

**CHARACTERIZING THE DISTRIBUTION OF DEPRESSION AND ALCOHOL USE
DISORDERS AMONG AN ADULT PERUVIAN POPULATION: PREVALENCE, RISK
FACTORS AND ASSOCIATIONS**

By

Alanna M. Mozena

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LIST OF ABBREVIATIONS

AUD	Alcohol Use Disorder
DALY	Disability Adjusted Life Years
DIS	Diagnostic Interview Schedule
DSM-IV	Diagnostic Statistical Manual – Fourth Edition
ICD	International Classification of Disease
MDD	Major Depressive Disorder
MDE	Major Depressive Episode
OR	Odds Ratio
STATA	Statistics and Data Analysis Software
WHO	World Health Organization
WMH-CIDI	World Mental Health Composite International Diagnostic Interview
WMHSI	World Mental Health Survey Initiative
YLD	Years Lived with Disability

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Thesis Committee

Dennis McCarty, PhD

Kim Hoffman, PhD

Javier Ponce Terashima, MD

Dongseok Choi, PhD

John Muench, MD, MPH

Unidad de Análisis y Generación de Evidencias en Salud Pública, Instituto Nacional de Salud, Lima, Perú

Marina Piazza, DSc, MPH

Fabián Fiestas, MD, PhD

Oregon Health and Science University

Priya Srikanth, MPH

Katrina Ramsey, MPH

Abstract

Background -- Though mood and substance use disorders account for a large majority of the years lived with disability (YLD) worldwide, there is a dearth of research regarding the epidemiology of these conditions (Whiteford, et al., 2013). In response, the global mental health community along with the World Health Organization (WHO) supports the World Mental Health Survey Initiative (WMHSI) to characterize the burden of mental and addictive disorders. This initiative also places mental health and substance use conditions firmly at the forefront of the global health agenda and addresses the tremendous disparities between demand and access to treatment (Sharan, et al., 2009). Major Depressive Disorder (MDD) and Alcohol Use Disorders (AUDs) are among the most prevalent and disabling mental health conditions worldwide and prior estimates of these conditions in Peru were based on small studies with limited populations. This secondary analysis is intended to provide insight into the sociodemographic associations of lifetime prevalence of Major Depressive Episodes and Alcohol Use Disorders (including alcohol abuse with and without dependence) in adults living in urban Peru.

Methods – This analysis was based on survey data gathered by the WMHSI among 3930 adults ages 18-65 living in five Peruvian cities (Arequipa, Chiclayo, Huancayo, Iquitos, Lima). A standardized, validated survey (World Health Organization – Composite International Diagnostic Interview) carried out by trained lay interviewers captured sociodemographic characteristics and symptoms based on DSM-IV criteria for Major Depressive Episode and Alcohol Abuse with and without Dependence. Univariate and multivariate analyses examined epidemiologic patterns of these conditions.

Results – The overall lifetime prevalence of Major Depressive Episode was 6.9%. Men were significantly less likely to have lifetime MDE compared to women (adjusted OR 0.63; 95% CI 0.49 – 0.83). Prevalence varied by geographic location; residents of Arequipa, Chiclayo and

Iquitos were less likely to have lifetime MDE compared to respondents in Lima. Previously or never married respondents had a significantly higher odds of having lifetime MDE compared to those who were married (adjusted ORs 2.48 and 1.48, respectively). The overall lifetime prevalence of AUDs was 5.6%. Men were significantly more likely to have lifetime AUD compared to women (adjusted OR 15.6; 95% CI 9.50 – 25.59). Respondents living in Arequipa and Chiclayo had a lower lifetime odds of AUD (adjusted ORs 0.36 and 0.44, respectively). Previously married respondents had a higher lifetime odds of AUD compared to those who were married (adjusted OR 1.90; 95% CI 1.14 – 3.17). Lower educational attainment was associated with higher odds of lifetime AUD compared to those who complete university level education (including primary, some secondary and completed secondary).

