familial, and neighborhood-level determinants. Adapted from the social-ecological theory, this model proved useful in theorizing the system of factors impacting individual ISU risk for this study. Each level interacts with and influences overall risk of ISU in a hierarchical manner that has been observed in multiple studies (Boardman et al., 2001; Carpiano et al., 2011; Karvonen & Rimpela, 1997; Schroeder et al., 2001; Sellstrom et al., 2011).

A longitudinal study published in 2011 found a 73% increase in the likelihood of hospital admission from drug abuse in populations of adults who spent their adolescence in neighborhoods with poor economic status compared to affluent neighborhoods (Sellstrom et al., 2011). This finding was born out despite controlling for individual factors including gender, housing, and income. In addition, the researchers found an 8% variation in drug abuse hospitalization rates between the high and low income neighborhoods which was deemed quite large compared to previous studies (Sellstrom et al., 2011). These results suggest an effect of neighborhood-level determinants that remains when individual risk factors are held constant.

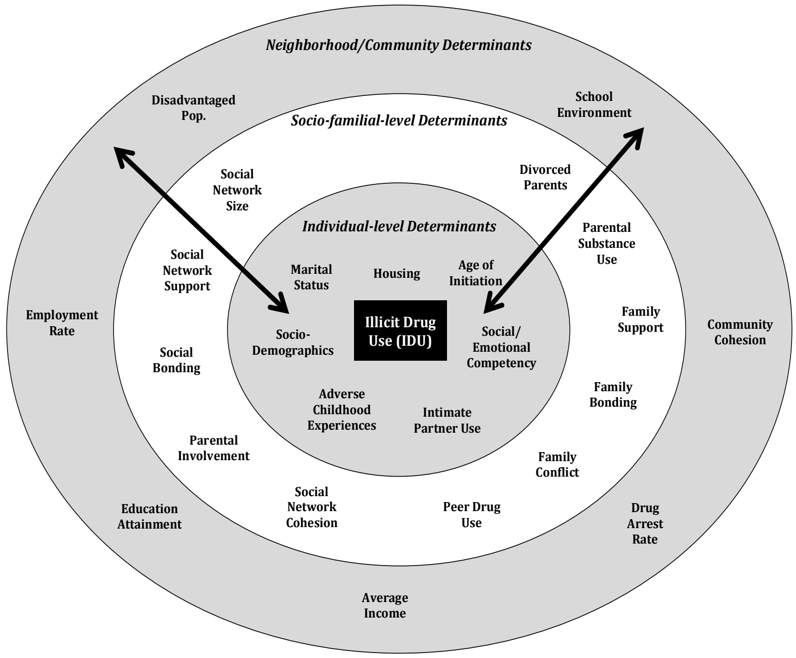


Figure 1. Social-Ecological Model of Illicit Substance Use
(adapted from McLeroy et al., 1988)

Another study published in 2007 involved a sample of 1305 adults from 249 neighborhoods in Baltimore, Maryland who were part of the Self-Help and Eliminating Life-Threatening Diseases study (SHEILD) (Williams & Latkin, 2007). The goal of the study was to examine the effects of social network and neighborhood factors on current heroin and cocaine use. Bivariate and multi-level analyses suggested the association between social network characteristics (i.e., drug influences, ties to full-time employees, and support) and ISU was significant. Results from the multi-level logistic models indicated that neighborhood-level indicators (poverty) were significantly associated with heroin and cocaine use but that its inclusion did not diminish the effect of social network characteristics (Williams & Latkin, 2007). This result further illustrates the complexities underlying the system of ISU determinants.

Other studies have explored the relationship between social networks and neighborhood with regard to individual ISU using similar modeling techniques with comparable results. Social network and neighborhood characteristics both play an important role in determining individual ISU risk. In his 2009 article, Galea is critical of the then current approach to risk analysis, claiming that its short sighted interpretation of cause and effect does not account for feedback interactions between multiple outcomes in the context of multi-level analyses. He advocates for the application of complex systems modeling, citing its utility in other scientific disciplines to illustrate the need for this perspective in the social sciences (Galea et al., 2009).

Short of applying these complex systems modeling methods, much progress can be made in ISU research if studies maintain a social epidemiology perspective. That is to say research should strive to account for multiple levels of determinants thus becoming ever more efficient at describing pathways of influence between and across levels of predictors. Moving into the discussion of NMPDU and then rural OUD, reference will be made back to this concept of the neighborhood's impact on the individual's ISU risk.

Non-Medical Prescription Drug Use (NMPDU)

NMPDU is unique in the world of ISU in that the substances being misused are socially and legally sanctioned for their therapeutic value in the health field. Prescription drugs are judged on their use vs. abuse potential. Illicit drugs, such as heroin and cocaine are classified by the Drug Enforcement Agency (DEA) as Schedule I because their use constitutes abuse or misuse, as they have no therapeutic value. Prescription drug schedules on the other hand range from II to V, with II having the most abuse potential (e.g., oxycodone, hydrocodone, fentanyl, etc.). Schedule classification affects dosage, dispensation, oversight, etc., and includes the therapeutic value of the individual drug in its calculus. When we consider that the health care system is dispensing these drugs for legitimate uses, it becomes clear that the production, availability, and perceived risk for these drugs will likely vary greatly from illicit drugs.

The following discussion will concentrate on the study of NMOU determinants, as prescription analgesics tend to be the most abused and are consequently responsible for 72% of all pharmaceutical overdose deaths (Centers for Disease Control and Prevention, 2014a). Considering NMOU in a historical context, we have vastly more OPRs available for use, both legitimate and illicit, in the community than ever before (King et al., 2014). The prevalence and distribution of OUD along with overdose mortality has changed over the last 20 years, trending upward in most areas right along with prescribing rates. The data indicating greater availability coupled with reports from over 60% of past-year non-medical prescription drug that they are getting their most recent supply from a friend or relative, who got their OPRs from a single doctor suggests that legitimate prescribing practices in the medical community today are contributing heavily to NMOU and overdose (Substance Abuse and Mental Health Data Archive, 2014).

The legitimate commercial distribution element is missing in the system of ISU determinants. There is no sanctioned infrastructure for the distribution of heroin or crack cocaine. Because of the duality inherent in public policy governing prescription drugs, the community is confused about how to feel regarding the dangers of non-medical or even medical use of OPRs. National surveys have revealed that aside from alcohol and marijuana, adolescents perceive prescription drug abuse to be less risky than any other drug use (Johnston et al., 2010). This perception could be changing as we now see much more attention paid to NMOU in the media; however, low perception of risk remains a contributing factor to the prevalence of NMOU.

An ecological study conducted in 2009 found significant associations between the volume of media coverage and overdose mortality rates (Dasgupta et al., 2009). A temporal relationship between media coverage and opioid overdose mortality was established using time-lagged regression techniques producing results that indicated much of the variance in mortality was explained by the model (R^2: 88%) (Dasgupta et al., 2009). This association is tenuous at best and does not imply causation, which the authors recognize; however, it does bring the role of responsible media coverage into the conversation around public risk perception of NMOU.

In addition to prescribing practices and harm perception, NMOU is influenced by programs established to reduce the opportunity for what is referred to as doctor shopping, a practice employed by high risk users to access more OPRs by procuring multiple prescriptions from different providers. Prescription drug monitoring programs (PDMPs) have been established in 47 states as of 2014, with the remaining states pushing legislation through currently (National Alliance for Model State Drug Laws, 2014). These PDMPs are databases that physicians and pharmacists can reference and append in order to identify individuals attempting to doctor shop.

While PDMPs represent a positive step toward a forward thinking system for distributing OPRs and other prescription pills with abuse potential, it does not necessarily reduce NMOU in the majority of at-risk populations. As mentioned above, most non-medical users report getting their pills from a friend or family member with a legitimate prescription, not through doctor shopping. Despite this fact, a study has shown that the implementation of PDMPs can reduce overdose mortality rates (King et al., 2014).

<u>“Rurality” as a Neighborhood-Level Determinant</u>

The fact that rural America continues to experience disparate rates of ISU compared to the rest of the nation as evidenced by the comparatively meteoric rise in unintentional overdose deaths in these areas during the early 21st century has been discussed in previous sections (Paulozzi & Xi, 2008).

Figure 2 shows the OPR prescribing patterns in the US for 2010 (Centers for Disease Control and Prevention, 2014a). The effect of “rurality” on prescribing practices however, is not constant across the US. In fact the ten highest prescribing states are in the Southeast, with Alabama ranking number one at 1.43 OPR prescriptions per state resident (Centers for Disease Control and Prevention, 2014b). For the past two decades prescribing patterns have been trending upward with drug overdose mortality, suggesting the impact of OPR dispensation on overall ISU is significant (Figure 3).

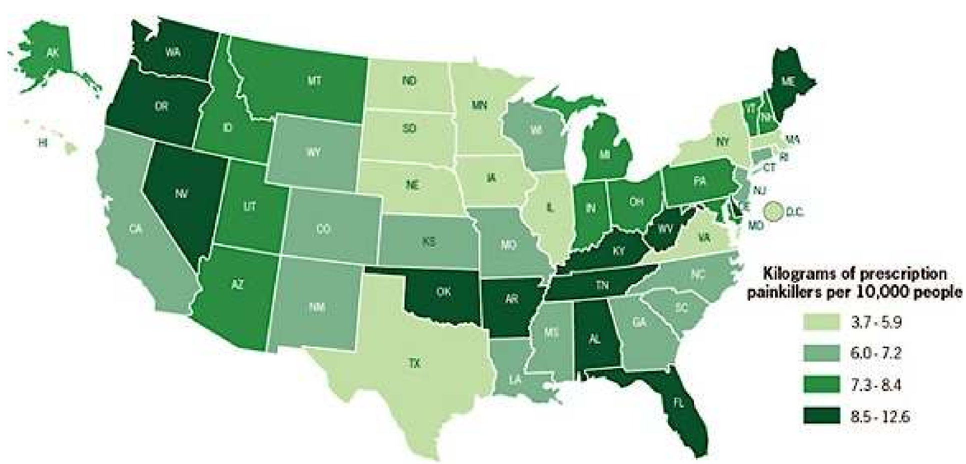


Figure 2. Painkiller prescribing rates per 100,000 residents by state, 2010
Source: CDC, 2014a

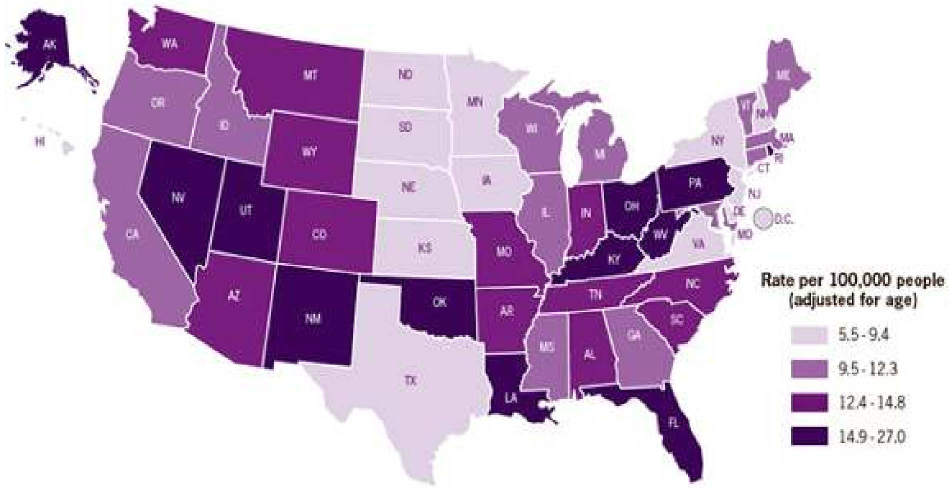


Figure 3. Drug overdose deaths per 100,000 by state, 2008.
Source: CDC, 2014a

Through a discussion of the existing literature, a set of individual, social, institutional, and community-level factors associated with ISU risk has been identified. These elements have been included in a proposed model of their inter-related nature regarding potential influence on ISU and NMOU. This model is now applied to a discussion of identified risk factors in rural populations and their contribution to the rise in NMOU outcomes in the last two decades.

When considering determinants for NMOU in rural America, the most obvious element is that the supply of prescription medications available for abuse in rural areas is higher on average than suburban and urban areas. Those states with 20% or more of their populations living in rural areas, specifically those in Appalachia, tend to have the highest OPR prescribing rates in the nation (Centers for Disease Control and Prevention, 2014b).

While these figures illustrate the connection between prescribing and drug overdose deaths on the ecological level that cannot be assumed to hold for the individual, there remains the strong indication of a significant impact on NMOU rates from overprescribing across the US, particularly in rural areas.

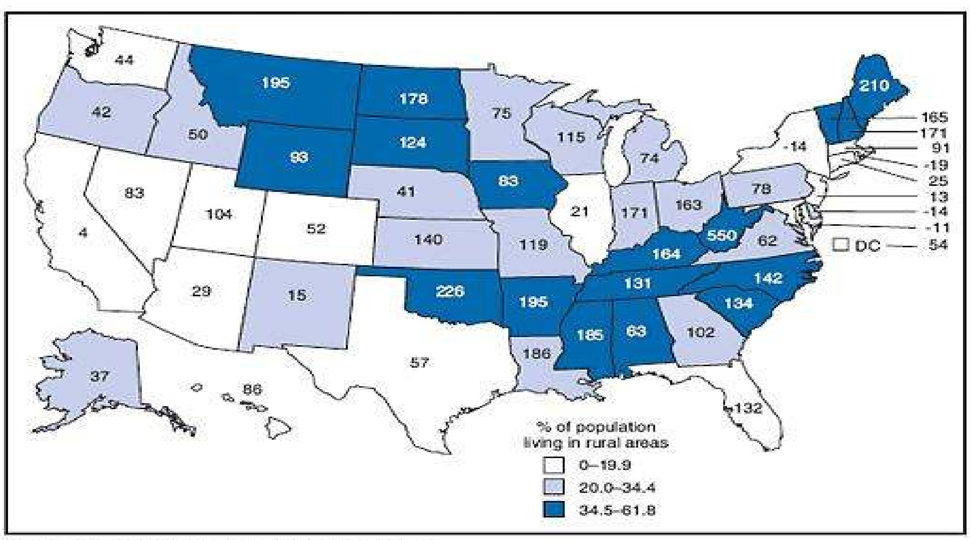
Figure 4 below indicates the percent change in unintentional overdose deaths between 1999 and 2004, by percent state population living in rural areas (Centers for Disease Control and Prevention, 2007). The map clearly indicates that states with higher percentages of people living in rural areas experienced a steeper increase in unintentional mortality from overdose.

According the Appalachian Regional Commission's 2012 report, personal income for the Appalachian region, which is 42% rural, was 82% that of the US average indicating fewer employment opportunities for people living in Appalachia (United States Department of Agriculture, Economic Research Service, 2014).

Rural areas in general experience a depressed economic state, with higher unemployment and poverty compared to the rest of the nation. In 2012 the United States Department of Agriculture (USDA) estimated that 12.2 percent of children in rural areas lived in deep poverty, income less than half the poverty level, compared to 9.2 percent of children in metro areas (United States Department of Agriculture, Economic Research Service, 2014). The roots of these socioeconomic disparities are found in systemic changes in economic resources and thus overall availability of resources in rural areas.

During the last half of the 20th century, rural areas in the U.S. underwent a significant decline in economic viability, causing disparate rates of unemployment, low education, and poverty as mentioned above (Thomas et al., 2009). This economic distress in rural America has lead to a dramatic emigration of young adults aged 18-24 years, contributing to further economic decline and a possible concentration in rural areas of populations at risk for substance abuse disorder. Individuals remaining in areas of low economic opportunity may exhibit fewer qualities, such as higher educational aspiration, that are protective against risky behavior (Leukefeld et al., 2007; Roscigno & Crowle, 2001). This clustering of individuals at higher risk is one possible explanation for the high prevalence of NMOU in rural America.

Mental health in rural America is an important contributing factor to NMOU, as rates of anxiety and depression are high in these areas. Historically rates of serious mental illness (SMI) have been comparable with those found in urban areas; however, accessibility and acceptability of prevention and treatment services in rural areas is quite different (US Department of Health and Human Services, Health Resources and Services Administration, Office of Rural Health Policy, 2005). Rural populations tend to enter treatment at a later age and at higher SMI severity, indicating decreased treatment service access and utilization (US Department of Health and Human Services, Health Resources and Services Administration, Office of Rural Health Policy, 2005).



* Age-adjusted rates per 100,000 population.
† Defined as the percentage of the population living in census blocks below a certain population density, based on U.S. Census data for 2000 (*4*).

Figure 4. Percentage change in unintentional poisoning mortality rates, by rural state, 1999-2004
Source: CDC, 2014b

The impact of SMI such as major depressive episodes (MDE) and anxiety disorders on the risk of ISU has been shown to be significant in nationally representative samples. A longitudinal study conducted using data from the National Comorbidity Survey (NCS) indicated that individuals reporting no SUD at baseline were 3 to 5 times as likely to report SUD at a ten year follow-up if they experienced MDE or various anxiety disorders in the interim (Swendsen et al., 2010). This is consistent with findings from the study of adolescent NMOU in rural areas (Havens et al., 2011). In addition, a study done in 2008 indicated higher rates of treatment for MDE in the adult population within Appalachia (National Opinion Research Center, 2008).

Rural communities report greater cohesion within their neighborhoods as well as larger family and social networks. NSDUH data show that more than 60% of individuals reporting NMOU indicate that they most recently got drugs from a family member or friend (Substance Abuse and Mental Health Services Administration, 2014). This has profound implications for NMOU in rural areas. With a wider and more cohesive social network, rural NMOU could be moderated by the impact of what amounts to an increased availability of prescription pills. Individuals with risk factors such as unemployment, low educational attainment, and SMI would essentially have a larger pool of individuals from which to solicit drugs (Keyes et al., 2014).

As illustrated in figures 2 and 3 above, availability appears to have a significant impact on NMOU; therefore the rural resident with risk factors common across geographic regions has increased likelihood of NMOU, and transitively OUD, by virtue of, among other factors, the social network characteristics found in rural areas.

Rural designation is applied within this study as a proxy for the matrix of socio-familial and community-level determinants found to be common in these areas (i.e., social network characteristics, educational resources, unemployment rates, etc.). Individual level risk factors will be included as covariates, thus controlling for their effect, in order to identify the impact of "rurality" on the measurement OUD and the latent classification of SUD.

Abuse and Dependency Measurement

The valid assessment of SUD is important, not only for the health of the individuals diagnosed, but also for the development of public policy dictating the need for specific interventions within targeted populations. Public health officials and agencies must be able to trust the functioning of diagnostic tools within and across populations. The DSM-IV is currently the preferred instrument for the measurement of self-reported SUD used for population-based survey assessment. Because of its wide use, this study has far reaching implications for public health practice and research.

Currently our understanding of the prevalence of SUD comes from studies like the NSDUH, which is administered via interview assisted computer-based methods in the home, based on a randomized census block sampling frame. The sample is clustered, weighted and stratified to produce nationally representative estimates of SUD. Study of instrument validity across sub-groups is vital to trusting statistics produced from the survey, such as 4.5% of adults in the US report past year NMOU and of those 12.9% meets the criteria for SUD (Becker et al., 2008). This 0.58% of the population indicated in the Becker et al. study is at high risk for overdose, therefore that percentage must be as accurate as possible if the burden of unintentional overdose in the population is to be reduced.

Much research has been done on the functioning of the DSM-IV SUD criteria, assessing for DIF in ethnic, gender, age, and other sub-groups. Prevalence of NMOU in rural and urban populations has been researched extensively as outlined above. What remains to be fully understood are differences in OUD prevalence in rural and urban populations and perhaps more importantly, the functioning of the DSM-IV instrument across rural and urban sub-groups. Below is a discussion of the history of the DSM and its development, with an eye on DIF and measurement invariance assessment.

Since the 1950s when alcoholism was declared a medical condition by the American Medical Association, the diagnosis of SUDs has been evolving in the US. The basis for our current approach to dependency diagnosis, as first published in 1987 by the American Psychiatric Association's (APA) DSM-III, was established in 1976 when Edwards and Gross wrote on the alcohol dependence syndrome (American Psychiatric Association, 1980; Fenton et al., 2013). Following the inclusion of dependency criteria in its third edition, the APA revised the DSM multiple times to incorporate the results of extensive study into the validity of these criteria and their application. In 1987 the DSM-III-R was published and in it was included many of the abuse and dependency measures found in the DSM-IV and V which are in use today (Fenton et al., 2013).

Table 1 lists the 11 criteria for the DSM IV SUD diagnosis, cross-walking those measures with the DSM-V substance abuse disorder severity scale (American Psychiatric Association, 2000; American Psychiatric Association, 2013). For both instruments, there are 11 items making up the measurement of the SUD construct. The primary difference between the two is the dimensionality applied to the criteria.

In the DSM-IV abuse and dependence were measured separately as unique but related phenomena. Both constructs are measured on a threshold scale in order to establish a dichotomous measure of each (i.e., yes or no; individual exhibits SUD).

Table 1. DSM IV, V Abuse and Dependence/ SUD Severity Scale Criteria

Criteria	DSM-IV	DSM-V
	Dependence	Substance Use Disorder
Tolerance	x	x
Withdrawal	x	x
Taken more/longer than intended	x	x
Desire/ unsuccessful efforts to quit use	x	x
Great deal of time taken by activities involved in use	x	x
Use despite knowledge of problems associated with use	x	x
Important activities given up because of use	x	x
	Abuse	
Recurrent use resulting in a failure to fulfill important role obligations	x	x
Recurrent use resulting in physically hazardous behavior(e.g., driving)	x	x
Continued use despite recurrent social problems associated with use	x	x
Craving for the substance		x
Recurrent substance related legal issues	x	

An individual is identified as engaging in substance abuse if they endorse one or more of the abuse criteria. Dependence diagnosis is based on the endorsement of 3 or more items (American Psychiatric Association, 2000).

The DSM-V criteria are applied to a substance abuse severity scale, which is a one-dimensional categorical construct in which all items are weighted equally on a scale from 1 to 11 (American Psychiatric Association, 2013). An individual diagnosis can therefore land along the spectrum as mild (2-3 items endorsed), moderate (4-5 items), or severe (6+ items). For the move from DSM-IV to DSM-V SUD diagnosis, the APA dropped one item, recurrent substance use related legal issues, due to poor performance. This item was replaced by a measure of craving.

The move from a multi-dimensional, hierarchical assessment of SUD to a uni-dimensional categorical severity scale was based on multiple studies that supported the change (Gillespie et al., 2007; Hasin & Beseler, 2009; Saha et al., 2012; Wu et al., 2009a; Wu et al., 2011). Within the DSM-IV SUD diagnosis was a hierarchy of severity presumed between abuse and dependency, in which it was held that individuals with dependency were exhibiting a higher level of SUD; the argument being that to reach the level of dependence one had to abuse a substance for a period of time. In the DSM-V, all 11 items are weighted the same, the accumulation of which constitutes SUD severity rather than any itemization into abuse or dependence.

As mentioned above, much research has focused on the functioning of the DSM SUD criteria and its appropriateness as a tool for the assessment of the SUD construct. In a study conducted in 2008 using data from the 2006 NSDUH, researchers found that SUD measurement in adolescents (n=1291) was best assessed along a single factor continuum (Wu et al., 2009a). In other words, the hierarchical abuse and dependence formation of the SUD construct was not found to be appropriate. Results of their factor analysis and IRT indicated that the single factor construct was most parsimonious and that abuse did not necessarily occur at a lower level of OUD severity than dependence (Wu et al., 2009a).

Other studies of the factor structure of the DSM-IV criteria have found the progression from abuse to dependence present in alcoholics but not other substance users

(Ridenour et al., 2003). This suggests a potential need for drug specific items for the assessment of SUD, as well as casting doubt on the hierarchical nature of abuse and dependency. A twin study conducted in 2007 found that the DSM-IV criteria tended toward a single factor continuum rather than a two or three (Gillespie et al., 2007). They conducted a maximum likelihood factor analysis to test the dimensionality of the criteria and found that, despite the slightly better fit of the two and three factor structures, factor loadings were multi-dimensional making interpretation very difficult. In addition, correlation between the abuse and dependence factors were high dictating the need for a single level approach (Gillespie et al., 2007). Wu et al. interpreted their results in the same manner to reach the same conclusions in 2009 (Wu et al., 2009a).

These results were further confirmed in 2012 through study of data from the 2001-2002 NESARC, in which factor analysis was applied to the DSM criteria for multiple drugs including amphetamine, cocaine, and prescription drugs (Saha et al., 2012). In addition to concluding that the criteria fit a one-factor structure most parsimoniously, the researchers determined that no significant change was seen in the model fit when the "legal problems" criteria was removed, thus supporting the DSM-V revision (Saha et al., 2012). Wu et al. came to the same conclusion regarding this criterion, citing its poor discrimination and high severity as an indication of measurement error (Wu et al., 2011). The inclusion of the craving criteria has yet to be fully vetted, as the DSM-V instrument has not been used for national survey research at the time of this writing.

Measurement invariance assessment of DSM-IV criteria has produced mixed results, often dependent on the specific grouping variables analyzed. In 2009 Wu et al.

assessed for DIF by applying MIMIC methods to the 2006 public use NSDUH data (Wu et al., 2009a). The results of this analysis indicated that the items measuring withdrawal, time spent using, and continued use despite medical/ psychological problems functioned differently based on gender, race and ethnicity (Wu et al., 2009a). Females were more likely to endorse the withdrawal item as compared to males. African Americans were more likely to endorse time spent using compared to whites, but along with Hispanics, they were less likely to endorse continued use despite medical/ psychological problems (Wu et al., 2009a). Demographic characteristics and OUD liability were controlled for in the analysis. What this suggests is that there is some effect of gender, race and ethnicity on how an individual answers items of the diagnostic instrument.

In 2012, another study compared the prevalence of cannabis use disorder between a population of Native Americans and individuals of European descent. The study found that five of the DSM-IV measures varied in their likelihood of endorsement across ethnic groups (Gizer et al., 2013). The items they found to have DIF were those measuring withdrawal, caused physical or emotional problems, role failure, hazardous use, and social problems. The authors' interpretation of these results was most interesting for the psychosocial measures of abuse (i.e., role failure, hazardous use, and social problems). They suggest that DIF in these items constitutes a difference in the impacts of use across cultural groups, that despite being similar in SUD liability, the effects are not the same regarding employment and social function (Gizer et al., 2013).

Multiple studies have shown that DSM-IV criteria for assessing SUD fit a single factor, continuous severity scale structure, making assessment of DIF through IRT and MIMIC analyses possible. Research into the measurement invariance of these items has uncovered potential problems with the way they function across gender, race, and ethnicity. Because of this fact, along with the rising burden of OUD in rural America as measured by the DSM-IV instrument, it is important to understand how it functions across populations identified as rural and urban. This study will attempt to validate the DSM-IV measurement of OUD, apply the results of that analysis to the assessment of OUD in rural America as well as any possible interaction between "rurality" and SUD class.

The following three chapters will detail the statistical approaches taken (i.e. IRT, MIMIC, and LCA) in the analysis of data associated with OUD and SUD diagnosis within data collected from the 2011-2012 NSDUH. Results from each analysis will be discussed in each respective chapter as well as a brief summary of the findings and their implications. The final chapter will draw conclusions from all three analyses in an attempt to synthesize their results into a cogent discussion of the implications for public health and clinical practice.

CHAPTER 2

DESCRIPTIVE ANALYSIS OF DSM-IV ABUSE AND DEPENDENCE CRITERIA IN ADULT POPULATIONS OF RURAL AND URBAN PAST-YEAR NON-MEDICAL OPIOID USERS: AN APPLICATION OF ITEM RESPONSE THEORY

The objective of this study is to describe the functioning of the DSM-IV SUD criteria across rural and urban populations using IRT methods of assessment. The target population for this analysis is adult past-year non-medical users of prescription pain reliever. These individuals report using a prescription pain killer for purposes other than for which it was described or for the feeling it generated. Potential measurement invariance between the groups is assessed through the comparison of item characteristic curves, total information curves, and conditional standard errors of measurement.

Study Sample

Data from the 2011-2012 iterations of the NSDUH public use data file were sorted and merged on the case identifier using SAS 9.2 (N = 113,665). Data were cleaned and limited in SAS 9.2, selecting for adults who reported past-year NMOU living in large metro or non-metro areas (N = 3,369). Once the merged and limited data set was produced, MPlus 7 was used to account for clustering, stratification and weighting as dictated by the sampling methodology.

The NSDUH is a population-based survey developed to gather information about substance abuse prevalence and determinants by drawing a nationally representative sample of individuals 12 years and older (Substance Abuse and Mental Health Data Archive, 2014). Formerly known as the National Household Survey on Drug Abuse, the NSDUH has been employing a multi-stage area probability sampling strategy for all 50 states and the District of Columbia since 1999. The primary geographical sampling unit for the survey is census tracts that are aggregated under state sampling regions in cases where low population density dictates the need. This is done in order to include, for each census track, a minimum of 150 households in urban areas and 100 households in rural areas.

Administration of the survey is done via audio computer assisted self-interview, computer-assisted personal interview, and computer-assisted self-interview. These methods are intended to offer increased anonymity for respondents to ensure greater validity of the data. The restricted use data file for 2011 contains 70,109 records, which are limited to 58,397 for the public-use file. The 2012 public-use file contains 55,268 records, making the merged total 113,665. After limiting the data to adults in rural or urban areas, the final sample size used in the analysis was 3,369. The un-weighted percentage of this sample that was from a rural area was 20.54% (692).

Measurement Items

In the study sample, adult past-year NMOU was identified as those individuals 18 years or older reporting use of "any opioid pain reliever that was not prescribed for you or that you took only for the experience or feeling it caused" in the past year (Substance Abuse and Mental Health Data Archive, 2014). The outcome of interest was a diagnosis of abuse or dependence, referred to hereafter as substance use disorder (SUD), on prescription pain relievers based on the DSM-IV SUD criteria included in the survey. The main predictor was the three-level variable identifying sample regions as large metro, small metro, and non-metro. Large metro was defined as being within a metropolitan area and having a population greater than 1,000,000.

Small metro was within a metropolitan area with a population smaller than 1,000,000 and non-metro was outside of any metropolitan area and having a population smaller than 1,000,000. For the analysis, this variable was limited to two levels; large metro and non-metro. This was done in order to focus the analysis on differences between rural and urban populations as well as to encourage as much differentiation within the study sample as possible. The geographic identifier described is very limited and does not allow for the consideration of the continuum of rurality, nor the urbanization of small metro regions. In order to increase confidence in the levels of the main predictor, the more ambiguous small metro category was excluded. Throughout this article large metro will be referred to as urban while non-metro will be identified as rural.

Table 2 lists the 11 items used within the DSM-IV to diagnose opioid use disorder (OUD). This set of items has changed in the new edition of the manual, the DSM-V, dropping the legal item for one that addresses craving. The details of this change and its implication for the factor structure of SUD are discussed in Chapter 1. Table 3 lists definitions for each item as it is asked in the NSDUH, as well as the items used to create the composite measures.

Table 2. DSM-IV Abuse and Dependence Criteria

Criteria (Variable Name)	Dependence
Tolerance (TOLERANCE)	x
Withdrawal (WITHDRAW)	x
Taken more/longer than intended (LIMIT)	x
Desire/ unsuccessful efforts to quit use (REDUCE)	x
Great deal of time taken by activities involved in use (TIME)	x
Use despite knowledge of problems associated with use (TOTPROB)	x
Important activities given up because of use (ACTIVE)	x
	Abuse
Recurrent use causing failure to fulfill important role obligations (WORKPROB)	x
Recurrent use resulting in physically hazardous behavior (RISK)	x
Continued use despite recurrent social problems associated with use (FAMPROB)	x
Recurrent substance related legal issues (LEGAL)	x

Table 3. Variable Codes for NSDUH Survey Items Addressing DSM-IV SUD Criteria

USETIME	Spent a great deal of time over a period of a month getting and using
OVERTIME	Spent a great deal of time over a period of a month getting over the effects of pain relievers
TIME**	Spent a great deal of time over a period of a month getting, using, or getting over the effects of pain relievers
LIMIT	Used pain relievers more often than intended or was unable to keep set limits on pain reliever use
USEMORE	Needed to use pain relievers more than before to get desired effects
LESEFFECT	Noticed that same amount of pain reliever use had less effect than before
TOLERANCE**	Needed to use pain relievers more than before to get desired effects or noticed that same amount of pain reliever use had less effect than before
REDUCE	Inability to cut down or stop using pain relievers every time tried or wanted to
EMOTPROB	Continued to use pain relievers even though they were causing problems with emotions, nerves, mental health
PHYSPROB	Continued to use pain relievers even though they were causing physical problems
TOTPROB**	Continued to use pain relievers even though they were causing problems with emotions, nerves, mental health, or physical problems
ACTIVE	Pain reliever use reduced or eliminated involvement or participation in important activities
WITHDRAW*	Reported experiencing three or more pain reliever withdrawal symptoms at the same time that lasted longer than a day after pain reliever use was cut back or stopped
WORKPROB*	Serious problems at home, work, or school caused by using pain relievers
RISK	Used pain relievers regularly and then did something that might have put you in physical danger
LEGAL	Use of pain relievers caused you to do things that repeatedly got you in trouble with the law
FAMPROB	Problems with family or friends probably caused by using pain relievers

*WITHDRAW symptoms include (i) feeling kind of blue or down, (ii) vomiting or feeling nauseous, (iii) having cramps or muscle aches, (iv) having teary eyes or a runny nose, (v) feeling sweaty, having enlarged pupils, or having body hair standing up on skin,(vi)having diarrhea, (vii) yawning, (viii) having a fever, and (ix) having trouble sleeping

*WORKPROB includes neglecting their children, missing work or school, doing a poor job at work or school, losing a job or dropping out of school

**Composite item

When considering the structure of the DSM-IV SUD instrument and its application to the current study, some issues arose regarding low response frequencies for at least one of the SUD items; specifically the *FAMPROB* item. Meeting this criterion for abuse requires responding affirmative to problems with family AND affirmative to continued use, which equates to a survey skip logic that reduces the response rate associated with this item (i.e. continued use given family problems). Limiting the data in this way may contribute to poor standard error estimates; therefore the less stringent measure of *FAMPROB* was adopted. Previous studies have taken this approach with this criterion for IRT and MIMIC analyses (L. T. Wu et al., 2009).

In addition to making adjustments for the family problems criterion, the fit of a measurement model that included 14 items instead of the standard DSM-IV 11 items was explored. These fourteen items were made up eight indictors directly from the DSM-IV instrument along with 6 items used to build the remaining 3 composite measures. These composite indicators are identified in table 3 above by a ** next to the variable name. The indicators making up the composite measures are listed above each respective item.

Within the NSDUH survey, respondents are asked six questions that are used to calculate response to three criteria of the SUD instrument. One of these criteria is the *TIME* indicator, in which an either/or logic is applied to responses from the *USETIME* and *OVERTIME* indicators to calculate this criterion. The other two criteria are the *TOTPROB* and *TOLERANCE* measures that are similarly computed through an either/or logic. For this study of measurement invariance, which is an assessment of individual respondents' characteristics and their effects on the probability of endorsement, it was important to work with the items asked directly to respondents rather than those computed from multiple items. Before moving on to IRT assessment of the 11-item instrument, it was important to rule out the need for a 14-item model.

Statistical Analysis

Item Selection

The first step in the analysis was to test the fit of the 14-item instrument against the 11-item, through the application of confirmatory factor analysis (CFA). Chi-difference tests were not available for this analysis since these models are not functionally nested; therefore comparisons were made using standard indices: CFI > 0.90, RMSEA less than 0.10. In addition, item characteristic curves (ICC) were consulted to further inform the model selection.

Confirmatory Factor Analysis (CFA)

A CFA considering the fit of a two-factor and single-factor model was conducted as an added layer of validity of the study approach. Exploratory factor analysis (EFA) was not necessary in this case because the study objective was to validate an existing instrument rather than to build a new one with theorized constructs and factor structures. Figure 5 illustrates the two models considered in the CFA. The 2-factor model is one that hypothesizes individual constructs for abuse and dependence, whereas the single-factor approach theorizes one construct, SUD, which is measured by all 11 items.

Option DIFFTEST was used in Mplus 7 to determine the best model fit comparing the 2-factor abuse and dependence model and the single-factor SUD model. This option calls up a chi-square difference test between nested models. As with the previous CFA, other considerations were taken into account in choosing the model for analysis, including correlation between factors and multi-dimensionality of indicators.

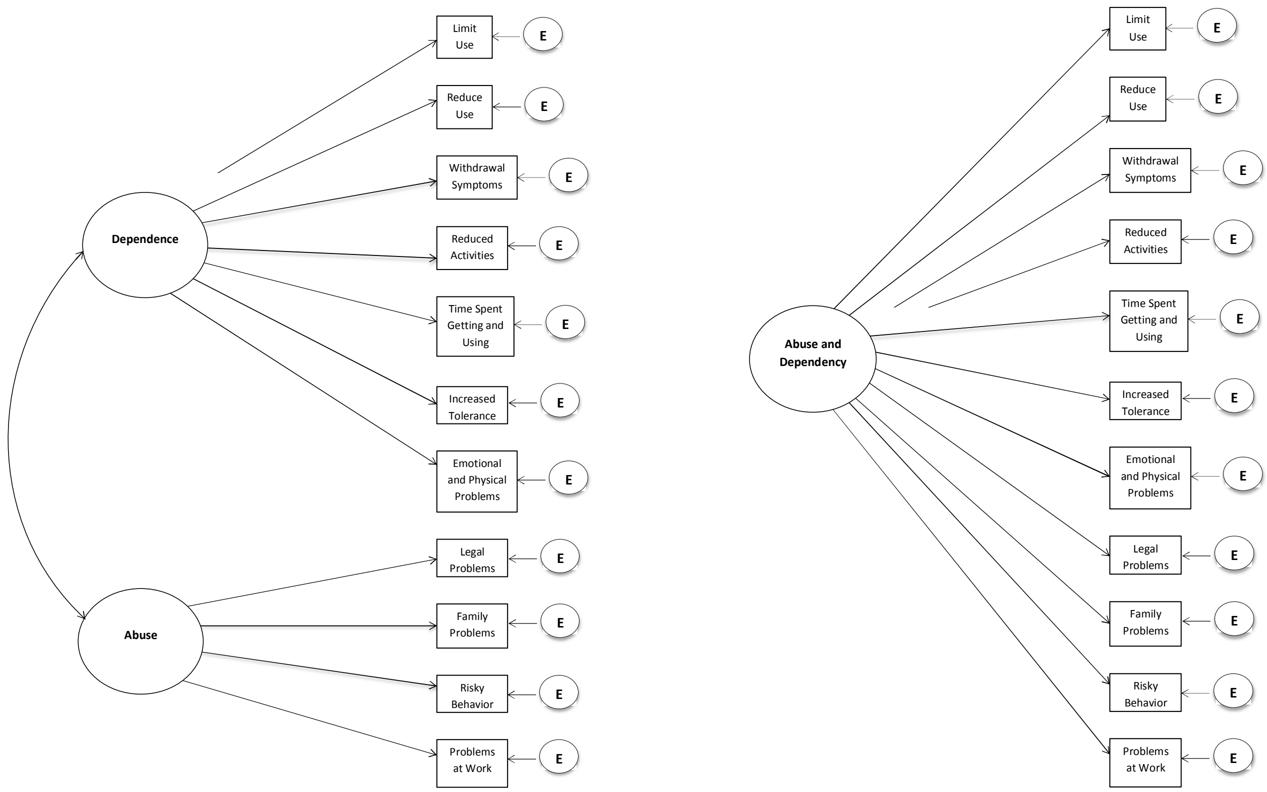


Figure 5. Single and Two-Factor Confirmatory Factor Analysis of Abuse and Dependence

Once factor structure was established IRT methods were applied to assess measurement invariance in the DSM-IV criteria among the population of rural and urban adult past-year non-medical opioid users.

Item Response Theory

The data were modeled using the two-parameter (2PL) item response function (IRF) below,

$$P(Y_i = Yes|\theta, b_i, a_i) = \frac{\exp[a_i(\theta - b_i)]}{1 + \exp[a_i(\theta - b_i)]} \quad (2.1)$$

where *a* is the discrimination or slope of the curve for each item, *b* is the difficulty or probability of endorsing the item ≥ 50%, and Y_i is the response to the ith item given OUD severity (θ) (Thorpe & Favia, 2012) . This model was chosen over the 1 or 3 parameter item response functions because it allows for the estimation of the item discrimination (a) but does not include the guessing parameter estimate, which applies more to test scoring for scholastic research and was not deemed relevant to this study.

The IRF produces item characteristic curves (ICC), which are logistic curves that can be used to visualize the functioning of each item in the instrument in comparison to all other items. The x-axis for the ICC plot measures θ along a z-scale with mean 0 and variance 1, and the y-axis indicates the probability of endorsing each item (Figure 2.2).

Therefore the difficulty (b) of an item corresponds to a z-score value of θ for which a horizontal line can be drawn through the point on the curve indicating a 50% probability of endorsing the item.

The IRF above was used to plot ICCs for the 11-item and 14-item instruments, in order to inform selection of an appropriate model. Response rates for each indicator

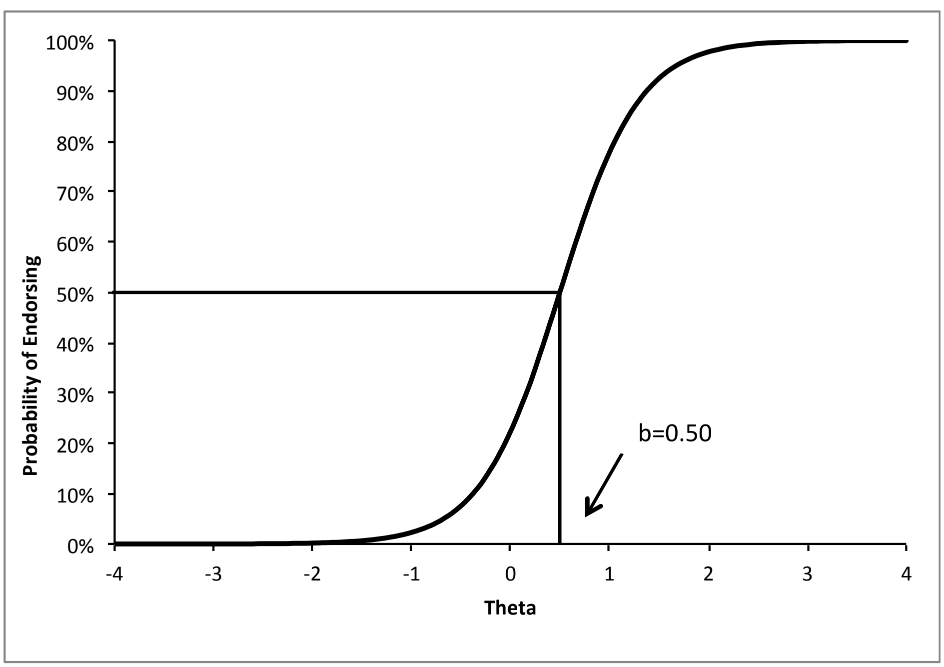


Figure 6. ICC Plot Example

making up composite measures (i.e. physical problems, emotional problems, time spent using and time spent getting over, taking more than before, same amount had less effect) were considered to ensure proper interpretation of item difficulties and discrimination parameter estimates.

In addition to the ICC plots, total information curves (TIC) were plotted to assess the factor score values at which the instrument is most functional. The curve that is plotted is a function of the derivative of the probability of $Y_i = 1$ at θ,

$$(2.2) \qquad I(\theta) = \sum_{k=1}^{K} \frac{1}{P_{ik}} \left(\frac{dP_{ik}(\theta)}{d(\theta)} \right)^2$$

where P_{ik} is the probability of responding in the affirmative for item i at value k of θ (Thorpe & Favia, 2012). The function above generates a TIC that depicts the variable estimation quality of the IRF across the factor score continuum.