Conclusion – Major depression and AUDs are significant public health concerns for urban Peru. Moving forward, recognizing the epidemiological trends of these conditions by providers and policy-makers will be important in designing targeted prevention and treatment campaigns.

Introduction

Mental health and substance use disorders are leading causes of years lived with disability (YLD) worldwide (Whiteford, et al., 2013). Despite the magnitude of disability related to these conditions, relatively little is known about their epidemiologic distribution in low- and middle-income countries (Razzouk, et al., 2008). Efforts to understand the burden of these conditions are a priority on the global health agenda because demand for treatment outweighs access to and availability of care (Sharan, et al., 2009).

WMH Survey Initiative

The World Health Organization supported the World Mental Health Survey Initiative (WMHSI) to characterize the global burden of mental and addictive disorders and to highlight the need for adequate care and treatment for those suffering from mental health and substance use disorders (Kessler, Haro, Herringa, Pennell & Ustun, 2006; Kessler & Ustun, 2004). The WMHSI trained lay interviewers to administer a fully structured psychiatric diagnostic interview that approximated clinical diagnoses (Kessler & Ustun, 2004).

The WMHSI was based on experience with the Diagnostic Interview Schedule (DIS), the first fully-structured psychiatric diagnostic interview administered by lay interviewers in five communities in the United States (the Epidemiologic Catchment Area Study). The World Health Organization World Mental Health Composite International Diagnostic Interview (WMH-CIDI) was developed as an expanded version of DIS to include the International Classification of Disease (ICD) guidelines (Robins & Regier, 1991; Kessler & Ustun, 2004). The ICD guidelines are useful for cross-national comparative research and are the international standard diagnostic system for psychiatric disorders (Kessler & Ustun, 2004). Twenty-eight countries including Peru representing all regions of the world participated in the WMHSI.

General Description of the WMHSI

The WMHSI conducted rigorous general population surveys to capture the prevalence of mental disorders, and assess potential risk factors, patterns of and barriers to the use of mental health services (The World Mental Health Survey Initiative, 2005). The WMH-CIDI has 41 sections (i.e., an introductory screening and lifetime review section, 22 diagnostic sections, 4 sections on functioning and physical comorbidity, 2 sections assess treatment of mental health disorders, 4 sections examine risk factors, 6 assess sociodemographics, 2 final sections are methodological). See Table 1. Generally, the whole interview requires about 2 hours to complete, but interview time varies drastically depending on the whether or not the respondent screens positive for having a mental health or substance use disorder (Kessler & Ustun, 2004).

I.	Screening and lifetime review	
II.	Disorders	
	Mood	Major depression, mania
	Anxiety Disorders	Panic disorder, specific phobia, agoraphobia, generalized anxiety disorder, post-traumatic stress disorder, obsessive-compulsive disorder, social phobia
	Substance Use Disorders	Alcohol abuse, alcohol dependence, drug abuse, drug dependence, nicotine dependence
	Childhood Disorders	Attention-deficit/hyperactivity disorder, oppositional-defiant disorder, conduct disorder, separation anxiety disorder
	Other	Intermittent explosive disorder, eating disorders, premenstrual disorder, non-affective psychoses screen, pathological gambling, neurasthenia, personality disorders screens
III.	Functioning and physical disorders	Suicidality, 30-day functioning, 30-day psychological distress, physical comorbidity
IV.	Treatment	Services, pharmacoepidemiology
V.	Risk Factors	Personality, social networks, childhood experiences, family burden
VI.	Socio-demographics	Employment, finances, marriage, children, childhood demographics, adult demographics
VII.	Methodological	Part I – Part II selection, interviewer observations

* (Kessler & Ustun, 2004)

Uniquely, the WMH-CIDI requires lay interviewers to be trained to administer the survey by participating in a standardized computer module in addition to a face-to-face training session.