The TIC can be easily transformed in order to plot the conditional standard error of measurement (CSEM), which displays a curve of the standard errors along the factor score continuum. This plot provides a more conventionally understood illustration of the quality of parameter estimation.

The conditional SEM is calculated as the square root of the inverse of the TIC (Thorpe & Favia, 2012) .

$$(2.3) \qquad CSEM = \sqrt{\frac{1}{I(\theta)}}$$

Comparisons were made between ICC, TIC, and CSEM plots of data from rural and urban samples. Criteria for comparison were based on visual assessment of these plots as well as a review of model parameters for each group.

Results

The results of the item selection analysis indicated that the 11-item instrument would fit the data best and that composite items functioned better than the individual indicators used to calculate them. The CFI for the 14-item model was 0.972 which is above the threshold for good fit; however the RMSEA was between 0.055 and 0.062 which is above the cut off of 0.05 for acceptable fit.

In addition, the ICC plot for the 14-item model displays the poor functioning of the *PHYSPROB* and *LESEFFECT* items (Figure 7). These items have low discrimination parameter estimates (a = 0.089 and a = 0.053 respectively) with slopes approaching zero, making them inappropriate as individual items (see also table 4).

In addition to the poor discrimination, the *LESEFFECT* item has a difficulty that is more than 27 standard deviations above the mean OUD factor score. Since theta is on a z-scale, meaning 99.73% of the population is within 3 standard deviations, a difficulty of 27 for an item suggests the item is not functional in assessing theta. Only a tiny fraction

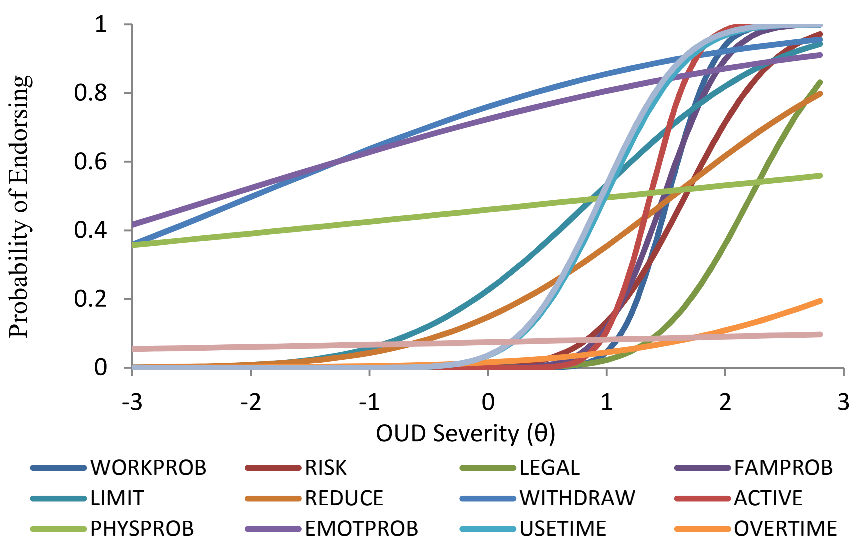


Figure 7. ICC Plot of 14-Item Instrument

of a percent of the population should ever endorse *LESEFFECT*. The fact that 7.4% of the sample in this study endorsed the *LESEFFECT* item is an artifact of the poor discrimination, which makes estimating difficulty with any precision impossible.

Figure 8 is the ICC plot for the 11-item instrument. An examination of the curves for composite measures, TOTPROB and TOLERANCE, indicates that the items paired with *PHYSPROB* and *LESEFFECT* (i.e. *EMOTPROB* and *USEMOR*, respectively) function very closely to the composite measures themselves, suggesting either a low response frequency for the *PHYSPROB* and *LESEFFECT* items, or that the composite measure of problems and tolerance are driven by responses to the *EMOTPROB* and *USEMOR* indicators, respectively.

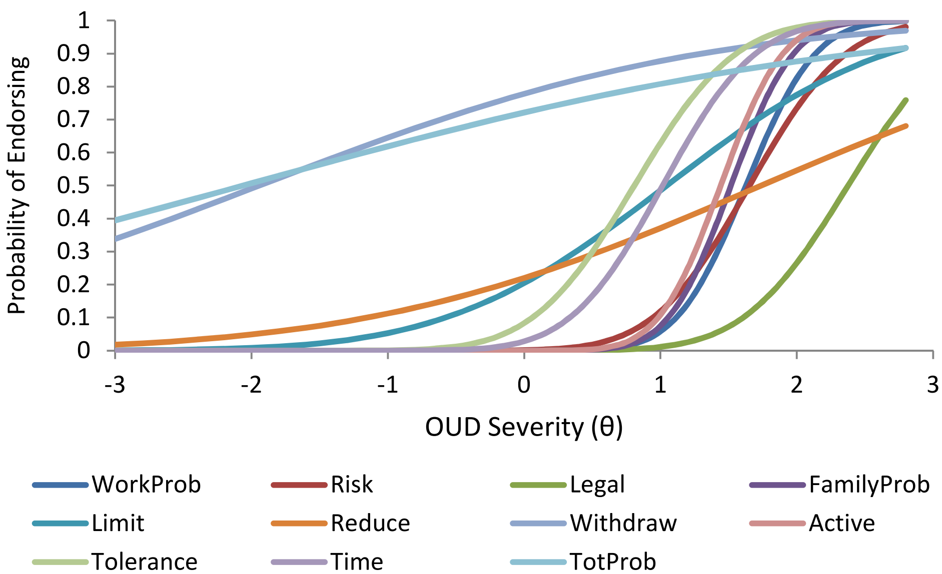


Figure 8. ICC Plot of 11-Item Instrument

Fit indices for the 11-item model were only marginally better than the 14-item estimates (CFI = 0.985 and RMSEA = (0.051, 0.060)). The selection of a model was then based on theory, which is grounded in the 11-item consensus measure instrument from the DSM-IV, as well as a comparison of parameter estimates and ICC plots for the two models.

Data in Table 4 indicate that each of the composite items (*TOTPROB, TIME,* and *TOLERANCE*) have greater discrimination than either of their paired items (PHYSPROB/EMOTPROB, USETIME/OVERTIME, USEMOR/LESEFFECT, respectively) with the exception of *TOLERANCE,* which has a smaller discrimination value than *USEMORE.*

The difficulty associated with the *LESEFFECT* item dictates the use of the composite item rather than the pair in that case. The item information curves in Figure 9 illustrate the functioning of each item in its estimation of OUD factor score. The plot suggests that the *WORKPROB*, *RISK*, and *FAMPROB* items function better than other items and that *PHYSPROB* and *LESEFFECT* exhibit very low TIC maximum values.

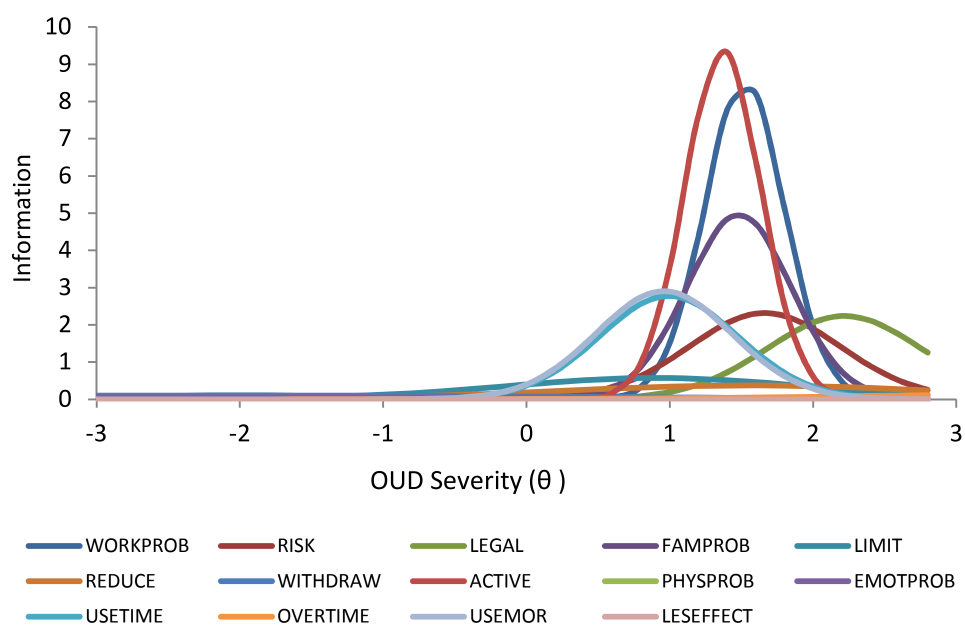


Figure 9. Item Information Curve for 14-Item Model

Table 4. 2-Parameter Model Estimates for 14-item and 11-item Instruments

			14-Item Instrument		11-Item Instrument	
	Total Responses	% Endorsed	Discrimination (S.E.)	Difficulty (S.E.)	Discrimination (S.E.)	Difficulty (S.E.)
WORKPROB	3281	7.3	3.227 (0.341)	1.521 (0.038)	3.251 (0.352)	1.52 (0.038)
RISK	3280	7.7	1.679 (0.117)	1.663 (0.052)	1.677 (0.116)	1.664 (0.052)
LEGAL	3281	2.9	1.649 (0.156)	2.218 (0.085)	1.651 (0.156)	2.217 (0.085)
FAMPROB	3099	8.5	2.458 (0.19)	1.484 (0.039)	2.481 (0.195)	1.482 (0.039)
LIMIT	962	28.2	0.833 (0.049)	0.903 (0.072)	0.816 (0.048)	0.914 (0.073)
REDUCE	1123	19.2	0.672 (0.049)	1.558 (0.113)	0.662 (0.049)	1.575 (0.115)
WITHDRAW	569	74.7	0.357 (0.037)	-1.98 (0.268)	0.343 (0.036)	-2.048 (0.279)
ACTIVE	3280	9.5	3.378 (0.314)	1.37 (0.034)	3.388 (0.323)	1.369 (0.034)
TOTPROB	-	-	-	-	0.272 (0.03)	-2.227 (0.348)
PHYSPROB	63	46	0.089 (0.077)	1.126 (2.031)	-	-
EMOTPROB	435	71.7	0.268 (0.033)	-2.216 (0.373)	-	-
TIME	-	-	-	-	1.975 (0.117)	0.896 (0.03)
USETIME	3289	19.2	1.838 (0.109)	0.992 (0.032)	-	-
OVERTIME	2657	2.5	0.465 (0.046)	4.651 (0.418)	-	-
TOLERANCE	-	-	-	-	1.783 (0.098)	0.745 (0.029)
USEMORE	3282	19.9	1.88 (0.116)	0.959 (0.032)	-	-
LESEFFECT	2625	7.4	0.053 (0.009)	27.328 (4.617)	-	-

The results of the CFA DIFFTEST procedure suggested the 2-factor model was a better fit for the data (Chi-square= 20.481, df=1, p-value <0.0001); however, as has been the case in previous studies (Gillespie et al., 2007; L. T. Wu et al., 2009b) the two factors were highly correlated and there was evidence of multidimensionality with 9 of the 11 measures. Because of these two facts as well as the overlap of abuse and dependence items seen in the ICC plots, I chose to fit the single-factor model to the data, which was also supported by my theory.

Item characteristic curve (ICC) plots were generated for the rural and urban samples (Figures 10 and 11), which indicated some potential differences in difficulty and differentiation between the rural and urban samples. One item in particular, *WORKPROB,* had a discrimination parameter estimate 1.72 times higher in the rural sample compared to the urban (Table 5). Other indicators (i.e. *LIMIT, REDUCE, WITHDRAW,* and TOTPROB) had low discrimination estimates in both samples suggesting they functioned poorly independent of the grouping variable.

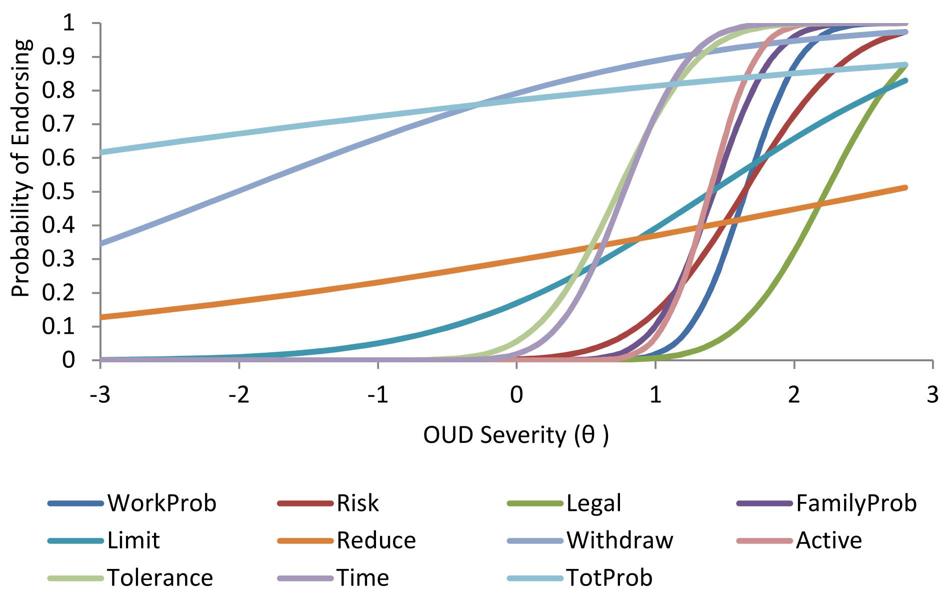


Figure 10. ICC Plot for Rural Sample

A visual assessment of the ICC plots for each sample suggests that the instrument functions marginally better in the urban population. Items like *REDUCE* appear to be more discriminant in the urban group. The same is true for the *LIMIT* item, which has a more dramatic slope in the urban ICC than in the rural. The majority of the indicators' ICCs do not differ greatly between the two plots; however, suggesting the instrument may function similarly in both rural and urban populations.

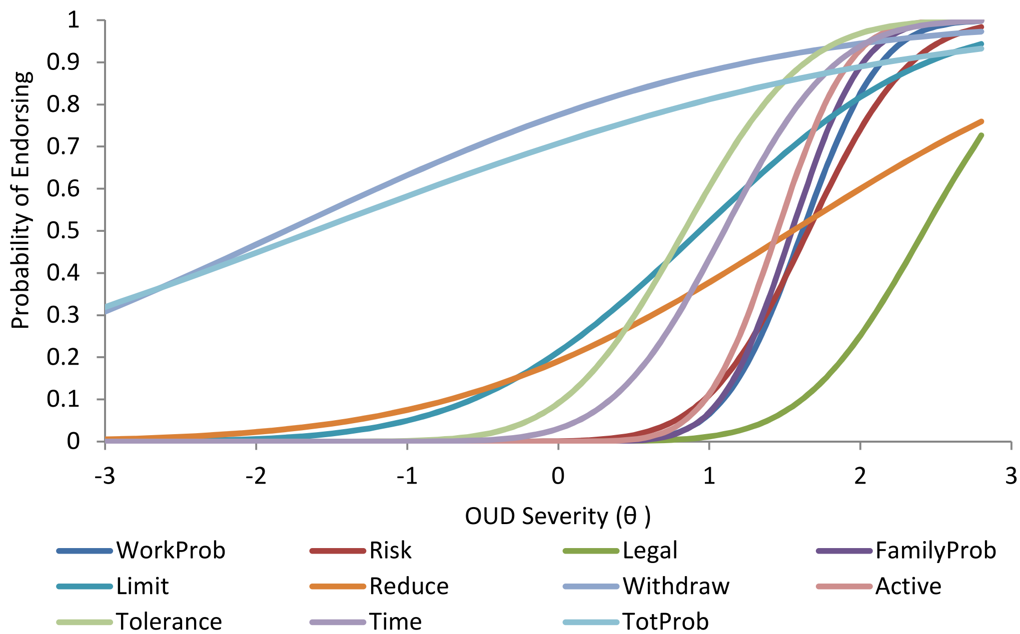


Figure 11. ICC Plots for Urban Sample

The range of differentiation values for the rural sample was 0.184 to 5.003 for the WORKPROB item (Table 5). The urban sample range for the same parameter was 0.331 to 3.106 for the ACTIVE item. Difficulty for the rural sample ranged from a low of -3.667 to 2.218 for the LEGAL item. The urban sample difficulty ranged from -1.854 to 2.215 (Table 5).

Table 5. 2-Parameter Model Estimates for Rural and Urban Samples

	Rural Parameters				Urban Parameters			
	Total Responses	% Endorsed	Discrimination (S.E.)	Difficulty (S.E.)	Total Responses	% Endorsed	Discrimination (S.E.)	Difficulty (S.E.)
WORKPROB	1032	7.3%	5.003 (1.555)	1.485 (0.063)	2249	7.3%	2.917 (0.352)	1.534 (0.048)
RISK	1032	8.6%	1.53 (0.17)	1.63 (0.093)	2248	7.2%	1.774 (0.158)	1.677 (0.062)
LEGAL	1032	2.8%	1.692 (0.279)	2.218 (0.149)	2249	2.9%	1.637 (0.189)	2.215 (0.104)
FAMPROB	1031	9.3%	2.165 (0.255)	1.456 (0.071)	2251	8.1%	2.686 (0.285)	1.493 (0.047)
LIMIT	331	28.7%	0.826 (0.084)	0.883 (0.123)	631	27.9%	0.814 (0.058)	0.928 (0.091)
REDUCE	381	20.2%	0.578 (0.079)	1.667 (0.23)	742	18.7%	0.712 (0.062)	1.531 (0.131)
WITHDRAW	195	74.9%	0.25 (0.061)	-2.767 (0.787)	374	74.6%	0.398 (0.045)	-1.789 (0.279)
ACTIVE	1031	9.3%	4.914 (1.198)	1.349 (0.058)	2249	9.5%	3.106 (0.338)	1.376 (0.042)
TOTPROB	150	74.7%	0.184 (0.053)	-3.667 (1.234)	323	70.9%	0.311 (0.037)	-1.854 (0.341)
TIME	1034	23.8%	2.095 (0.239)	0.79 (0.051)	2255	20.0%	1.937 (0.136)	0.947 (0.037)
TOLERANCE	1034	27.0%	1.66 (0.164)	0.716 (0.053)	2251	25.2%	1.843 (0.118)	0.759 (0.034)

An examination of the TIC for the instrument by rural verses urban samples suggests the criteria function better as a whole in the rural group (Figure 12). This assessment is based on a comparison of the maximum values for each curve. The rural sample has a higher TIC maximum. This difference is likely due to the higher overall discrimination values in the rural sample.

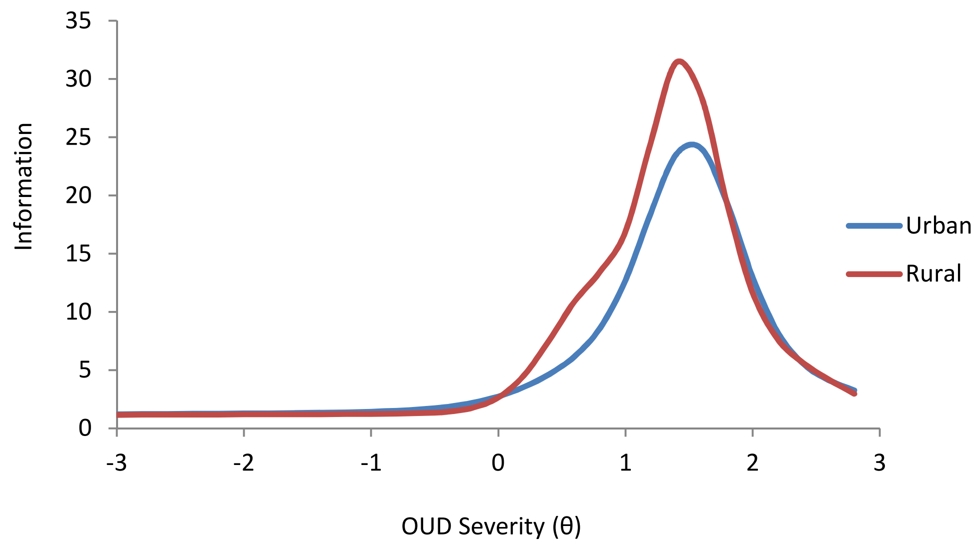


Figure 12. Total Information Curves, Rural v. Urban

Averaging the discrimination values for each item in the rural and urban groups generated an estimated total information area index, which is the integral of the area underneath the TIC. The area index for the rural sample was 2.17 and the urban was 1.65. The difference in area index values is reflected in higher rural TIC maximum in figure 12.

Through the application of some basic algebra to the TIC values, conditional standard error of measurement (CSEM) estimates can be generated that display instrument precision in terms of standard error. The curves for the urban and full samples overlay each other, while the rural CSEM deviates somewhat from both until close to factor scores of 2 or higher (Figure 13). Application of the instrument in both the rural and urban population appears to have approximately the same minimum CSEM at factor score 1.6 (Full=0.20, Rural 0.19, Urban=0.20).

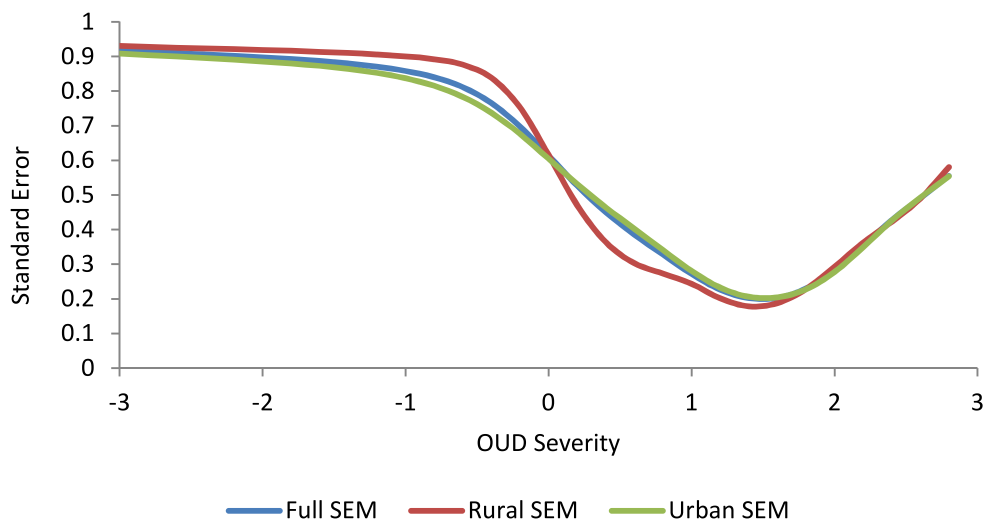


Figure 13. Conditional SEM for Rural, Urban and Full Sample

Discussion

Based on the IRT analysis it appears the DSM-IV instrument functions similarly across rural and urban populations. Some differences were seen in the range of both discrimination and difficulty parameters that was evident in the TIC plot as well as the area index calculation. This study applied descriptive methods to assess the function of the instrument. Statistical confirmation of discrimination differences requires methods such as multiple group analysis, which can test for variance in this parameter between groups. Difficulty variance is assessed using multiple indicators, multiple causes (MIMIC) in the following chapter.

In both groups, the instrument functions primarily to identify individuals on the higher end of OUD severity (1 to 2 standard deviations above the mean), which is appropriate for this type of instrument. The DSM-IV is of greater value for diagnostics if the most precise measurement is done within the population of users at the highest risk for negative outcomes from SUD. This is not necessarily the case for surveillance systems meant to identify early signs of SUD in the population. It is possible that another tool that is used for early intervention assessment perhaps would be more appropriate for inclusion in the NSDUH and other similar national surveys. Any instrument included in the NSDUH would, however need to be short as is the case with the DSM tool.

Based on these results, there is some cause for concern in the overall function of several items in the scale (i.e. *LIMIT, REDUCE, WITHDRAW,* and TOTPROB). These indicators had low discrimination in both the rural and urban samples, making them less useful in the diagnosis of SUD. This group of poorly functioning items represents over 36% of the indicators used to assess for SUD in the instrument, which calls into question the functioning of the entire set of criteria.

A significance test of differences in discrimination estimates between rural and urban samples conducted using confidence intervals resulted in four indicators being significantly different (*WORKPROB, WITHDRAW, ACTIVE,* and *TOTPROB*). Two of these indicators (*WITHDRAW* and *TOTPROB*) had very low discrimination in both samples and are of less interest. The other two items, *WORKPROB* and *ACTIVE*, had relatively high discrimination estimates in both samples (Table 5); however discrimination parameters were significantly higher in the rural sample for both items. This suggests measurement of these criteria is more precise when applied within rural communities.

The PHYSPROB received very few responses (63) in the full sample and the rate of endorsement was nearly 50%. This distribution is troublesome because it would suggest that continued use despite physical problems is the most common symptom of SUD; however, without a larger sample this conclusion cannot be drawn. The LESEFFECT item functioned very poorly, displaying a low discrimination and high difficulty, despite having a useful number of responses (2625). When combined with the USEMORE item its effect disappears and the composite item, TOLERANCE, displays a reasonable discrimination and difficulty placing it firmly in the middle of the other item parameter estimates (a=1.783, b=0.745). Further study into the relationship between individual items and SUD outcomes would be useful for understanding any qualitative differences between the different items.

CHAPTER 3

MULTIPLE INDICATORS, MULTIPLE CAUSES (MIMIC) ASSESSMENT OF MEASUREMENT INVARIANCE IN DSM-IV DIAGNOSIS OF OPIOID USE DISORDER ACROSS RURAL AND URBAN U.S. POPULATIONS

The objective of this study is to assess measurement invariance of DSM-IV opioid use disorder (OUD) criteria across rural and urban populations, identifying differential item functioning (DIF) within the instrument. Multiple indicators, multiple causes (MIMIC) model; a form of structural equation modeling (SEM) that employs factor analysis and regression to test the effect of sub-group categories (e.g., gender, race, rural vs. urban, etc.) on the probability of endorsing a measurement item, was applied a nationally representative sample of rural and urban survey respondents. In addition to identifying potential differences in item function across sub-groups, effects of covariates on OUD factor scores were calculated controlling for DIF found in MIMIC analysis.

Background

MIMIC is an approach used to test for invariance among survey items as they are administered across groups of sub-populations. First proposed in 1975 by Joreskog and Goldberg, MIMIC is designed to test measurement invariance by combining measurement modeling on one side with regression analysis on the other (Joreskog & Goldberger, 1975). Through this approach we can assess the potential association between multiple grouping variables and the measurement items.

In the previous chapter, a descriptive analysis IRT analysis was conducted the on data from the DSM-IV OUD instrument within the NSDUH. This step was taken in order to identify any variance in discrimination and difficulty parameters across rural and urban groups. Chapter 3 discusses the application of a statistically rigorous approach to testing measurement invariance within the difficulty parameter. Variance in this parameter across groups is referred to as uniform DIF. Non-uniform DIF will not be assessed as that requires a third approach, multiple-groups IRT or factor analysis, that is not likely to yield significant results in this case.

MIMIC analysis has been applied to many studies of DIF among test criteria (Joreskog & Goldberger, 1975). It has been shown to function as well or better when compared to other methods of uniform DIF detection such as factor analysis, SIBTEST, Mantel-Haenszel, and item response theory (Finch, 2005; Kim et al., 2012; Macintosh & Hashim, 2003; Shih & Wang, 2009; Willse & Goodman, 2008).

One limitation of MIMIC is its inability to detect non-uniform DIF, which occurs when the IRF differs across groups not only in its difficulty but its discrimination as well (Woods et al., 2009). In non-uniform DIF, the discrimination parameter varies across the levels of grouping variables, which in this study is the rural/ urban explanatory variable. When this variance occurs, probabilities of endorsement can shift to favor a different group at higher levels of the latent factor than the one evidenced at lower levels.

Figure 14 illustrates the difference between uniform and non-uniform DIF. The plots show that uniform DIF causes the difficulty, or latent factor score severity needed for endorsing probability to cross 50%, to be higher for the blue curve. In the non-uniform DIF example, the rate of change in endorsing probability is higher for the blue curve, meaning the item is better at discriminating between one level of the factor and the next compared to the red.

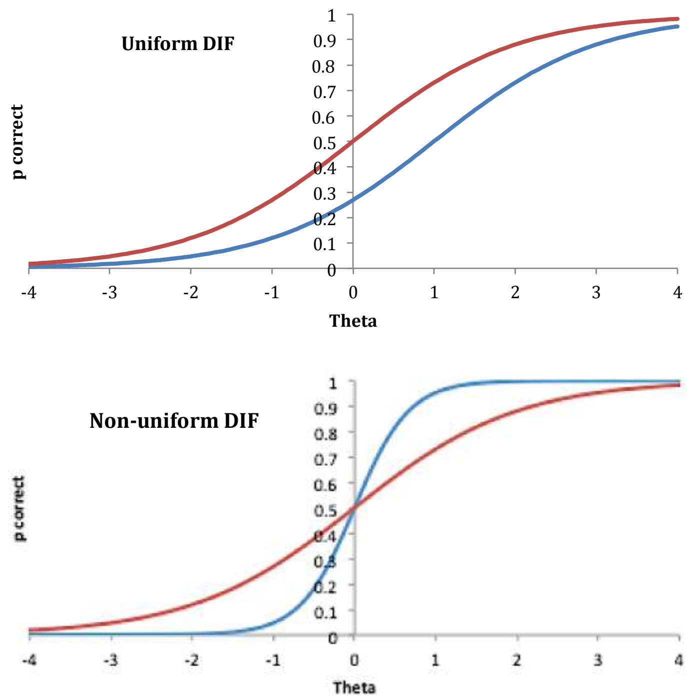


Figure 14. Uniform and non-uniform DIF

Despite its limitations, MIMIC was chosen for this analysis based on its ability to model multiple grouping variables and covariates simultaneously. In addition, parameter estimates produced by MIMIC are comparable to those estimated in IRT which is useful for discussing the results of this analysis in the context of the previous chapter's work. For this study, MIMIC was employed to assess for differences in item difficulty across rural and urban populations as well as a set of selected covariates.

Testing for the direct path between grouping variables and measurement criteria can be represented linearly as

$$Y_{ij} = \lambda_j \eta_i + \beta_j X_i + \varepsilon_{ij}, \quad (3.1)$$

$$\eta_i = \gamma X_i + \zeta,$$

where Y_{ij} is the observable manifestation of the latent construct for the ith respondent at the jth item, in this case SUD as measured by the 11 criteria. The observed outcome is modeled by the variable factor loading (λ_j), the latent factor (η_i), the effect of the grouping variable (β_j) on the observed measure (X_i), and the random effect (ε_{ij}) (Kim et al., 2012).

Effects on the latent factor score (η_i) are modeled in the second equation where (γ) is the slope estimate of the grouping variable in relation to the latent factor. The final element (ζ) indicates error associated with unmeasured variables.

The null hypothesis in the MIMIC analysis is $\beta_j = 0$ for all grouping variables included in the model. One distinct benefit of using the MIMIC approach is the ability to include all variables of interest to be tested against the probability of endorsing each item in the instrument simultaneously. Figure 15 illustrates the proposed MIMIC model. Only the rural/urban variable and a single β_j were included in the figure for illustrative purposes. The final model will test the effect of "rurality" (β_j) and several covariates on the probability of endorsing each item.

In addition to the assessment of uniform measurement invariance, the MIMIC model provides a method for controlling DIF when estimating the effects of model covariates on the latent factor score. This allows for a rigorous understanding of OUD determinants and their association with the latent factor itself. Once the final model has been selected, parameter estimates between covariates and the latent factor represent this relationship when controlling for DIF within all indicators in the model.

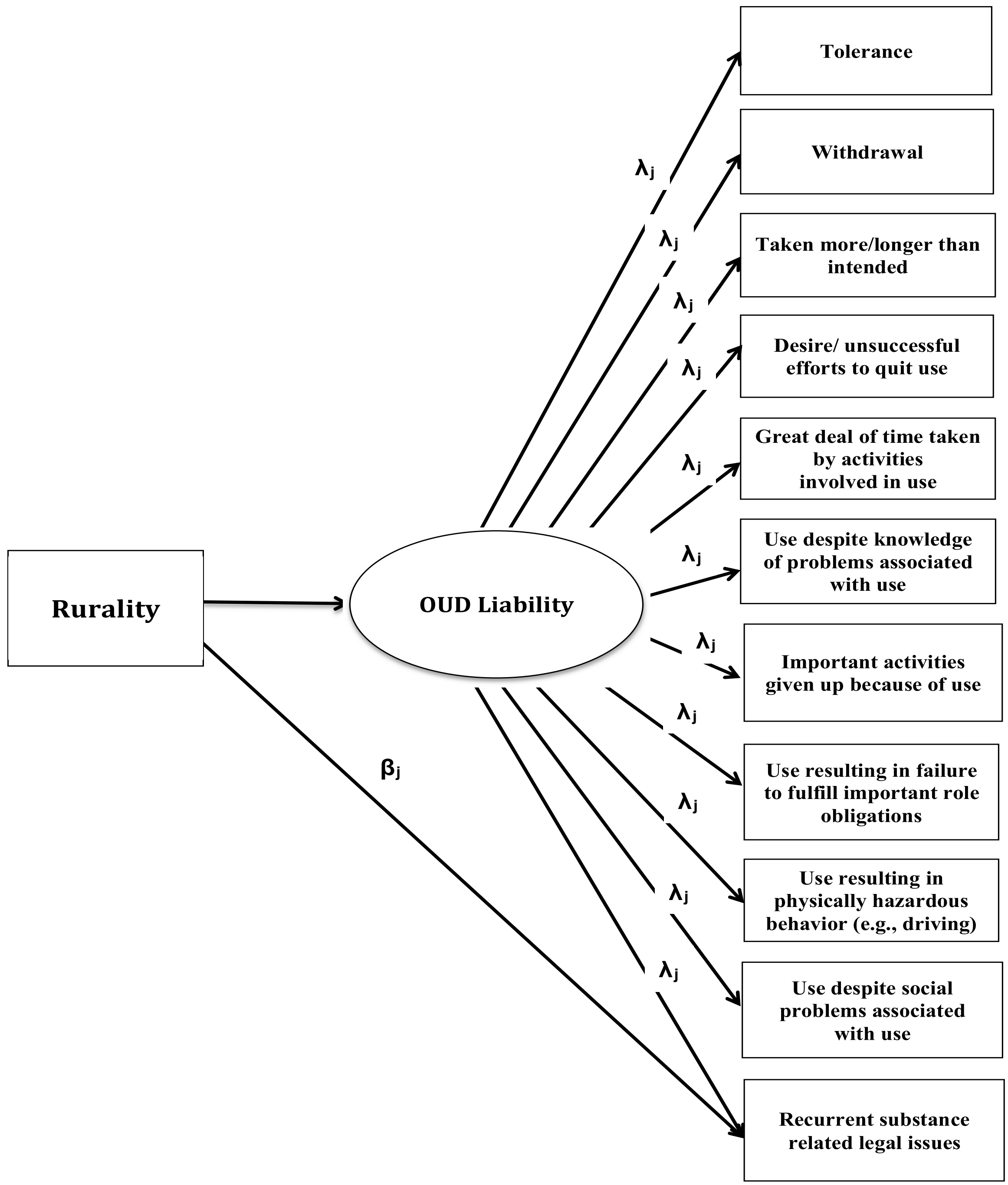


Figure 15. Multiple Indicators, Multiple Causes Model

Study Sample

Data from the 2011 and 2012 iterations of the National Survey on Drug Use and Health, (NSDUH) public use data file were sorted and merged on the case identifier using SAS 9.2 (N = 113,665). Data were cleaned and limited in SAS, selecting for adults who reported past-year non-medical opioid use (NMOU) living in large metro or non-metro areas (N = 3369). Once the merged and limited data set was produced, MPlus 7 was used to account for clustering, stratification and weighting in the MIMIC model as dictated by the sampling methodology.

Measurement Items

In the study, past-year non-medical opioid use was identified as those individuals 18 years and older reporting use of "any opioid pain reliever that was not prescribed for you or that you took only for the experience or feeling it caused" in the past year (Substance Abuse and Mental Health Data Archive, 2014). The main explanatory variable was the three-level variable identifying sample regions as large metro, small metro, and non-metro. Large metro was defined as being within a metropolitan area and having a population greater than 1,000,000. Small metro was within a metropolitan area with a population smaller than 1,000,000 and non-metro was outside of any metropolitan area and having a population smaller than 1,000,000. For the analysis, this variable was limited to two levels; large metro and non-metro. The justification for limiting the explanatory variable in such a way is discussed in the previous chapter. Throughout this chapter, large and small metro is referred to as urban while non-metro will be identified as rural.

Covariates included in the model were age, race, gender, income, self-reported health, marital status, employment status, insurance coverage, serious psychological distress, educational attainment, as well as age when first tried cigarettes and alcohol.

Self-reported health status was measured on a categorical scale of poor, fair, good, very good, and excellent. The variable used in my analysis was dichotomized poor/fair vs. good/very good/ excellent. This was done for ease of interpretation and was grounded in results from previous research indicating higher substance abuse risk in populations of individuals reporting poor/fair health (Simoni-Wastila & Strickler, 2004).

Respondents to the survey were asked to indicate if they were married, widowed, divorced, or never married. For the analysis individuals were categorized as married or other, again justified by previous findings (Substance Abuse and Mental Health Services Administration, 2014). Insurance coverage was evaluated as having insurance of any kind (i.e. private or Medicaid/CHIP) or none. The educational attainment variable was dichotomized from an 11-level categorical variable ranging from fifth grade to graduate school. This step generated a binary response indicating less than 12th grade or high school and greater. As was the case with the marital status variable, the insurance and education covariates recoding was justified based on previous summary of the NSDUH data (Substance Abuse and Mental Health Services Administration, 2014).

A composite measure of psychological distress was generated based on the Kessler-6 psychological distress scale. Respondents to the NSDUH survey were asked to rank their experience with feelings of sadness, restlessness, and hopelessness as some of the time to all of the time. These scores were used to develop a major psychological distress scale of 0-24. In the survey, participants were asked to score the last 30 days as well as the worst

30 days in the last year. The highest score between these two months was used in the analysis.

For ease of interpretation within the model; age, race, income, age when first tried cigarettes, and age of alcohol use initiation were dummy coded. The referent categories were age 18-25, white, income less than $20,000, never smoked and never tried alcohol.

Statistical Analysis

Within the MIMIC model a latent factor, opioid use disorder, is assumed which varies from negative infinity to positive infinity. The observed value of OUD = 1, indicating presence of OUD, is associated with higher values of the underlying, unmeasured latent OUD factor. IRT parameters, difficulty and discrimination, associate the probability of each item equaling 1 given placement along the continuum of OUD.

Item responses were assessed in Mplus 7 based on a PROBIT model using a means and variance adjusted weighted least squares estimation (wlsmv) that produces coefficients measuring the increased or decreased probability of endorsing the item. PROBIT coefficients are not as easily interpreted as LOGIT or linear regression estimates. They require calculation of the cumulative function that accounts for the values of all coefficients as well as the starting value for the predictor of interest.

Within MPlus 7, replicate weighting variables (i.e. weight, stratification, cluster) were applied to the data. These variables were provided in the dataset to account for the complex sampling design, and making results representative of the U.S. population. All covariates were included with direct paths to all 11 indicators of the OUD instrument constrained at 0. These paths can be interpreted as beta coefficients, which is consistent with other latent factor models (e.g. EFA, CFA, SEM, etc.).

Free paths between covariates and the latent factor were also included for the first step of model selection. These paths assess any effects of the covariates on the latent factor score directly. Modification indices (MI) set at 3.84 were consulted to identify significant estimates indicating fit improvement if parameters are freed. MI values higher than 3.84 for paths between covariates and indicators suggested that freeing those parameters would significantly improve the model chi-square making for a better fit. Indicators with the highest MI were freed and the model was run with the new unconstrained pathway until no significant MI values remained.

The modification index is a univariate Lagrange Multiplier (LM) tested as a chi-square with df of 1. The value expressed is an estimate of model chi-square improvement given the inclusion of the freed parameter. Actual change in the model chi-square may not be reflected in the MI as this value is produced through matrix algebra considering the current covariance matrix. After all significant MI estimates were addressed, chi-square DIFFTEST was conducted to assess significance of fit difference between the new, less restricted model and the previous model. Replicate weights (REPSE) were used to generate modification indices but were not used during the DIFFTEST analysis, as this is not possible in Mplus7 in conjunction with REPSE command.

Once DIFFTEST was complete, a manual backwards selection of the final model was conducted, which included significant effects (alpha = 0.05) between covariates and the latent factor, covariates and indicators, and non-significant pathways between the main explanatory (or independent) variable as well as the covariates that had significant effect on any indicator and the latent factor.

Results

The sample was nationally representative with roughly 20% of individuals in sample living in rural, non-metro areas (Table 6). The largest age group was 18-25 years (31.59%) and the sample was predominantly white (65.73%). Most respondents were unmarried, divorced or widowed (65.94%) and started smoking and drinking alcohol before the age of 18 (64.6 and 73.5% respectively).

The percentage of adult past-year non-medical opioid users who did not meet the criteria for abuse or dependence was 81.8%. The prevalence of non-medical opioid abuse in the sample was 3.1% and the dependence prevalence was 15.1%. Non-Hispanic whites appeared to have the highest prevalence of dependence yet African Americans appeared to have the highest prevalence of abuse. The group with the largest percentage of dependence was made up of individuals reporting past-year psychological distress.

Results of the MIMIC model selection indicated the main independent variable, rurality, did not have a significant effect on any of the measurement items, nor did it predict OUD severity. However, eight of the covariates tested in the model had significant beta values for the covariate to indicator path, meaning DIF was present in those items based on the levels of the covariate. These are indicated in figure 16 as having a direct path to one of the OUD indicators.

Table 6. Descriptive Statistics for Covariates and Abuse and Dependence Diagnosis

Weighted Percent %	All Users	Users Without SUD	Users With Abuse	Users With Dependence
Sample Size	3369	2756	104	509
Rural County Designation	20.54	79.5	2.9	17.6
Male	53.69	85.4	2.9	11.7
Age				
18-25 Years Old	31.59	81.6	3.5	14.9
26-34 Years Old	26.08	80.8	3.7	15.5
35-49 Years Old	24.62	86.6	3.9	9.5
50 or Older	17.71	85.1	3.3	11.7
Race				
Non-Hispanic White	65.73	81.3	3.2	15.6
Non-Hispanic African American	12.54	85.1	5.2	9.7
Hispanic	17.18	87.8	4.6	7.6
Other	4.55	88.8	2.1	9
Total Family Income				
Less than $20,000	24.19	81.9	5.1	13.1
$20,000 - $49,999	34.35	82.6	3.5	13.9
$50,000 - $74,999	15.37	84.3	2.9	12.8
$75,000 or more	26.09	84.6	2.9	12.5
Uninsured	27.19	81.2	3.1	15.8
Fair/ Poor Overall Health	15.18	75	6.9	18.1
Unmarried	65.94	82.8	3.5	13.7
Unemployed	31.09	77.5	4.7	17.9
Less than High School	18.25	79.6	6.3	14.1
Age of First Cigarette Use				
Never	18.31	93.1	4.8	2.1
Less than 18	64.55	78.6	3.9	17.4
18-25	15.86	89.5	1.3	9.3
Older than 25	1.28	94.8	1.2	4
Age of First Alcohol Use				
Never	6.72	85.2	10	4.8
Less than 18	73.53	81.2	4	14.9
18-25	18.88	89.8	0.3	10
Older than 25	0.87	96.9	0	3.2
Past Year Serious Psychological Distress	27.55	71.6	5.4	23

Nine of the 11 measurement items showed DIF, or significant change in probability of endorsement in relation to a variable in the model (Table 7). Seven of the covariates (including dummy variables for race) remaining in the final model had significant effects on the level of OUD severity indicated in the figure as having a direct path to the latent factor OUD (Figure 16).