The rigorous training ensures that the diagnoses generated by the instruments are as consistent as possible with clinical interviewers.

Because of the sensitive nature of the content of the survey, considerable focus and research was done to increase the validity of the interview. Generally, it focused on four methodological problems:

- 1.) Respondents might not understand some of the CIDI questions, due to length or complexity;
- 2.) Some respondents might not understand the task implied by the questions, which necessitate difficult memory searches;
- 3.) Respondents might not be motivated to answer the questions correctly, especially because many of the questions pertain to potentially embarrassing or stigmatizing experiences;
- 4.) Respondents might not be able to answer some CIDI questions accurately (Kessler & Ustun, 2004).

To address these concerns, the components and questions included in the WMH-CIDI were studied and explicitly modified to minimize cross cultural ambiguity. For example, questions that might lead to confusion (such as those regarding phobias related to flying in an airplane in countries where most of the population doesn't regularly use air travel) were carefully edited or removed, as deemed appropriate by in-country survey staff (Robins, et al., 1988). Translations and back-translations used a standardized WHO protocol (Kessler & Ustun, 2004).

Peru-based WMH Survey Initiative

In 2005, the WMHSI, in collaboration with the Instituto Nacional de Salud, carried out a community survey in five metropolitan Peruvian cities (Arequipa, Chiclayo, Huancayo, Iquitos and Lima). Prior to the completion of these surveys, there were limited data regarding the burden of mental and behavioral disorders in Peru and few resources for care and treatment services. Based on the 1993 census, these cities together held more than 50% of the

population (Peru: Instituto Nacional de Estadística e Informática). These five cities also represented the geographically diverse areas of Peru – the highlands, coastal and jungle regions.

At the time the WMH survey was completed, Peru had three specialized mental health facilities with 1,067 patient beds, all located in the capital, Lima (J. Ponce Terashima, personal communication, February 2015). Although some general hospitals were required by law to provide patient beds for psychiatry, most patients were referred to the mental health institutions. Many patients at the mental health facilities were hospitalized for extended periods of time. In 2008, an estimated 44% of patients were hospitalized for more than 10 years and 4% had been hospitalized for 1-4 years (Peru - Ministerio de Salud, 2008). Given the duration of hospitalization for the majority of the patients at the mental health facilities in Lima, these institutions appear to provide care for patients with severe disease and/or few community supports.

Epidemiology of Major Depression

Independently, Major Depressive Disorder (MDD) is among the most prevalent and disabling mental health conditions worldwide (Whiteford, et al., 2013). Cross-national data collected on behalf of the WMHSI asserts that MDD has a relatively early age-of-onset leading to adverse outcomes and affects educational attainment, marital timing and stability, childbearing and occupation (Kessler & Bromet, 2013). Common mental health disorders like depression have also been associated with the social and economic milieu of poverty in low- and middle-income countries (Lund, et al., 2010). Understanding the epidemiology of MDD is increasingly important as low- and middle-income countries become more urbanized and transition economically, as income inequality has been associated with increased morbidity and mortality related to depression (Weich, Lewis, & Jenkins, 2001).

Looking at trends in the Global Burden of Disease from 1990 through 2010, there was an increase in 37.5% in years of life lived with disability (YLD) related to MDD (Ferrari, et al.,

2013). This increase was attributed to population growth and aging, as most of the burden of MDD occurs among adults of working age (Ferrari, et al., 2013). Further, the burden of MDD is higher among women compared to men (Ferrari, et al., 2013; Kessler & Bromet, 2013; Van de Velde, Bracke, & Levecque, 2010; Piccinelli & Wilkinson, 2000). Other global trends in depression have found that increasing age and being currently married are associated with decreased prevalence of MDD (Kessler & Bromet, 2013).