Table 7. Differential Item Functioning of DSM-IV Abuse and Dependence Criteria

Criteria	
Tolerance	DIF
Withdrawal	-
Unable to limit use	DIF
Unable to quit or reduce use	DIF
Great deal of time taken by activities involved in use	DIF
Use despite family problems associated with use	-
Important activities given up because of use	DIF
Recurrent use resulting in a failure to fulfill important role obligations	DIF
Recurrent use resulting in physically hazardous behavior(e.g., driving)	DIF
Continued use despite recurrent social problems associated with use	DIF
Recurrent substance abuse related legal issues	DIF

All indicators loaded strongly on the OUD factor suggesting the items are all good measures of the latent factor opioid use disorder. Results of the DIFFTEST between the fully restricted model and final, less restricted model containing freed parameters, indicted significant improvement in fit for the less restricted model (Chi-square=43.45, df=15, p-value <=0.0001). Based on this result, the model that controlled for DIF in the measurement items was assumed to fit the data better as a measure of OUD (RMSEA = (0.019, 0.023); CFI = 0.982; and TLI = 0.98).

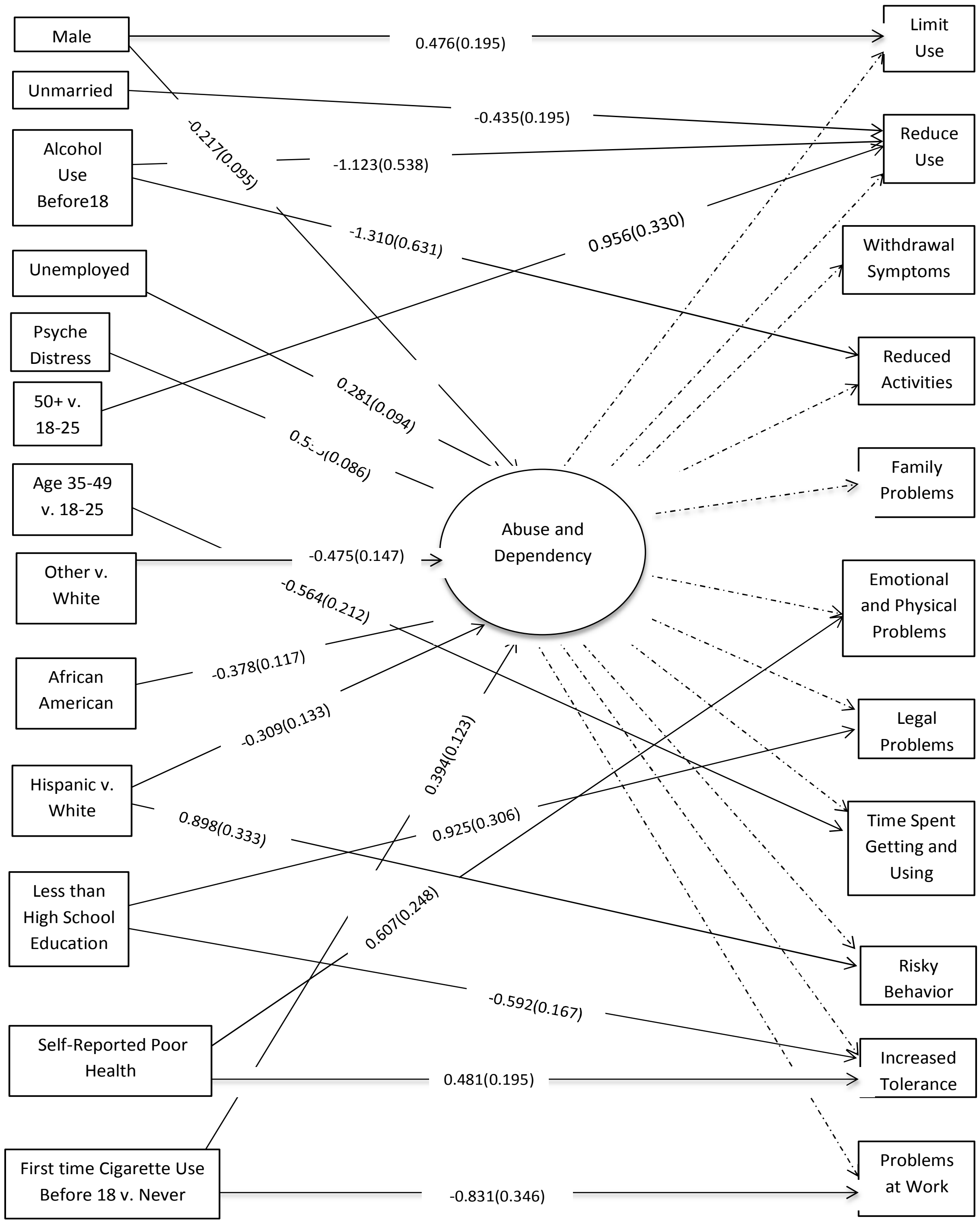


Figure 16. MIMIC model of DSM-IV criteria including covariates and pathways significant at alpha 0.05. Values indicated are PROBIT Estimates (SE)

A closer examination of the parameter estimates allows for the comparison of DIF estimates across covariates remaining in final model (Table 8). For example, the table below indicates underage alcohol consumption had the most impact on the response probability for a single indicator of all the covariates. This variable affected the difficulty of endorsing the Less Activity indicator negatively, meaning individuals reporting alcohol consumption before the age of 18 had a probability of forsaking activities to use OPRs for a given OUD severity that was higher than individuals that did not.

Table 8. Results of MIMIC model analysis including beta estimates and associated p-values for paths between covariates and indicators

		Estimate	S.E.	Lower CL	Upper CL	P-value
Male						
	Limit Use	0.476	0.195	0.281	0.671	0.014
Self-Reported Health						
	Tolerance	0.481	0.195	0.286	0.676	0.016
	Emotional/Physical Problems	0.607	0.248	0.359	0.855	0.015
Less than High School				0.000	0.000	
	Tolerance	-0.592	0.167	-0.759	-0.425	<0.0001
	Legal Problems	0.925	0.306	0.619	1.231	0.0003
Unmarried						
	Reduce Use	-0.435	0.195	-0.630	-0.240	0.025
Under 18 Alcohol Initiation				0.000	0.000	
	Reduce Use	-1.123	0.538	-1.661	-0.585	0.037
	Less Active	-1.31	0.631	-1.941	-0.679	0.038
Income $75,000+ vs. Less than $20,000						
	Legal Problems	-0.771	0.44	-1.211	-0.331	0.08
Age 50+ vs. 18-25						
	Reduce Use	0.956	0.33	0.626	1.286	0.004
Age 35-49 vs. 18-25						
	Much Time Spent Getting, Using, Recovering	-0.564	0.212	-0.776	-0.352	0.008
Hispanic vs. White						
	Risky Behavior	0.898	0.333	0.565	1.231	0.007

When DIF was removed from the model by constraining all remaining parameters between covariates and indicators to zero, differences in the beta estimates for pathways between covariates and the latent factor OUD were seen in all variables that had a significant effect on item response (i.e. DIF) (Table 9). Of the covariates displaying significant DIF and a significant effect on OUD (i.e. Hispanic vs. White, Male, and First Cigarette Use under 18), the Hispanic dummy variable had the most change in its beta estimate (16%). This variable is of important note as it is the one variable that was not significant in the constrained model with regard to its association with OUD severity, yet became significant in the freed model that controlled for DIF. The Under 18 Alcohol Initiation variable also exhibited a notable shift in the unconstrained model, becoming non-significant when DIF was controlled.

Table 3.4 PROBIT estimates, standard errors, p-values, and percent change in PROBIT estimates for unconstrained model (w/DIF) and constrained model (w/o DIF)

	Unconstrained		Constrained			
	Estimate (S.E.)	P-value	Estimate (S.E.)	P-value	% Est. Change	DIF
Rural	-0.024 (0.084)	0.776	-0.024 (0.084)	0.776	-	No
Unemployed	0.281(0.094)	0.003	0.281 (0.094)	0.003	-	No
Psychological Distress	0.535(0.086)	<0.0001	0.535 (0.086)	<0.0001	-	No
Race Other	-0.475(0.147)	0.001	-0.475 (0.147)	0.001	-	No
African American vs. White*	-0.378(0.117)	0.001	-0.392 (0.118)	0.001	-3.7%	No
Hispanic vs. White**	-0.309(0.133)	0.02	-0.259 (0.134)	0.053	16.2%	Yes
Male	-0.217(0.095)	0.022	-0.196(0.097)	0.044	-10.7%	Yes
Self-Reported Health	0.041 (0.119)	0.729	0.112 (0.111)	0.315	173.2%	Yes
Unmarried	0.094 (0.111)	0.397	0.077 (0.11)	0.485	18.1%	Yes
Income $75,000+ vs. < $20,000	0.107 (0.123)	0.384	0.08 (0.12)	0.504	-25.2%	Yes
Less than High School	0.13 (0.112)	0.247	0.118 (0.106)	0.266	-9.2%	Yes
Age 35-49 vs. 18-25	-0.096 (0.125)	0.443	-0.163 (0.118)	0.165	-69.8%	Yes
Age 50+ vs. 18-25	-0.027 (0.205)	0.894	0.025 (0.204)	0.903	192.6%	Yes
First Cigarette Use Under 18	0.394(0.123)	0.001	0.358 (0.119)	0.003	-9.1%	Yes
Under 18 Alcohol Initiation	-0.247 (0.176)	0.161	-0.393 (0.168)	0.019	-59.1%	Yes

*Path from covariate to indicator kept in final model based on significant MI value;
**Effect on OUD prediction became significant in unconstrained model.

As expected, variables without significant DIF pathways (i.e. Rural, Unemployed, Psychological Distress, and Race Other) did not exhibit change in their beta values between the constrained and unconstrained models. The largest change in beta estimate was seen in the over 50 age and self-reported health variables (193% and 173%, respectively). As these remained non-significant when DIF was removed (i.e. no direct path to OUD factor score), their effect on OUD factor score is not considered further.

Discussion

This analysis further suggests a lack of significant difference in measurement of OUD using the DSM-IV criteria between rural and urban samples. Results indicated no significant DIF between the groups with regard to any of the measurement items, nor were there any significant effects of rurality on level of OUD factor scores. That said there were a large number of significant effects on the measure items from the covariates included in the model. This is consistent with previous studies that found similar effects of income, age, gender, and race (Wu et al., 2008; Wu et al., 2009a).

The DIF identified and controlled for in the MIMIC model highlighted two important factors and their change in association with OUD severity. The Hispanic and Under 18 Alcohol Initiation variables both had significant shifts in this association when DIF was controlled for in the model. This is important for the assessment of OUD predictors in future research. These results show that if DIF is not controlled for and predictors are identified through traditional regression techniques erroneous conclusions may be drawn in regards to the association between OUD and study covariates.

The results found here are useful in the development of future research approaches that use factor models to control for OUD severity when assessing the predictive power of different covariates. These results do not however, have application for the diagnosis of OUD, other than anecdotal assessment of diagnosis results in context of age, gender, race, and other demographics. Clinicians cannot be expected to apply advanced modeling techniques to the evaluation of patient OUD status.

This study utilized a large, nationally representative sample of adult past-year non-medical opioid users and explored the effects of a much larger number of covariates as compared to previous studies. Moreover, the addition of rurality as the main independent variable has not been studied using the MIMIC modeling approach before. These results suggest the DSM-IV can be applied across rural and urban populations to assess for OUD without concern regarding DIF.

Low cell frequency in some of the indicators when cross-tabulated with Under 18 Alcohol Initiation variable may have inflated the effect seen for this variable in the model. Results showed a negative 59% change in the parameter estimate between constrained and unconstrained models. These results should be replicated in a second, ideally larger sample in order to confirm them.

In addition, the large number of DIF found in this study could be the product of the inclusion of several variables. It may be the case that any psychometric scale will evidence DIF when tested against enough covariates. This fact makes results generated through this approach exploratory in nature requiring confirmation through the application of the model in an independent study sample, such as one of the many other years of NSDUH data available.

The DSM-IV appears to be an effective assessment tool for identifying OUD in the population. Social science researchers using the NSDUH data to study OUD in the population should consider these results when exploring the prevalence and correlates of OUD in populations.

CHAPTER 4

THE EFFECT OF "RURALITY" ON SUBSTANCE USE DISORDER LATENT CLASS MEMBERSHIP: A MULTIPLE-GROUPS LATENT CLASS ANALYSIS WITH COVARIATES

The objective of this study was to apply multiple-groups LCA with covariates to examine potential differences in latent classifications of multiple drug substance use disorder (SUD) between rural and urban populations. Nine different drug categories including cannabis, stimulants, hallucinogens, opiates, cocaine, sedatives, inhalants, heroin, and tranquilizers were used to identify latent classes of SUD based on the groupings of different illicit and prescription drugs. This approach resulted in the identification of drugs that are likely to be abused in tandem as well as a stratum of classes indicating level of SUD. Once the class structure was established for rural and urban samples, the second step was to test the effect of "rurality" on the likelihood of being a member of any particular class of SUD while controlling for potential confounders identified in the literature.

Background

Latent class analysis (LCA) is one of several types of latent factor models that use measured variables to describe a phenomenon that cannot be directly observed. In models of this type latent factors, or constructs, are assumed to be error free and are responsible for the probability of individual manifestations of specific behaviors or responses. These measured responses are not error free but are dictated by their liability with respect to the latent factor along with any un-modeled disturbance. Figure 17 below illustrates the concept of latent factor modeling.

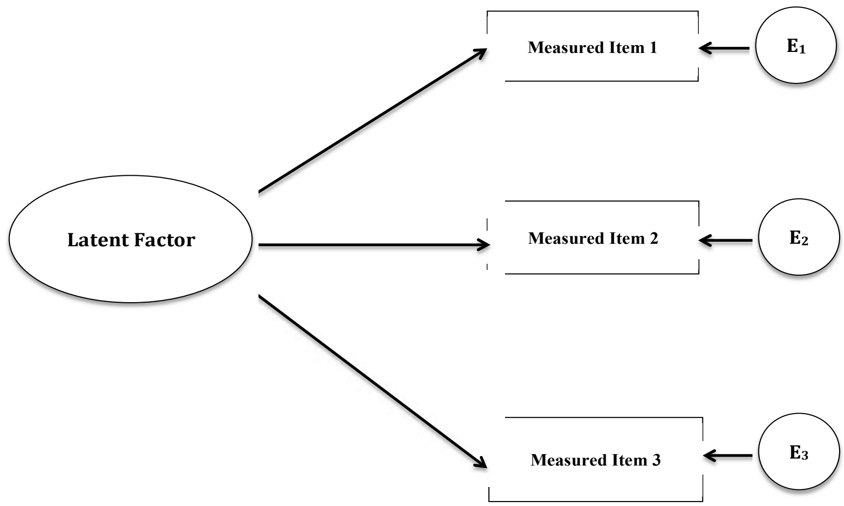


Figure 17. Latent factor model

The MIMIC model discussed in previous chapters is one example of the latent factor model, a CFA, in which the latent factor is assumed to be continuous. In LCA the latent factor is treated as categorical along with the measurement items (Collins LM, 2010). The purpose of LCA is to identify classes of the latent factor by modeling the measured items (Figure 18).

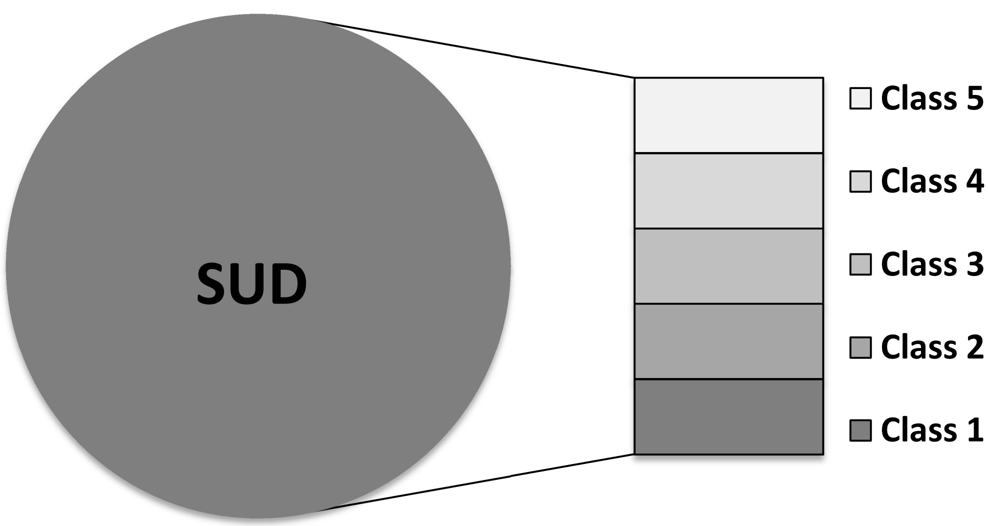


Figure 18. Latent class factor model

The number and type of latent classes assumed to be present in a particular factor are identified based on the distribution of item response probabilities. Each class of the factor has individual probabilities of endorsement for each item measured. The probability of obtaining a response pattern, P(Y=y), can be conceptualized by the following equation

$$P(Y = y) = \sum_{x=1}^{C} P(X = x)P(Y = y|X = x) \tag{4.1}$$

where x is an individual latent class, y is a single pattern of responses, P(X = x) is the proportion of individuals belonging to latent class x, and C is the number of classes (Vermunt J & Magidson J, 2003). Each observed variable L is assumed to be independent of the others, an assumption that is motivated in equation 4.2. This equation illustrates that response pattern probability for a given number of classes is a function of the product of response pattern probability for each item (Vermunt & Magidson, 2003).

$$P(Y = y|X = x) = \prod_{l=1}^{L} P(Y_l = y_l|X = x) \tag{4.2}$$

Finally the two equations above are combined to form the conditional response pattern probability function, equation 4.3.

$$P(Y = y) = \sum_{x=1}^{C} P(X = x) \prod_{l=1}^{L} P(Y_l = y_l|X = x) \tag{4.3}$$

In this way, classes can be developed and evaluated based on the specific items likely to be endorsed within each. Labels for classes can then be generated based on this evaluation. Traditionally, the selection of the number of classes within a latent factor is done using the Bayesian Information Criteria (BIC); however a more rigorous test employed today and in this study is the parametric bootstrap likelihood ratio test (BLRT) (Nylund, Asparouhov, & Muthen, 2007).

Using a derivation of the above equations that applies Bayesian probability theory, a class of most probable membership, or posterior membership probability can be calculated for each respondent in a given dataset (Vermunt J & Magidson J, 2003). This method was used in the study to produce a dataset of most probable class membership for each individual to be utilized for multinomial regression analyses.

$$P(X = x|Y = y) = \frac{P(X = x)P(Y = y|X = x)}{P(Y = y)} \quad (4.4)$$

Study into the latent classification of illicit substance users has identified distinct groups of users based on the probability of engaging in illicit use of different drugs. One study found that a five-class structure fit their data best: low use, moderate use, party drugs, opioids/ sedatives, and polydrug use (Lynskey et al., 2006). Labels were generated post hoc as the probabilities of class membership were evaluated. Individuals in the low use class had minimal probabilities of any drug use except cannabis. The moderate use group was characterized by the probable use of cannabis, stimulants, and hallucinogens. The third class, or party drug class, exhibited probabilities similar to class 2 with the addition of cocaine and a low probability of sedative use. The 4th class was almost exclusively opioids and sedatives, while the polydrug class was the highest risk group engaging in frequent use of multiple substances (Lynskey et al., 2006).

The authors also found significant differences in the rates of psychopathology among the different classes, suggesting that the association between serious mental illness (SMI) and substance use is drug use latent class specific (Lynskey et al., 2006).

For instance, the opioids/ sedatives class had the highest odds ratio for major depressive disorder and ORs comparable to the polydrug use class for social anxiety and sexual abuse (Lynskey et al., 2006). This is particularly interesting as the polydrug class could be considered the highest risk group, yet the opioids/ sedatives class exhibits some of the same psychometric qualities.

Another study done in 2006 examined the latent class structure of SUD among a nationally representative sample of non-institutionalized adults (Agrawal et al., 2007). Rather than modeling the class structure for IDU, Agrawal et al. tried to identify the classes of SUD for multiple drugs. The result was a 5-class structure as was the case in the Lynskey study; however, the characteristics of the classes were different.

Firstly, the low-risk group, which represented 92.5% of the sample, was identified as not having SUD (Agrawal et al., 2007). The second class was characterized by a high probability for cannabis SUD and modest cocaine SUD probability. Class three had probabilities similar to class 2 with the added probability of stimulants and hallucinogen SUD. The fourth class was the cannabis, sedatives, and opioids class with the fifth class representing the polysubstance SUD group (Agrawal et al., 2007).

As seen in the Lynskey study, the latent class for opioids and sedatives bore similar predictive characteristics as the polysubstance class with regard to the covariates chosen for the study. For every psychopathological measure, the opioid class exhibited a significant increase in the likelihood of membership compared to the first class. In addition, class 4 did not differ significantly from the polysubstance class in any of these same measures (Agrawal et al., 2007). This suggests that risk of SUD for opioids and sedatives is similar to that associated with polysubstance use when considering SMI.

The goal of this study was to illuminate any potential moderation of latent class SUD membership by “rurality.” Individuals living in rural settings often experience a matrix of determinants dissimilar to populations in urban areas. The tested hypothesis is that the effects of “rurality” would be seen in the latent class membership probability distribution.

Study Sample

AS with the previous two analyses in this study, data from the 2011 and 2012 NSDUH were merged on the response identification variable (QUESTID2). For the LCA, data were limited to adults in large metro (urban) and non-metro (rural) regions reporting past-year use of nine drug classes (prescription analgesics, cocaine, heroin, marijuana, hallucinogens, sedatives, stimulants, tranquilizers, and inhalants). The final sample used for analysis consisted of 12,140 records, with 3,409 individuals aged 18 and older from rural areas and 8,731 from urban settings.