Results from the WMHSI data collected in Central and South America suggest that the prevalence of lifetime MDD is relatively high. Epidemiologic studies in Columbia based on the WMHSI study data estimated a 12% lifetime prevalence of MDD (Posada-Villa, Rodriguez, Duque, Garzon, Aguilar-Gaxiola, & Breslau, 2008). In Mexico, the prevalence of MDD was 4.6% (SE 0.6) in men and 9.7% (SE 0.6) in women (Medina-Mora, et al., 2008). The relatively high burden of MDD was also found using the WMH-CIDI in the *Sao Paulo Megacity Mental Health Survey*, conducted in Brazil; where the lifetime prevalence for MDD was 16.9% (SE 0.9) (Viana & Andrade, 2012). In Peru, the WMHSI estimated that 6.4% (CI: 5.6-7.2%) have major depression (Fiestas & Piazza, 2014).

Cross-sectional studies that use methodologies besides the WMHS methodology also report a high prevalence of MDD. In a community survey completed in Buenos Aires using an Argentine-validated Spanish version of the Beck Depression Inventory, 20% of the surveyed population were positive for clinical depression (Leiderman, Lolich, Vazquez, & Baldessarini, 2012).

Epidemiology of Alcohol Use Disorders

Along with MDD, Alcohol Use Disorders (AUDs) are among the most prevalent mental health disorders and they contribute 9.6% of disability-adjusted life-years (DALYs) caused by mental health and substance use disorders globally (Whiteford, et al., 2013). Though AUDs contribute significantly to DALYs in most countries, the treatment rates are also remarkably low (Whiteford, Ferrari, Degenhardt, Feigin, & Vos, 2015). Broadly, those between the ages of 25-

50 years have the highest burden of AUDs, after which there is a gradual decline (Whiteford, et al., 2013). AUDs are unique because they increased in prevalence on a global level between the years of 1990 and 2010, whereas the prevalence of other mental health disorders did not (Whiteford, et al., 2013). This is attributed to an increase in the true prevalence, not to demographic transitions such as aging populations (Whiteford, et al., 2013).

The burden of AUDs varies widely among the countries studied by the WMHSI. Recently published literature based on the WMH Survey data in Peru found that 5.6% have an alcohol use disorder (CI: 5.0 – 6.2%) (Fiestas & Piazza, 2014). An older study looking at the prevalence of AUDs based on a Spanish version of the DIS in the Independencia district of Lima, Peru, found that the prevalence of lifetime AUDs was higher in men (34.8%) compared to women (2.46%) (Yamamoto, Silva, Sasao, Wang, & Nguyen, 1993).

In Columbia, the lifetime prevalence of AUDs was 9.2% (SE 0.6) (Posada-Villa, Rodriguez, Duque, Garzon, Aguilar-Gaxiola, & Breslau, 2008). In Mexico, alcohol abuse was more common among men (14.5%) than among women (1.3%) (Medina-Mora, et al., 2008). Men (9.8%) were also more likely than women (3.3%) to have a lifetime diagnosis of alcohol abuse and dependence in the *Sao Paulo Megacity Mental Health Survey* (Viana & Andrade, 2012).

Comorbid Major Depressive Disorder and Alcohol-Use Disorders

Comorbid psychiatric disorders are pervasive among a variety of populations and comprise the majority of lifetime disorders in samples in the United States (Kessler, et al., 1994). Despite the important implications of comorbid disorders, the epidemiology and risk factors are frequently under-recognized (Swendson, Merikangas, Canino, Kessler, Rubio-Stipec, & Angst, 1998).

Extensive literature supports the association between MDD and AUDs and this connection has been identified as a priority in the field of global mental health research (Merikangas, et al., 1998; Boden & Fergusson, 2010). A systematic review concluded that

alcohol problems were associated with worse outcomes with respect to depression course, risk of suicide and death, social functioning and health care utilization (Sullivan, Fiellin, & O'Connor, 2005). Thus, this population is at risk for more severe morbidity and higher mortality than those who are suffering from a single condition.

A cross-national study examining the comorbidity between substance use disorders and mood and anxiety disorders using the WHO-CIDI reported that 20% of persons with alcohol problems and 26% of those with alcohol dependence had a lifetime history of any mood disorder (Merikangas, et al., 1998). In a study of former drinkers (sober for more than 12 months), a previous diagnosis of DSM-IV alcohol dependence significantly increased the risk of having a current episode of major depressive disorder (adjusted OR 4.21; 95% CI 2.82-6.28) (Hasin & Grant, 2002). This builds the evidence that major depressive episodes in those with alcohol problems are not merely an artifact or symptoms of acute alcohol intoxication or withdrawal (Hasin & Grant, 2002). From a clinical and public health standpoint, it is important to recognize the increased risk of MDD in those who have AUDs because substance-induced mental health disorders have unique treatments and require tailored interventions (Schuckit, 2006).

Alcohol Use Disorders: Sociocultural context

Globally, alcohol has long been an integral part of human society and culture. Demographic and economic trends influence the consumption of alcohol and alcohol use is higher where it is more affordable and available (Anderson, 2006). Historically, partnerships associated with alcohol were a structural feature of the Inca state and played an important role in engaging and expressing social bonds (Jennings & Bowser, 2008). Alcohol continues to be widely used and accepted in Peru and an estimated 90% of individuals between the ages of 12 and 64 living in urban areas have drunk alcohol at least once (Comision Nacional para el Desarrollo y Vida sin Drogas, 2002). Generally, mass-produced beer is most commonly consumed in highly urbanized areas, whereas traditional brews made from sugarcane (*canazo* /

aguardiente), yucca and corn (*chichi de jora*) are consumed in more rural regions (Peele & Grant, 1999). Alcohol is an integral part of religious holidays, indigenous festivals and national or regional holidays (Jennings & Bowser, 2008). Major holidays are celebrated over a period of 3-4 days and include heavy drinking, music and dancing by a large portion of those partaking in the festivities.

Social mores in Peru and other parts of Latin America, including the *machismo factor*, have been hypothesized to contribute to the differences in drinking behavior by gender. Drinking alcohol is generally viewed as masculine and this may facilitate heavier lifelong drinking behaviors among men in Peru (Yamamoto, Silva, Sasao, Wang, & Nguyen, 1993).

Summary

Based on the significant individual and societal burden of MDD and AUDs, I examined the major sociodemographic associations and risk factors for these conditions in Peru. This secondary analysis is based on data collected by the World Mental Health Survey Initiative in collaboration with the Instituto de Salud Publica y Administración.

Methods

Overview of Design

This was a secondary analysis of a cross-sectional survey completed in 2005 in five Peruvian cities (Arequipa, Chiclayo, Huancayo, Iquitos, Lima) as part of the World Mental Health Survey Initiative. Respondents were 18-65 years of age at the time of the interview.

Sample Size

The anticipated sample size was 6,000 completed interviews, including 3,376 from Lima and 2,624 from the other four cities. Due to budget restrictions, the sample size was reduced outside of Lima to 1,184 interviews per community. The sample size reduction was recalculated to be representative of the four cities. The final sample size was 4,560 interviews. In Lima, 3,376 respondents were selected and 2,794 interviews were completed (82.1% response rate).

In the other four cities, there were 1,184 respondents selected and 1,134 interviews completed (96.1% response rate) with a 90.2% overall response rate. The total number of respondents surveyed was 3,930.

Selection Criteria

Respondents were required to living in a formally-registered non-agricultural family household within the urban limits of Arequipa, Chiclayo, Huancayo, Iquitos, and Lima. Institutionalized people in hospitals, prisons, shelters, military institutions or similar public or private institutions were excluded.

Respondent Recruitment

Respondents were identified for interviews through a stratified, three-stage systematic selection scheme (Kessler, et al., 2004). All steps in the sampling process were carried out with close coordination between the sampling specialist, the central field manager and the local supervisor in each city.