Measurement Items

The observed outcome for this analysis was past-year drug-specific SUD defined through the administration of the DSM-IV diagnostic criteria. Each drug class was associated with a diagnosis of that particular substance. Within the NSDUH, each set of SUD items are tailored to the drug of reference, creating a drug-specific diagnosis indicator. These indicators were used to identify SUD for each individual in the sample.

The grouping variable, or main predictor, for the LCA portion of the analysis was the three-level variable identifying sample regions as large metro, small metro, and non-metro. Large metro was defined as being within a metropolitan area and having a population greater than 1,000,000. Small metro was within a metropolitan area with a population smaller than 1,000,000 and non-metro was outside of any metropolitan area and having a population smaller than 1,000,000 (Substance Abuse and Mental Health Data Archive, 2014). For the analysis, this variable was limited to two levels; the large metro and non-metro. Throughout this article large and small metro will be referred to as urban while non-metro will be identified as rural.

Covariates assessed in the study were age, race, gender, income, self-reported health, marital status, insurance coverage, educational attainment, and psychological distress. All variables were dichotomized for analysis to avoid quasi separation of data within the model due to low cell frequency. Other variables, such as employment status and age of initiation were omitted for this same reason.

Self-reported health status was measured on a categorical scale of poor, fair, good, very good, and excellent. The variable used in my analysis was dichotomized poor/fair vs. good/ very good/ excellent. Respondents to the survey were asked to indicate if they were married, widowed, divorced, or never married. For the analysis, individuals were coded as married or other. Insurance coverage was evaluated as having insurance (i.e. private or Medicaid/CHIP) or none. The educational attainment variable was dichotomized from an 11 level categorical variable ranging from fifth grade to graduate school, making it a binary response indicating less than 12th grade or high school and greater. All of these categorizations were justified based on previous summary of the NSDUH data (Substance Abuse and Mental Health Services Administration, 2014).

Age was dichotomized 18-25 vs. all other age categories based on results from the MIMIC analysis in chapter 3, as well as previous data analyses indicating higher prevalence of illicit substance use in this group compared to older and younger age categories (Substance Abuse and Mental Health Services Administration, 2014). Race was coded white vs. non-white. As outlined in Chapter 3, a composite measure of psychological distress was generated based on the Kessler-6 psychological distress scale that was dichotomized into scores above and below 12 (Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Behavioral Health Statistics and Quality., 2012). Income was coded as less than $20,000 vs. $20,000 and greater income per year based on previous research indicating higher prevalence of illicit drug use in this economic category compared to others (Blum et al., 2000).

Statistical Analysis

This analysis applies LCA to identify latent classes of SUD as defined by the probability of being diagnosed for 9 different drugs including cannabis, stimulants, hallucinogens, opiates, cocaine, sedatives, inhalants, heroin, and tranquilizers. These categories of drugs were chosen for comparison to previous LCA studies conducted around SUD (Agrawal et al., 2007). Once the best fitting model of classes was determined, the association between "rurality" and latent class membership was then assessed controlling for a set of covariates.

All latent class models were fit in MPlus 7 considering 1 to 8 level class structures. The parametric bootstrap likelihood ratio test (BLRT) was consulted to determine the best fitting model with the most parsimonious number of classes. In order to ensure the best likelihood ratio was replicated and avoid the influence of local maxima, the number of initial and final random starts was adjusted until it was achieved. This process of selecting the number of random starts was also implemented within the BLRT to establish the needed number of bootstrap draws.

Using the BLRT approach, the first step in the LCA was to determine the class structure for the full sample (n=12,140), identifying the number of classes within the structure, as well as the prevalence of class membership. Once the general class structure was established, the same criteria were applied to test for differences in the class structure for the rural and urban samples. This was accomplished by analyzing the populations separately to establish class structure. Once the best model was selected for both groups, depending on whether a difference was seen or not, the next step was to test for measurement invariance. Figure 19 illustrates the flow of procedures employed for the LCA analysis. The sample size for the urban analysis was 8,731 while the rural sample was 3,409, or 28.1% of the total sample used for the study.

Once the class structure was determined for the full, rural and urban groups, a data set of posterior membership probabilities was generated in Mplus 7, consisting of a variable that identified an individual's most likely class of membership. This data set was then merged separately for each group with the data containing covariates of interest for analysis. The class membership variable was then used as the dependent variable in a multinomial regression for the full, urban, and rural samples with 5, 6, and 3 level outcome class variables respectively, testing for any association with an individual's class identification and the covariates listed above.

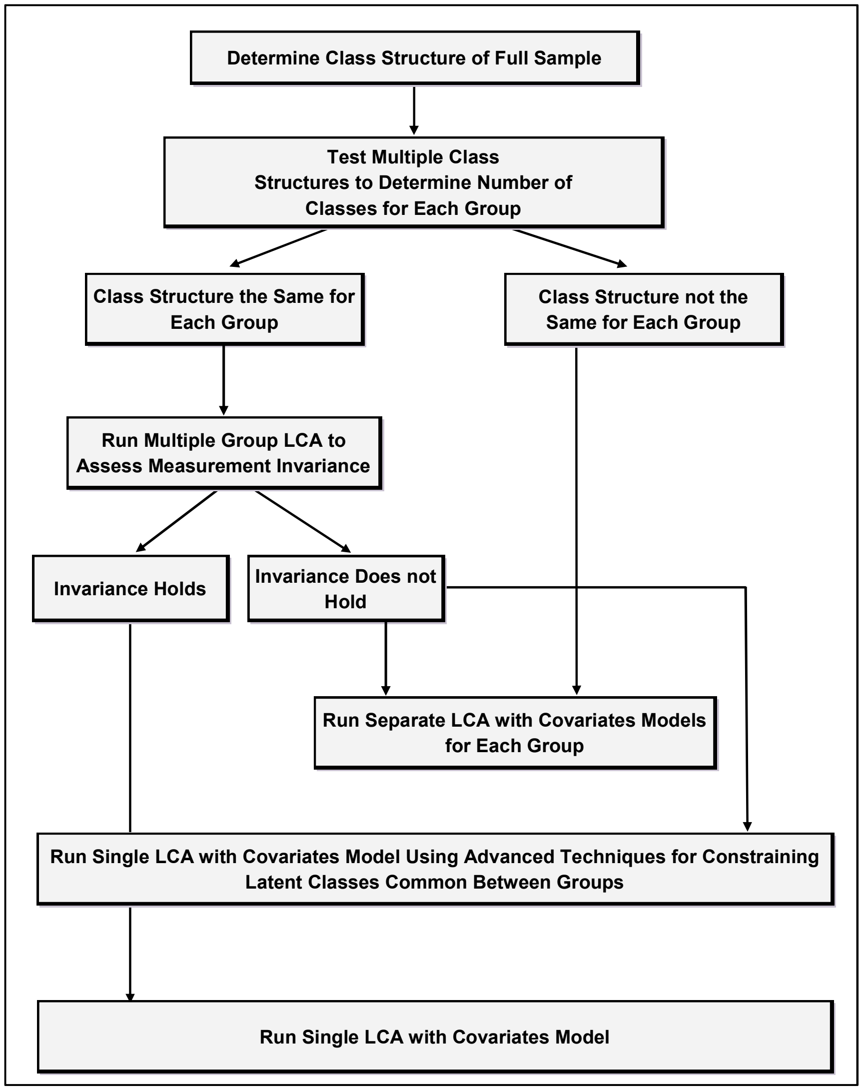


Figure 19. LCA Analysis Flow Chart

Variable inclusion into initial model was based on an 80% confidence level, final model selection was conducted through manual backward selection at a 95% confidence level. Age, race and gender remained in the final model whether they proved to be significantly associated with the outcome or not.

Results

Results of the descriptive analysis indicated that the most prevalent substance use disorder diagnosis in rural and urban communities was for marijuana use (12.2% and

13.3%, respectively, Table 4.1). This result is likely due to the disproportionately high rates of marijuana use in the entire sample compared to other drugs (83.1%). Respondents in rural areas were more likely to report past-year NMOU compared to urban respondents (p-value<0.0001). Individuals in rural areas were also more likely to meet the criteria for OUD than respondents in urban settings (p-value=0.0002). Urban respondents were more likely to report past-year use of cocaine, hallucinogens, and marijuana as compared to rural respondents (p-value=0.0002, p-value=0.0002, and p-value=0.0089 respectively). This sample also exhibited higher rates of cocaine and heroin use disorder compared to the rural sample (p-value=0.0029 and p-value=0.0066 respectively).

The majority of the sample was aged 18 to 25 years (69.71%) and unmarried, widowed or divorced (84.73%). The distribution of gender and race were consistent with national census data with the proportion of non-white individuals in rural areas much smaller than that found in urban areas. Compared to the urban sample, the rural sample had a significantly higher percentage of individuals reporting income below $20,000 (29.4% vs. 37.8%, p-value<0.0001).

Multiple Groups LCA

The multiple groups LCA indicated a 5-class structure in the full sample, a 6-class structure in the urban sample and a 3-class structure in the rural sample. This suggests a qualitative difference in classes of SUD between rural and urban populations. Selection for correct number of classes was accomplished through the application of the parametric bootstrap likelihood ratio test. In the full sample, the BLRT chi-square assessed comparative fit between 6, 5, and 4 classes.

Table 10. Descriptive statistics for LCA covariates and SUD diagnosis along with chi-square test p-values

	Total n (%)	Rural n (%)	Urban n (%)	P-value
Total Sample	12140	3409 (28.1)	8731 (71.9)	-
Age 18 to 25 years	8463 (69.7)	2341 (68.7)	6122 (70.1)	0.1190
Uninsured	3086 (25.4)	973 (28.5)	2113 (24.2)	<0.0001
Non-White	4746 (39.1)	866 (25.4)	3880 (44.4)	<0.0001
Male	6695 (55.2)	1926 (56.5)	4769 (54.6)	0.0618
Psychological Distress	2868 (23.6)	866 (25.4)	2002 (22.9)	0.0039
Fair to Poor Health	1219 (10.0)	383 (11.2)	836 (9.6)	0.0062
Less than High School	2155 (17.8)	748 (21.9)	1407 (16.1)	<0.0001
Unmarried	10286 (84.7)	2796 (82.0)	7490 (85.8)	<0.0001
Income Less than $20,000	3854 (31.8)	1288 (37.8)	2566 (29.4)	<0.0001
Reported Past-Year Use				
Rx Opioids	3369 (27.8)	1054 (30.9)	2315 (26.5)	<0.0001
Cocaine	1469 (12.1)	353 (10.4)	1116 (12.8)	0.0002
Hallucinogens	1763 (14.5)	431 (12.6)	1332 (15.3)	0.0002
Heroin	255 (2.1)	63 (1.9)	192 (2.2)	0.2255
Marijuana	10101 (83.1)	2788 (81.8)	7313 (83.8)	0.0089
Sedatives	130 (1.1)	30 (0.9)	100 (1.2)	0.2018
Stimulants	952 (7.8)	277 (8.1)	675 (7.7)	0.4675
Tranquilizers	1609 (13.3)	454 (13.3)	1155 (13.2)	0.8966
Inhalants	363 (3.0)	105 (3.1)	258 (3.0)	0.7161
SUD Diagnosis				
Rx Opioids	613 (5)	213 (6.2)	400 (4.6)	0.0002
Cocaine	253 (2.1)	50 (1.5)	203 (2.3)	0.0029
Hallucinogens	117 (1)	24 (0.7)	93 (1.1)	0.0672
Heroin	166 (1.4)	31 (0.9)	135 (1.5)	0.0066
Marijuana	1577 (13)	416 (12.2)	1161 (13.3)	0.1070
Sedatives	21 (0.2)	5 (0.1)	16 (0.2)	0.6629
Stimulants	128 (1.1)	44 (1.3)	84 (1)	0.1112
Tranquilizers	139 (1.1)	41 (1.2)	98 (1.1)	0.7087
Inhalants	23 (0.2)	9 (0.3)	14 (0.2)	0.2379

The results of the full sample analysis indicated that the 5 class structure fit was a better fit than the 6-class structure (p-value=0.0938) and that the 5-class structure fit significantly better than the 4-class model (p-value<0.0001). Therefore, I selected the 5-class structure as the model for the full sample. Figure 20 is the class membership plot for this analysis.

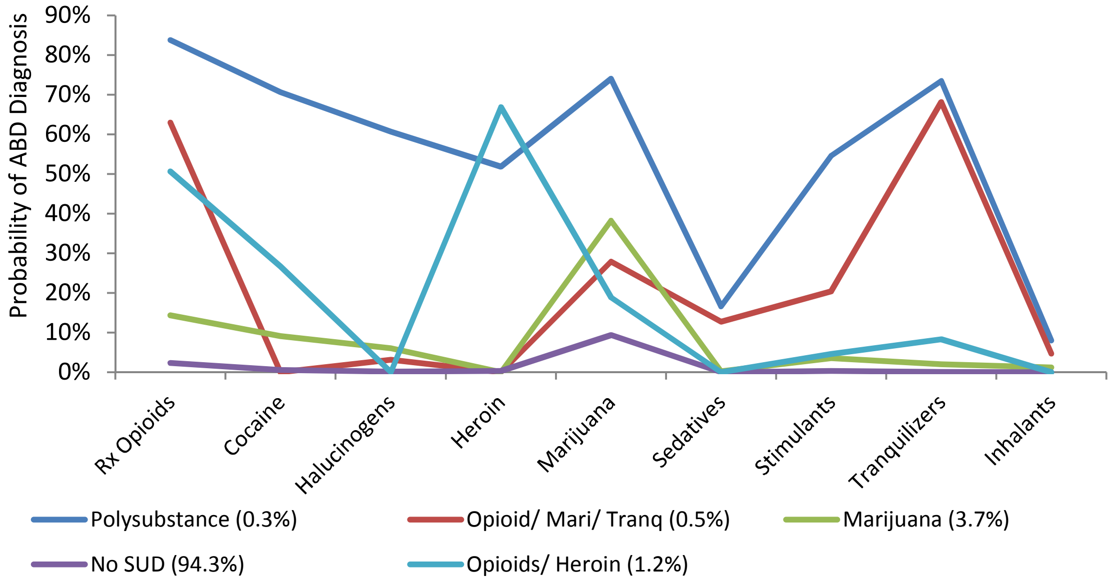


Figure 20. 5-class Full Sample Membership Plot

The most prevalent class by far was the class labeled No SUD (or no abuse and dependence) (94.3%). As shown in figure 20, this class is characterized by 9.3% probability of marijuana use disorder diagnosis and a 2.3% probability of Rx opioid use disorder. All other substance use disorder diagnosis probabilities are negligible for this class; therefore the No SUD class became the baseline class of no abuse or dependence diagnosis. The next most prevalent class was the marijuana class (3.7%). Individuals in this class had a 38.23% probability of marijuana use disorder diagnosis and a 14.29% chance of Rx opioid use disorder. Since other classes such as the opioid/mari/tranquilizer class, the opioids/heroin class, and the polysubstance class had a much greater probability of Rx opioid use disorder this class remained the marijuana class due to its high rate of marijuana use disorder diagnosis. The polysubstance class included high rates of diagnosis for all drugs except inhalants, which were not very prevalent in the sample.

The class structure for the rural sample was quite different than the full sample with only 3 classes of SUD rather than 5. For this sample, the results of the BLRT indicated that the 3-class model fit better than the 4 or the 2-class structure (p-value=0.03).

In figure 21, the class membership probabilities for the rural 3-class structure indicates a distinct marijuana class, an opioid/marijuana/ tranquilizer class, and a no abuse or dependence class. As is the case in the full sample class structure, the most prevalent class by far is the class (97.26%) represented by negligible probability for disorder diagnosis. In contrast to the full sample, however, the rural analysis indicated the opioid/marijuana, tranquilizer class was the second most prevalent (1.47%). The sample lacked what could be considered a polysubstance class as was seen in the other two analyses.

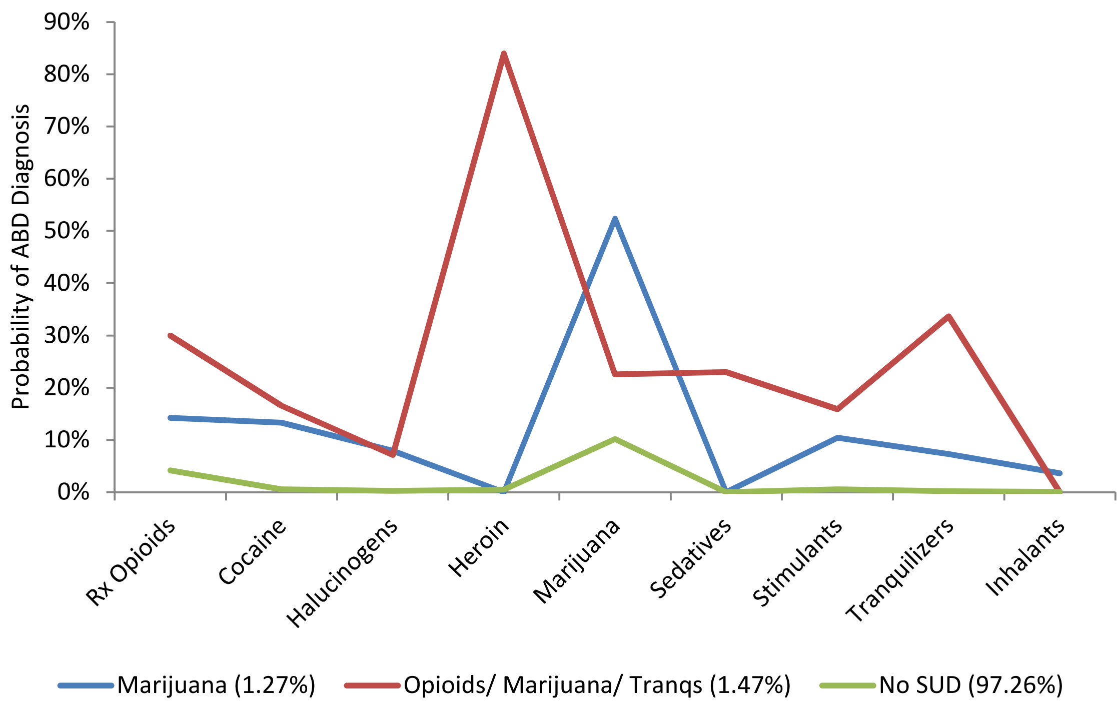


Figure 21. 3-class Rural Sample Membership Plot

The urban sample class structure differed from both the full and rural sample structures exhibiting a 6-class design (Figure 22). Most notable in this analysis was the presence of a class characterized by 100% probability of cocaine use disorder along with a 25.08% rate of marijuana use disorder diagnosis. As was seen in the full sample analysis, the urban group exhibited a polysubstance class that had high rates of all substance use disorders excepting the sedatives and inhalants. The selection of a 6-class structure was based on the BLRT that indicated that 6-classes fit better than the 7 or 5 class model (p-value=<0.0001).

Class prevalence was similar to the full and rural sample analyses in that the overwhelming majority of subjects were in the non-diagnosed class (95.21%). The most striking difference, and perhaps the most important between the three class structures, is that the second most prevalent class in the urban sample was the cocaine class (1.73%), which did not exist in either the full or rural LCA models.

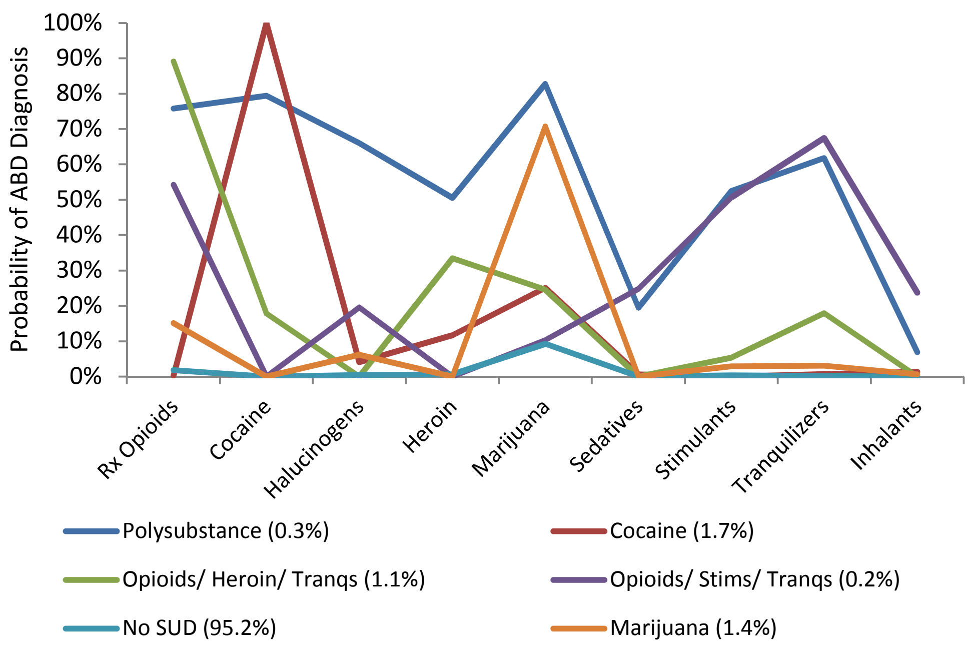


Figure 22. 6-class Urban Sample Membership Plot

Multinomial Logistic Regression

Results for the covariate analysis of class membership suggest that many demographic and socio-economic factors influence the likelihood of membership in different substance use disorder classes. In the full sample analysis individuals in the polysubstance class were more likely to be aged 18 to 25 years, white, males with fair to poor health, and with serious psychological distress compared to the reference, non-diagnosed class (Table 11). Single, uninsured males with less than high school education, fair to poor health and serious psychological distress were more likely to be members of the marijuana disorder class compared to the non-diagnosed class.

Those in the opioid/heroin class were more likely to be single, uninsured white males with less than high school education, fair to poor health, and serious psychological distress. The opioids/mari/tranq class was more likely to be populated with individuals reporting less than a high school education and serious psychological distress.

Respondents aged 18 to 25 were not significantly more likely to be members of any SUD class compared to the No SUD except for the polysubstance class. This suggests that individuals aged 18 to 25 years reporting past-year substance use are more likely to be diagnosed with more drug type use disorders than older individuals. The Opioid/Mari/Tranqs class had the least number of covariates significantly associated with membership than any other class, meaning membership in this class was not as driven by the included socio-demographic characteristics as other classes (Table 11).

Table 11. Full sample adjusted odds ratios from multinomial logistic regression

	Mari	Opioid/Mari/Tranqs.	Opioids/Heroin	Poly	P-Value
Age 18 to 25	0.968 (0.771,1.215)	0.705 (0.396,1.256)	0.763 (0.528,1.105)	3.512 (1.171,10.533)	0.0716
Less than High School	1.606 (1.29,1.999)	1.819 (1.017,3.255)	1.234 (0.83,1.835)	1.957 (0.949,4.039)	<0.0001
Fair to Poor Health	1.536 (1.18,1.999)	1.12 (0.534,2.347)	1.889 (1.242,2.871)	3.376 (1.592,7.163)	<0.0001
Unmarried	1.441 (1.041,1.996)	1.621 (0.697,3.771)	1.866 (1.054,3.3)	1.813 (0.408,8.056)	0.0291
Uninsured	1.396 (1.136,1.714)	1.312 (0.749,2.296)	1.716 (1.214,2.425)	0.737 (0.328,1.653)	0.0005
Non-white	0.976 (0.802,1.188)	0.566 (0.32,1.002)	0.384 (0.257,0.572)	0.456 (0.211,0.986)	<0.0001
Male	1.458 (1.193,1.78)	1.089 (0.645,1.839)	1.846 (1.302,2.618)	2.654 (1.284,5.482)	<0.0001
Psychological Distress	3.222 (2.648,3.92)	4.297 (2.544,7.259)	5.074 (3.615,7.121)	10.235 (4.728,22.156)	<0.0001

Covariate latent class analysis of the rural sample resulted in only two variables exhibiting significant association with class membership (Table 12). Compared with the non-diagnosed class, individuals in the marijuana class were more likely to be uninsured and report serious psychological distress. Only the psychological distress covariate effected the likelihood of membership in the opioid/marijuana/tranquilizer class (OR=2.827; 95% CI:1.588, 5.035).

Table 12. Rural sample adjusted odds ratios from multinomial logistic regression

	Marijuana	Opioids/Mari/Tranqs	P-Value
Age 18 to 25	2.239 (0.984, 5.096)	1.434 (0.743, 2.768)	0.0915
Uninsured	2.889 (1.544, 5.407)*	1.363 (0.75, 2.478)	0.0026
Non-White	0.835 (0.404, 1.727)	0.629 (0.303, 1.306)	0.415
Male	0.61 (0.316, 1.178)	0.771 (0.428, 1.387)	0.2383
Psychological Distress	5.111 (2.68, 9.747)*	2.827 (1.588, 5.035)*	<0.0001

*significant at alpha 0.01

In the urban sample, uninsured males who were older than 25 years of age, with less than a high school education, fair to poor health and serious psychological distress were more likely to be members of the cocaine group compared to the reference, non-diagnosed class (Table 13).

Members of the marijuana class were more likely to be white males, 18 to 25 years of age, with less than a high school education and serious psychological distress. White uninsured male respondents with serious psychological distress were more likely to be members of the opioids/heroin/tranquilizers class. Urban residents in the opioids/stimulants/tranquilizers class were more likely to report fair to poor health and

Table 13. Urban sample adjusted odds ratios for multinomial logistic regression

	Cocaine	Marijuana	Opioids,Heroin,Tranqs	Opioids,Stims,Tranqs	Poly	P-Value
Age 18 to 25	0.432 (0.31,0.603)	2.485 (1.475,4.189)	1.076 (0.687,1.687)	1.557 (0.552,4.39)	2.427 (0.908,6.487)	<0.0001
Less than High School	1.826 (1.264,2.639)	1.823 (1.191,2.792)	1.372 (0.824,2.283)	1.393 (0.484,4.007)	3.311 (1.521,7.209)	<0.0001
Fair to Poor Health	2.577 (1.76,3.774)	0.92 (0.495,1.712)	1.609 (0.934,2.77)	4.368 (1.645,11.598)	4.105 (1.85,9.108)	<0.0001
Uninsured	1.526 (1.079,2.159)	1.445 (0.965,2.164)	1.64 (1.05,2.56)	1.732 (0.67,4.477)	0.386 (0.131,1.143)	0.0038
Non-White	1.247 (0.892,1.744)	0.641 (0.436,0.943)	0.283 (0.171,0.469)	0.667 (0.266,1.671)	0.315 (0.131,0.757)	<0.0001
Male	1.609 (1.137,2.278)	1.895 (1.278,2.81)	1.558 (1.025,2.368)	0.633 (0.253,1.587)	2.817 (1.265,6.274)	<0.0001
Psychological Distress	3.192 (2.277,4.476)	4.083 (2.814,5.926)	7.595 (4.907,11.755)	3.386 (1.363,8.408)	11.113 (4.658,26.514)	<0.0001

serious psychological distress. White males populated the polysubstance class, reporting fair to poor health, less than a high school education, and serious psychological distress

Discussion

The primary finding of this study is that rural and urban populations of adult past-year illicit substance users are qualitatively different in their risk and type of SUD with respect to multiple classes of drugs. For instance, while the urban sample had a class of disorder diagnosis associated with 100% probability of cocaine diagnosis, the rural population lacked a cocaine class all together and relatively low probability of cocaine disorder in all three classes (0.6-13.3%). The urban cocaine latent class represents a group of individuals in the population that have a problem with cocaine that is associated with a possible marijuana and heroin use disorder (25.1% and 11.7%, respectively).

The prevalence of past-year use of prescription pain relievers in the sample analyzed was comparable across rural and urban substance users, though somewhat higher in the rural population (30.92% and 26.51%, respectively). Recent study has suggested that the prevalence of NMOU does not differ significantly between rural and urban adult non-institutionalized populations (Wang et al., 2013). It appears, based on the results of the LCA analysis described herein, that the rate of opioid use among past-year users does not differ across these populations either.

Figure 23 illustrates the differences in probability of disorder diagnosis across drug classes by study sample. It is clear by this graphic that heroin users are at much higher risk for SUD across populations compared to the other eight drug types, and that rural users are less likely to develop a disorder than urban users.

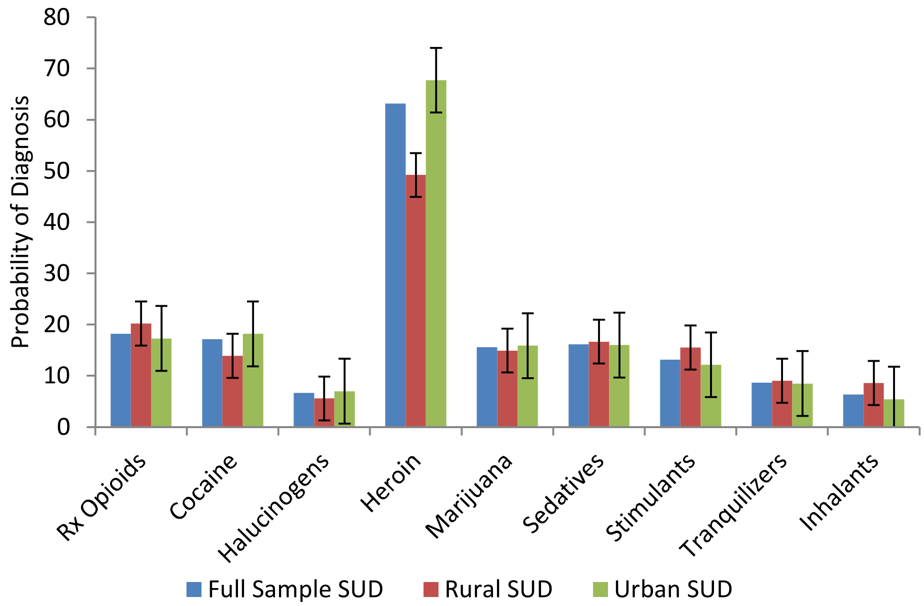


Figure 23. Substance Use Disorder Rate by Substance and Sample Area

The covariates portion of the analysis indicated that class membership in the rural sample did not have as much differentiation across levels of socio-demographics as did the urban population of past-year users. White males were at higher risk for multiple substance use disorder in the urban population yet these variables were not significantly associated with SUD in the rural sample, suggesting class membership is much less dependent on individual characteristics in rural communities of substance users. It is possible this is a product of the cultural homogeneity that exists in rural areas or rather the lack of homogeneity found in urban settings. As discussed in previous sections, rural communities tend to be more socially cohesive which can increase, or potentially equalize SUD risk, across sub-groups by way of family and peer group influence on the individual.

Psychological distress was highly significant in its association with membership in all disorder classes within the rural and the urban populations, further confirming the strong relationship between mental health and substance abuse. This finding, along with the effect of self-reported health status, has implications for public health policy development around mental health services and environmental prevention programing.

While marijuana was the most prevalent substance of use and abuse, prescription opioids played a big role in the class structure of all three analyses. It is important to note that relatively high probabilities of opioid use disorder were evidenced in three classes of the full and urban sample structures and one in the rural sample. This suggests that opioid use disorder is linked with other substance use disorders, most likely due to its lower perceived risk and greater availability.

This study is the first to apply the multiple-groups LCA with covariates approach to substance use disorder diagnosis in rural and urban past-year substance user populations. It utilized a large, nationally representative sample across multiple years, which was needed for parameter estimation of classes with low prevalence.

One major limitation that has been cited in previous sections is low specificity within the grouping variable. The large metro and non-metro designations over generalize the populations making it impossible to examine important cultural differences that might exist across populations such as rural Appalachia and rural non-Appalachia. The economic and cultural history of Appalachia is unique and should not be generalized with rural areas such as those found in Wyoming or the Dakotas for instance. Another potential limitation in the LCA analysis is the inability to apply the replicate weighting variables during model selection. The model commands required for conducting the LCA did not allow for this, therefore the results may have artificially small standard error. This is not likely to be a major flaw as all p-values were either well below alpha 0.05 or well above.

This work has great implication for public health initiatives around substance use disorder in the future. It is clear by this analysis that rural and urban populations of substance users are qualitatively different, making it necessary to tailor interventions to the populations. Programs considered evidence-based for preventing multiple substance use disorders in urban populations may not be effective in rural areas. In addition, the homogeneous nature within the rural latent classes suggests programing should focus less on gender-specific interventions and explore socio-familial approaches instead. By this approach, we may stem the negative effects of the close social ties within rural communities.

CHAPTER 5

DISCUSSION AND CONCLUSIONS

As the prevalence of NMOU and other substance use continues to rise in the U.S., it will become ever more important that researchers take deliberate steps to understand SUD diagnosis and surveillance methods. This study attempts to evaluate one diagnostic tool, the DSM-IV SUD instrument, for its function across populations of rural and urban respondents. The driving hypothesis behind the project is that cultural and demographic differences between these sub-populations likely affect the function of the instrument, making surveillance data of SUD rates biased.

Previous research has indicated that adolescents and adult probationers in rural areas are at higher risk for NMOU and that rates of unintentional overdose in rural communities has increased at an astonishing rate to now rival what is seen in the urban areas (Paulozzi & Xi, 2008). Other studies have shown that rates of NMOU within populations of non-institutionalized adults do not significantly differ between rural and urban environments (Wang et al., 2013). What is less understood, and was therefore the focus of this research, is the risk of SUD diagnosis in rural communities compared to urban. Before assessing for effects on OUD diagnosis between the two groups, it was important to address any potential bias in the diagnostic instrument. This was accomplished through the application of IRT and MIMIC methods. The latter in particular provided the opportunity to assess SUD risk in rural populations while controlling for bias.

Study into cultural differences and their impacts on DIF has been sparse but fruitful (Gillespie et al., 2007). Racial and ethnic variance has been seen regarding SUD measurement using the DSM-IV instrument. Most interesting are the results suggesting that social outcomes of chronic use are not as effectively measured as physical manifestations like tolerance and withdrawal. This suggests that the socio-cultural environment can influence an individual user's perspective on the impact their drug behavior is having on their social obligations. This idea was the central motivation for this study into measurement bias across rural and urban communities. The driving hypothesis was that the history, which shaped the communities in these areas, differed in such a way that measurement of social obligation failure for instance cannot be carried out using the same survey items or perhaps even factor structure.

Neither the IRT or MIMIC analyses conducted for this study indicated this socio-cultural factor at play in the measurement of SUD. While the TIC plot indicated some difference in the precision of the instrument across the groups (Figure 12), the CSEM was roughly the same for all samples with a minimum around factor scores of 1.6. This suggests socio-cultural differences between rural and urban communities do not affect the function of the DSM-IV SUD instrument.

There did appear to be some effect of this variable on the discrimination of some items in the scale (Figures 10 and 11). In the rural ICC plot, the *REDUCE, WITHDRAW*, and TOTPROB items had curves with relatively poor slopes that were only marginally improved in the urban sample. The discrimination estimate for the WORKPROB (Serious problems at home, work, or school caused by using pain relievers) in the rural sample was more than 70% higher than that that seen in the urban sample (Table 5). This suggests these social obligations are a much better estimate of OUD severity in the rural community than in the urban. The difficulty estimates were not significantly different between the two groups for this indicator.

One interesting finding that is consistent with previous studies but has not been fully addressed, is the tendency of the instrument to be more precise at factors scores between 1.4 and 1.6 (rural and urban TIC respectively) standard deviations above the mean (Figure 12). This means that 91% to 94% of the population in the sample has its factor scores estimated with varying degrees of precision. Factor scores below the mean are estimated poorly compared with those above the mean. This suggests that while the instrument is efficient at identifying individuals higher on the OUD severity scale, it may not accurately assess those with lower severity.

Given the choice between identifying the high risk or low risk population, it is preferable to be able to effectively identify those in the higher risk category; however, this does cause concern for secondary prevention efforts that are aimed at early intervention to prevent negative outcomes. With the DSM-IV SUD instrument, identification of individuals at risk for OUD may not occur until they experience higher severity and require more involved intervention with a lower success rate.

A study comparing the sensitivity and specificity of the DSM measures compared to a gold standard instrument is in order to fully understand the expected percent false positives and negatives. Possible options for this work could be the Addiction Severity Index (ASI) or the Screening, Brief Intervention, and Referral to Treatment (SBRT) assessment tools. Before either can be applied to a sensitivity/ specificity analysis each would have to be fully vetted for validity and reliability.

When considering IRT analysis of the DSM-IV SUD instrument applied within a population of adult past-year non-medical opioid users in rural and urban settings, it is clear that the instrument functions well and consistently across the sub-groups. Some items did have quite low discrimination in both groups suggesting these measures may not be as useful as others, but overall the findings are supportive of the application of this tool across rural and urban populations.

Chapter 2 explored the effect of rurality on the difficulty parameter variance in the sample using the MIMIC factor modeling approach. As stated above, the difficulty parameter did not vary significantly across the sub-groups nor did rurality predict factor scores (Figure 16). Differential item functioning was detected in 9 of the 11 measures when the set of covariates was tested for significant effects (Table 7). The MIMIC model indicated that items were influenced by gender, race, age, education, income, employment, history of underage alcohol and cigarette use, health status, and psychological distress. These results show that the instrument is measuring several other individual characteristics in addition to OUD severity.

The implications of these results are that individual demographic and sociocultural characteristics affect the probability of endorsing some items on the scale. There remains suspicion that the inclusion of a large number of covariates in the assessment of a psychometric scale such as the DSM SUD instrument creates a high likelihood of finding evidence of DIF. To that end, a follow-up, confirmatory analysis is in order to test the model generated in this study.

Despite the exploratory nature of this research, it is concerning that so many covariates had significant impact on so many of the items. The implication for epidemiological research is that the effects of identified predictors of OUD could be over or under estimated if DIF is not controlled for in the analysis. For instance, the protective effect of age (35-49 v. 18-25) on OUD was 69% greater when DIF was not controlled for in the model. This means that models that do not account for bias in the instrument will overestimate the impact age has on the likelihood of OUD diagnosis.

In the final MIMIC model, gender, race, employment status, psychological distress, and underage cigarette use history were all significantly predictive of OUD severity (Figure 16). White females had higher estimated OUD severity compared to African American and Other race males. Unemployed individuals reporting past-year psychological distress and a history of underage cigarette use were estimated in the model to have higher OUD severity as well. Confidence in these estimates is greater than previous studies due the control of DIF in the OUD indicators.

It is not reasonable to expect clinicians to apply complex statistical methods that can control for these covariates in order to produce a more rigorous assessment of individual OUD severity. The utility of these results is much more applicable to the surveillance of OUD as well as the identification of predictors. As stated above, the effect of some individual characteristics on OUD diagnosis can be over or under estimated if researchers do not account for instrument bias. Other instruments may not have the issues with DIF identified here (e.g. addiction severity index, etc.), which may make them better for national surveys such as the NSDUH. However, the length of the DSM instrument is conducive to response rates because it is short and can be easily included in a survey that is already quite long, as is the case with the NSDUH.

A mixed methods approach to the development of a new instrument may be in order if a suitable substitute for the DSM is not available. Qualitative data collection leading to a quantitative approach such as CFA can produce new items and constructs to be validated in subsequent studies. The bottom line is that public health infrastructure has to be as efficient as possible in order to effectively utilize ever-decreasing funds. It is then necessary to have assessment tools available that function without bias in order to produce accurate incidence and prevalence estimates.

The results of the latent class analysis were probably the most striking of all the approaches taken to analyze SUD diagnosis across rural and urban populations. While the full sample was consistent with previous studies indicating a 5-class structure of SUD (Agrawal et al., 2007), when the rural and urban samples were analyzed separately very different class structures emerged.

The rural sample, with its 3-class structure, was much more centered around opiate and marijuana SUD (Figure 21). Relative to the high rates of opiate and marijuana SUD, other drug SUD diagnosis such as cocaine, stimulants, tranquilizers and inhalants were not very prevalent in the sample. In addition, there was no evidence of what could be considered a polysubstance SUD class as was the case in the urban sample.

Based on these results, services for individuals with active SUD in rural areas should focus on programming for the identified classes in the study. In addition, trend analyses of the class structures would illuminate changes in the drug market and the impact of regulation on prescription medications. The demographic and cultural homogeneity of rural areas could be affecting the class structure, limiting diversity of SUD diagnosis. This can been seen in the greater racial diversity of the urban sample and the corollary increased likelihood of cocaine and heroin use disorder diagnosis. This is in line with the central hypothesis for the study.

As might be expected, several covariates proved to be predictive of class membership in both samples with psychological distress being the most predictive overall. In both the rural and urban samples, individuals reporting past-year psychological distress were more likely to be in any SUD class compared to none (Tables 12 and 13). Psychological distress was the most predictive of polysubstance use disorder in the urban sample and marijuana use disorder in the rural sample.

The results of these analyses support the application of the DSM-IV across rural and urban populations, as the instrument function does not vary across these groups. There is concern over the effect of socio-demographic characteristics on the individual items, suggesting need for further research into the instrument with regard to these variables, as well as the development of new instruments. The latent classification of SUD does differ between the two groups, further supporting the idea of cultural determinants of health and their impact on substance use disorder. These populations differ in the types of drugs that are abused, as well as how the use disorders cluster.

This research contributes to the SUD literature as well as the study of DSM-IV instrument validity. This work also applies to the new DSM-V revision as 10 of the 11 items remain in the instrument.

REFERENCES

Agrawal, A., & Lynskey, M. T. (2007). Does gender contribute to heterogeneity in criteria for cannabis abuse and dependence? results from the national epidemiological survey on alcohol and related conditions. *Drug and Alcohol Dependence, 88*(2-3), 300-307. doi:S0376-8716(06)00368-1 [pii]

Agrawal, A., Lynskey, M. T., Madden, P. A., Bucholz, K. K., & Heath, A. C. (2007). A latent class analysis of illicit drug abuse/dependence: Results from the national epidemiological survey on alcohol and related conditions. *Addiction (Abingdon, England), 102*(1), 94-104. doi:ADD1630 [pii]

American Psychiatric Association. (1980). Diagnostic and statistical manual of mental disorders (3rd ed.). *Washington DC,*

American Psychiatric Association (Ed.). (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev. ed.) doi:doi:10.1176/appi.books.9780890423349

American Psychiatric Association (Ed.). (2013). *Diagnostic and statistical manual of mental disorders* (5th ed. ed.) doi:doi:10.1176/appi.books.9780890423349

Becker, W. C., Sullivan, L. E., Tetrault, J. M., Desai, R. A., & Fiellin, D. A. (2008). Non-medical use, abuse and dependence on prescription opioids among U.S. adults: Psychiatric, medical and substance use correlates. *Drug and Alcohol Dependence, 94*(1-3), 38-47. doi:S0376-8716(07)00410-3 [pii]

Blanco, C., Rafful, C., Wall, M. M., Jin, C. J., Kerridge, B., & Schwartz, R. P. (2013). The latent structure and predictors of non-medical prescription drug use and prescription drug use disorders: A national study. *Drug and Alcohol Dependence, 133*(2), 473-479. doi:10.1016/j.drugalcdep.2013.07.011 [doi]

Blum, R. W., Beuhring, T., Shew, M. L., Bearinger, L. H., Sieving, R. E., & Resnick, M. D. (2000). The effects of race/ethnicity, income, and family structure on adolescent risk behaviors. *American Journal of Public Health, 90*(12), 1879-1884.

Boardman, J. D., Finch, B. K., Ellison, C. G., Williams, D. R., & Jackson, J. S. (2001). Neighborhood disadvantage, stress, and drug use among adults. *Journal of Health and Social Behavior, 42*(2), 151-165.

Carpiano, R. M., Kelly, B. C., Easterbrook, A., & Parsons, J. T. (2011). Community and drug use among gay men: The role of neighborhoods and networks. *Journal of Health and Social Behavior, 52*(1), 74-90. doi:10.1177/0022146510395026 [doi]

Centers for Disease Control and Prevention. (2007). Unintentional poisoning deaths -- united state, 1999-2004. *Morbidity and Mortality Weekly Report, 56*(5), 93-96.

Centers for Disease Control and Prevention. (2013). Policy impact: Prescription painkiller overdose. Retrieved from [http://www.cdc.gov/homeandrecreationalsafety/pdf/policyimpact-prescriptionpainkillerod.pdf.](http://www.cdc.gov/homeandrecreationalsafety/pdf/policyimpact-prescriptionpainkillerod.pdf)

Centers for Disease Control and Prevention. (2014a). Prescription drug overdose in the united states: Fact sheet. Retrieved from http://www.mayorsinnovation.org/images/uploads/pdf/1_-_Prescription_Drug_Overdose_in_the_United_States.pdf.

Centers for Disease Control and Prevention. (2014b). Vital signs: Variation among states in prescribing of opioid pain relievers and benzodiazepines - united states, 2012. *Morbidity and Mortality Weekly Report, 63*(26), 563-568.

Christiansen, E., Larsen, K. J., Agerbo, E., Bilenberg, N., & Stenager, E. (2014). Risk factors and study designs used in research of youths' suicide behaviour-an epidemiological discussion with focus on level of evidence. *Nordic Journal of Psychiatry,* doi:10.3109/08039488.2014.898092 [doi]

Chung, T., & Martin, C. S. (2005). Classification and short-term course of DSM-IV cannabis, hallucinogen, cocaine, and opioid disorders in treated adolescents. *Journal of Consulting and Clinical Psychology, 73*(6), 995-1004. doi:2005-16405-001 [pii]

Collins, L.M., & Lanza S.T. (2010). *Latent class and latent transition analysis with applications in the social, behavioral, and health sciences.* Wiley Series in Probability and Statistics.

Dasgupta, N., Mandl, K. D., & Brownstein, J. S. (2009). Breaking the news or fueling the epidemic? temporal association between news media report volume and opioid-related mortality. *PLoS ONE, 4*(11), e7758. Retrieved from http://dx.doi.org/10.1371%2Fjournal.pone.0007758

Derringer, J., Krueger, R. F., Dick, D. M., Agrawal, A., Bucholz, K. K., Foroud, T., . . . McGue, M. (2013). *Measurement invariance of DSM-IV alcohol, marijuana and cocaine dependence between community-sampled and clinically overselected studies*. United Kingdom: Wiley-Blackwell Publishing Ltd. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2013-33169-014&site=ehost-live

Fenton MC, Aivadyan C, & Hasin D. (2013). Epidemiology and diagnosis. *Addictions; A Comprehensive Guidebook,* , 73-107.

Finch, H. (2005). The MIMIC model as a method for detecting DIF: Comparison with mantel-haenszel, SIBTEST, and the IRT likelihood ratio. *Applied Psychological Measurement, 29*(4), 278-295.

Galea, S., Hall, C., & Kaplan, G. A. (2009). Social epidemiology and complex system dynamic modelling as applied to health behaviour and drug use research. *The International Journal on Drug Policy, 20*(3), 209-216. doi:10.1016/j.drugpo.2008.08.005 [doi]

Galea, S., Nandi, A., & Vlahov, D. (2004). The social epidemiology of substance use. *Epidemiologic Reviews, 26*, 36-52. doi:10.1093/epirev/mxh007 [doi]

Gillespie, N. A., Neale, M. C., Prescott, C. A., Aggen, S. H., & Kendler, K. S. (2007). Factor and item-response analysis DSM-IV criteria for abuse of and dependence on cannabis, cocaine, hallucinogens, sedatives, stimulants and opioids. *Addiction, 102*(6), 920-930. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2007-08481-017&site=ehost-live

Gizer, I. R., Gilder, D. A., Lau, P., Wang, T., Wilhelmsen, K. C., & Ehlers, C. L. (2013). Contributions of ethnicity to differential item functioning of cannabis abuse and dependence symptoms. *Journal of Studies on Alcohol and Drugs, 74*(2), 320-328. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2013-05838-015&site=ehost-live

Grant, J. D., Scherrer, J. F., Neuman, R. J., Todorov, A. A., Price, R. K., & Bucholz, K. K. (2006). A comparison of the latent class structure of cannabis problems among adult men and women who have used cannabis repeatedly. *Addiction (Abingdon, England), 101*(8), 1133-1142. doi:ADD1463 [pii]

Hasin, D. S., & Beseler, C. L. (2009). Dimensionality of lifetime alcohol abuse, dependence and binge drinking. *Drug and Alcohol Dependence, 101*(1-2), 53-61. doi:10.1016/j.drugalcdep.2008.10.025 [doi]

Havens, J.R., Young, A.M., Havens, C.E. (2011). Nonmedical prescription drug use in a nationally representative sample of adolescents: Evidence of greater use among rural adolescents. *Archives of Pediatrics & Adolescent Medicine, 165*(3), 250-255. doi:10.1001/archpediatrics.2010.217

Havens, J. R., Oser, C. B., Leukefeld, C. G., Webster, J. M., Martin, S. S., O'Connell, D. J., . . . Inciardi, J. A. (2007). Differences in prevalence of prescription opiate misuse among rural and urban probationers. *The American Journal of Drug and Alcohol Abuse, 33*(2), 309-317. doi:10.1080/00952990601175078

Johnston, L. D., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2010). Monitoring the future: National survey results on drug use, 1975-2009. volume II: College students and adults ages 19-50. NIH publication no. 10-7585. *National Institute on Drug Abuse (NIDA),*

Joreskog, K. G., & Goldberger, A. S. (1975). Estimation of a model with multiple indicators and multiple causes of a single latent variable. *Journal of the American Statistical Association, 70*(351, part 1), 631-639.

Karvonen, S., & Rimpela, A. H. (1997). Urban small area variation in adolescents' health behaviour. *Social Science & Medicine (1982), 45*(7), 1089-1098. doi:S0277953697000361 [pii]

Keyes, K. M., Cerda, M., Brady, J. E., Havens, J. R., & Galea, S. (2014). Understanding the Ruralâ€"Urban differences in nonmedical prescription opioid use and abuse in the united states. *Am J Public Health, 104*(2), e52-e59. doi:10.2105/AJPH.2013.301709

Kim, E. S., Yoon, M., & Lee, T. (2012). Testing measurement invariance using MIMIC: Likelihood ratio test with a critical value adjustment. *Educational and Psychological Measurement, 72*(3), 469-492. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2012-14870-007&site=ehost-live

King, N. B., Fraser, V., Boikos, C., Richardson, R., & Harper, S. (2014). Determinants of increased opioid-related mortality in the united states and canada, 1990-2013: A systematic review. *American Journal of Public Health, 104*(8), e32-42. doi:10.2105/AJPH.2014.301966 [doi]

Kopak, A., Proctor, S., & Hoffmann, N. (2014). The elimination of abuse and dependence in DSM-5 substance use disorders: What does this mean for treatment? *Current Addiction Reports, 1*(3), 166-171. doi:10.1007/s40429-014-0020-0

Leukefeld, C., Walker, R., Havens, J., Leedham, C.A., Tolbert, V. (2007). What does the community say: Key informant perceptions of rural prescription drug use. *Journal of Drug Issues, 37*(503) doi:10.1177/002204260703700302

Luthar, S. S., Cicchetti, D., & Becker, B. (2000). The construct of resilience: A critical evaluation and guidelines for future work. *Child Development, 71*(3), 543-562.

Luthar, S. S., & Zigler, E. (1991). Vulnerability and competence: A review of research on resilience in childhood. *The American Journal of Orthopsychiatry, 61*(1), 6-22.

Lynskey, M. T., Agrawal, A., Bucholz, K. K., Nelson, E. C., Madden, P. A., Todorov, A. A., . . . Heath, A. C. (2006). Subtypes of illicit drug users: A latent class analysis of data from an australian twin sample. *Twin Research and Human Genetics : The Official Journal of the International Society for Twin Studies, 9*(4), 523-530. doi:10.1375/183242706778024964 [doi]

Macintosh, R., & Hashim, S. (2003). Variance estimation for converting MIMIC model parameters to IRT parameters in DIF analysis. *Applied Psychological Measurement, 27*(5), 372-379. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2003-07626-004&site=ehost-live

McLeroy, K. R., Bibeau, D., Steckler, A., & Glanz, K. (1988). An ecological perspective on health promotion programs. *Health Education Quarterly, 15*(4), 351-377.

National Alliance for Model State Drug Laws. (2014). Status of state precription drug monitoring programs (PDMPs). Retrieved from http://www.namsdl.org/library/16666FCC-65BE-F4BB-A2BBAD44E1BC7031/

National Institute on Drug Abuse. (2011). Research report series: Prescription drugs: Abuse and addiction. Retrieved from http://www.drugabuse.gov/publications/research-reports/prescription-drugs/director.

National Institute on Drug Abuse (NIDA). (2003).
 Preventing drug use among children and adolescents (in brief). Retrieved from http://www.drugabuse.gov/publications/preventing-drug-abuse-among-children-adolescents/chapter-1-risk-factors-protective-factors/what-are-risk-factors

National Opinion Research Center. (2008). *An analysis of mental health and subtance abuse disparities and access to treatment services in the appalacian region.* ().Appalachian Regional Commission.

Nylund, K. L., Asparouhov, T., & Muthen, B. O. (2007). Deciding on the number of classes in latent class analysis and growth modeling: A monte carlo simulation study. *Structural Equation Modeling: A Multidisciplinary Journal, 14*(4), 535. doi:10.1080/10705510701575396

Office of Adolescent Health (OAH). (2013). Substance abuse. Retrieved from http://www.hhs.gov/ash/oah/adolescent-health-topics/substance-abuse/.

Paulozzi, L. J., & Xi, Y. (2008). Recent changes in drug poisoning mortality in the united states by urban-rural status and by drug type. *Pharmacoepidemiology and Drug Safety, 17*(10), 997-1005. doi:10.1002/pds.1626 [doi]

Resnick, M. D., Harris, L. J., & Blum, R. W. (1993). The impact of caring and connectedness on adolescent health and well-being. *Journal of Paediatrics and Child Health, 29 Suppl 1*, S3-9.

Ridenour, T. A., Cottler, L. B., Compton, W. M., Spitznagel, E. L., & Cunningham-Williams, R. M. (2003). Is there a progression from abuse disorders to dependence disorders? *Addiction (Abingdon, England), 98*(5), 635-644. doi:350 [pii]

Roscigno, V. J., & Crowle, M. L. (2001). Rurality, institutional disadvantage, and achievement/attainment*. *Rural Sociology, 66*(2), 268-292. doi:10.1111/j.1549-0831.2001.tb00067.x

Saha, T. D., Compton, W. M., Chou, S. P., Smith, S., Ruan, W. J., Huang, B., . . . Grant, B. F. (2012). Analyses related to the development of DSM-5 criteria for substance use related disorders: 1. toward amphetamine, cocaine and prescription drug use disorder continua using item response theory. *Drug and Alcohol Dependence, 122*(1-2), 38-46. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2012-10375-005&site=ehost-live

Schoeneberger, M. L., Leukefeld, C. G., Hiller, M. L., & Godlaski, T. (2006). Substance abuse among rural and very rural drug users at treatment entry. *American Journal of Drug & Alcohol Abuse, 32*(1), 87-110. doi:10.1080/00952990500328687

Schroeder, J. R., Latkin, C. A., Hoover, D. R., Curry, A. D., Knowlton, A. R., & Celentano, D. D. (2001). Illicit drug use in one's social network and in one's neighborhood predicts individual heroin and cocaine use. *Annals of Epidemiology, 11*(6), 389-394. doi:S1047-2797(01)00225-3 [pii]

Sellstrom, E., O'Campo, P., Muntaner, C., Arnoldsson, G., & Hjern, A. (2011). Hospital admissions of young persons for illicit drug use or abuse: Does neighborhood of residence matter? *Health & Place, 17*(2), 551-557. doi:10.1016/j.healthplace.2010.12.013 [doi]

Shih, C., & Wang, W. (2009). Differential item functioning detection using the multiple indicators, multiple causes method with a pure short anchor. *Applied Psychological Measurement, 33*(3), 184-199. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2009-06747-002&site=ehost-live

Simoni-Wastila, L., & Strickler, G. (2004; 2003). Risk factors associated with problem use of prescription drugs. *American Journal of Public Health, 94*(2), 266-268.

Substance Abuse and Mental Health Data Archive. (2014). National survey on drug use and health (NSDUH, 2012). Retrieved from http://www.icpsr.umich.edu/icpsrweb/SAMHDA/studies/34933)

Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Behavioral Health Statistics and Quality. (2012). National survey on drug use and health, 2005, 2006 to 2010, and 2011.

Substance Abuse and Mental Health Services Administration,. (2014). *Results from the 2013 national survey on drug use and health: Summary of national findings*
. NSDUH Series H-48, HHS Publication no. (SMA) 14-4863. Rockville, MD: Substance Abuse and Mental Health Services Administration,

Swendsen, J., Conway, K. P., Degenhardt, L., Glantz, M., Jin, R., Merikangas, K. R., . . . Kessler, R. C. (2010). Mental disorders as risk factors for substance use, abuse and dependence: Results from the 10-year follow-up of the national comorbidity survey. *Addiction (Abingdon, England), 105*(6), 1117-1128. doi:10.1111/j.1360-0443.2010.02902.x [doi]

Thomas, K. C., Ellis, A. R., Konrad, T. R., Holzer, C. E., & Morrissey, J. P. (2009). County-level estimates of mental health professional shortage in the united states. *Psychiatric Services (Washington, D.C.), 60*(10), 1323-1328. doi:10.1176/appi.ps.60.10.1323; 10.1176/appi.ps.60.10.1323

Thorpe, G. L., & Favia, A. (2012). *Data analysis using item response theory methodology: An introduction to selected programs and applications.* Unpublished manuscript.

United States Department of Agriculture. (2013). Rural-urban continuum codes. Retrieved from http://www.ers.usda.gov/data-products/rural-urban-continuum-codes.aspx#.VEEh0iuwL6c

United States Department of Agriculture, Economic Research Service. (2014). Poverty and deep paverty increasing in rural america. Retrieved from http://www.ers.usda.gov/amber-waves/2014-march/poverty-and-deep-poverty-increasing-in-rural-america.aspx#.VEfe1yuwL6c

US Census Bureau. (2013). 2010 census urban and rural classification and urban area criteria. Retrieved from https://www.census.gov/geo/reference/ua/urban-rural-2010.html

US Department of Health and Human Services, Health Resources and Services Administration, Office of Rural Health Policy. (2005). *Mental health and rural america: 1994-2005.* ().US Department of Health and Human Services.

Vermunt J & Magidson J. (2003). Latent class analysis. *Encyclopedia of social science research methods* (). London: Sage.

Wang, K. H., Becker, W. C., & Fiellin, D. A. (2013). Prevalence and correlates for nonmedical use of prescription opioids among urban and rural residents. *Drug and Alcohol Dependence, 127*(1-3), 156-162. doi:10.1016/j.drugalcdep.2012.06.027 [doi]

Williams, C. T., & Latkin, C. A. (2007). Neighborhood socioeconomic status, personal network attributes, and use of heroin and cocaine. *American Journal of Preventive Medicine, 32*(6 Suppl), S203-10. doi:S0749-3797(07)00063-3 [pii]

Willse, J. T., & Goodman, J. T. (2008). Comparison of multiple-indicators, multiple-causes-- and item response theory--based analyses of subgroup differences. *Educational and Psychological Measurement, 68*(4), 587-602. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2008-11338-004&site=ehost-live

Woods, C., Oltmanns, T., & Turkheimer, E. (2009). Illustration of MIMIC-model DIF testing with the schedule for nonadaptive and adaptive personality. *Journal of Psychopathology and Behavioral Assessment, 31*(4), 320-330. doi:10.1007/s10862-008-9118-9

Wu, L. T., Pan, J. J., Blazer, D. G., Tai, B., Brooner, R. K., Stitzer, M. L., . . . Blaine, J. D. (2009). The construct and measurement equivalence of cocaine and opioid dependences: A national drug abuse treatment clinical trials network (CTN) study. *Drug and Alcohol Dependence, 103*(3), 114-123. doi:10.1016/j.drugalcdep.2009.01.018 [doi]

Wu, L. T., Ringwalt, C. L., Mannelli, P., & Patkar, A. A. (2008). Prescription pain reliever abuse and dependence among adolescents: A nationally representative study. *Journal of the American Academy of Child and Adolescent Psychiatry, 47*(9), 1020-1029. doi:10.1097/CHI.0b013e31817eed4d [doi]

Wu, L. T., Ringwalt, C. L., Yang, C., Reeve, B. B., Pan, J. J., & Blazer, D. G. (2009a). Construct and differential item functioning in the assessment of prescription opioid use disorders among american adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 48*(5), 563-572. doi:10.1097/CHI.0b013e31819e3f45 [doi]

Wu, L. T., Ringwalt, C. L., Yang, C., Reeve, B. B., Pan, J. J., & Blazer, D. G. (2009b). Construct and differential item functioning in the assessment of prescription opioid use disorders among american adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 48*(5), 563-572. doi:10.1097/CHI.0b013e31819e3f45 [doi]

Wu, L. T., Woody, G. E., Yang, C., Pan, J. J., & Blazer, D. G. (2011). Abuse and dependence on prescription opioids in adults: A mixture categorical and dimensional approach to diagnostic classification. *Psychological Medicine, 41*(3), 653-664. doi:10.1017/S0033291710000954 [doi]

Wu, L., Pilowsky, D. J., & Patkar, A. A. (2008). Non-prescribed use of pain relievers among adolescents in the united states. *Drug and Alcohol Dependence, 94*(1–3), 1-11. doi:http://dx.doi.org/10.1016/j.drugalcdep.2007.09.023

Young, A. M., Havens, J. R., & Leukefeld, C. G. (2012). A comparison of rural and urban nonmedical prescription opioid users' lifetime and recent drug use. *The American Journal of Drug and Alcohol Abuse, 38*(3), 220-227. doi:10.3109/00952990.2011.643971; 10.3109/00952990.2011.643971

APPENDIX

Human Subjects Protection

January 20, 2015

Billy Brooks
149 Lamb Hall, Dossett Drive
Johnson City, TN 37614

Dear Mr. Brooks,
Thank you for recently submitting information regarding your proposed project "Rural Opioid and Other Drug Use Disorder Diagnosis: Assessing Measurement Invariance and Latent Classification of DSM-IV Abuse and Dependency Criteria."

I have reviewed the information, which includes a completed Form 129.

The determination is that this proposed activity as described meets neither the FDA nor the DHHS definition of research involving human subjects. Therefore, it does not fall under the purview of the ETSU/VA IRB.

IRB review and IRB approval by East Tennessee State University is not required. This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made and there are questions about whether these activities are human subject research in which the organization is engaged, please submit a new request to the IRB for a determination.

Thank you for your commitment to excellence.

Sincerely,
George Youngberg, M.D.
Chair, ETSU/VA IRB

VITA

BILLY BROOKS

Education:	Doctor of Public Health, August 2015 Concentration: Epidemiology East Tennessee State University (ETSU), Johnson City, TN
	Master of Public Health, May 2012 Concentration: Biostatistics East Tennessee State University (ETSU), Johnson City, TN
	Bachelor of Arts, May 2010 Major: Statistics Minor: Environmental Studies University of North Carolina (UNCA) Asheville, NC
Professional Experience:	External Evaluator – Community Awareness Recovery Effort (CARE) - Transylvania County, Jan.- Sept. 2015
	Research Assistant – NIDA R-24: Diversity promoting Institutions Drug Abuse Research Project (DIDARP), ETSU College of Public Health
	External Evaluator - RHA Behavioral Health Services, Inc. Strengthening Families Program – Asheville
	TA Provider – North Carolina Coalition Initiative Community Awareness Recovery Effort (CARE) - Transylvania County, Jan.- April 2014

Publications:

Wang, L., Mamudu, H. M., Alamian, A., Anderson, J. L., & Brooks, B. (2014). Independent and joint effects of prenatal maternal smoking and maternal exposure to second-hand smoke on the development of adolescent obesity: A longitudinal study. *Journal of Paediatrics and Child Health,* doi:10.1111/jpc.12667 [doi]

Brooks, B., Blackley, D., Masters, P., May, A. S., Mayes, G., Williams, C., & Pack, R. (2014). Developing an academic health department in northeast tennessee: A sustainable approach through student leadership.*Journal of Public Health Management and Practice : JPHMP, 20*(3), 315-323. doi:10.1097/PHH.0b013e3182980c1d [doi]

Ward, R. K., Blackley, D., & Brooks, B. (2014). The development and implementation of a student-led farmers' market on a public university campus. *Journal of Hunger & Environmental Nutrition, 9*(1), 81-95. doi:10.1080/19320248.2013.873007

Veeranki Sreenivas P, Brooks Billy, Bolick Susan, Robichaux Mary, Aldrich Timothy. Quality of Care: The Role of Disease Registries. Journal of Registry Management. 2010;37(4): 133-136.

Patch Steven, Goodman Catherine, Brooks Billy. The Effect of Chromated Copper Arsenate Structures on Adjacent Soil Arsenic Concentrations. Bulletin of Environmental Contamination and Toxicology. <u>Volume 86, Number 6</u> (2011), 662-665, DOI: 10.1007/s00128-011-0270-7

Honors and Awards: Undergraduate Research Scholar, UNCA 2010
Dept. of Biostatistics and Epidemiology Outstanding MPH Student, ETSU 2012
Public Health Student Association Leadership Award, ETSU 2012
Dept. of Biostatistics and Epidemiology Chair Service Award, ETSU 2013
Dept. of Biostatistics and Epidemiology DrPH Student Award of Excellence, ETSU 2014