1. Primary sampling unit: Based on census data from 1993 and pre-census data from 1999, the sampling framework of each city was divided into two strata: neighborhoods that existed in the 1993 census and those that appeared after the 1993 census. Based on these strata, the primary sampling unit consisted of neighborhoods of about 80 housing units (*conglomerados*), which were chosen with probabilities proportional to size measures.
2. Secondary sampling unit: A housing unit was selected from a list of all the housing units within the limits of each of the chosen neighborhoods. Ten housing units were selected using simple randomization methods.
3. Tertiary sampling unit: One eligible adult was chosen from each of the housing units selected. This was completed through compiling a list of all of the eligible adults in the household, then choosing one from the Kish table. No substitution was allowed.

The final sample was selected from 422 neighborhoods in metropolitan Lima and 148 neighborhoods in the rest of the cities.

Measurement and Data Collection

The content of the survey was a version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) that was developed specifically for the WHO World Mental Health Survey Initiative. Translation into Spanish was completed through an expert panel convened by the WHO and panel members were clinicians and researchers from Chile, Colombia, Mexico, Panama, Spain and the United States (including Puerto Rico) (Medina-Mora, et al., 2006).

The interviews were divided into two parts: Part I was administered to all respondents and captured all the core WMH-CIDI disorders, Part II was administered to a specific subset of the Part I respondents and included assessments of risk factors, consequences, services and other correlates of the core disorders and the assessment of other disorders that were of secondary importance or too time-consuming to assess in all respondents. Part II was weighted towards those with clinically significant psychopathology and included three subgroups: 1.) Those that met lifetime criteria for a mental health disorder, were sub-threshold lifetime criteria for a mental health disorder and sought treatment, or those who planned to commit suicide or had attempted suicide; 2.) Those respondents that met sub-threshold criteria for a mental health disorder, those who have sought treatment for an emotional or substance use problem, those who have ever had suicidal ideation, or those who have used psychotropic medications in the past 12 months; 3.) 25% of all respondents to Part I were given Part II. See Appendix A for a chart representing those that were included in Part II.

Survey Weights

Weighting of the data collected based on the person-level sample in Peru incorporated sample selection, nonresponse and poststratification factors (Kessler & Ustun, 2008). The primary reason for applying weights to these data is to reduce or eliminate potential sources of

bias that may be present in unweighted analysis. The analysis weights for these data were completed by the Harvard Data Analysis Coordination Centre using data from local project teams.

The Part I (n = 3930) weight comprised of four main steps:

- I. Non-response weight: Takes into account the number of eligible persons (complete and incomplete) compared to the number of eligible persons who completed Part I of the survey.
- II. Post-stratification weight: This was based on the 2005 census data and weighted on city, age and sex.
- III. Normalization of weights: This ensured that the sum of the weights was equal to the total sample size of Part I data.
- IV. Trimming of normalized weights: The upper and lower 5% of each tail were trimmed.

Only a portion of those completing Part I went on to take Part II and inclusion in Part II was partially based on the presence or absence of symptoms as prescribed in the WHO-CIDI interview (see *Measurement and Data Collection* section above).

The four main steps of Part II (n = 1801) weighting:

- I. Part II selection weight: This takes into account the probability that one may complete Part II of the survey.
 - a. Those fulfilling the criteria for a mental health diagnosis based on Part I were selected into Part II with a probability of 1.0.
 - b. All others completing Part I were selected to complete Part II with a probability of 0.25.
- II. Post-stratification weight: Like Part I, this was based on the 2005 census data and weighted based on city, age and sex.

- III. Part II weight: This was a compilation of Part I weight, Part II weight and the post-stratification weight.
- IV. Normalize Part II weight: This ensures that the sum of the weight is equal to the total sample size of the Part II data (n = 1801).

A more detailed description of the weighting techniques used by the WMHSI research team and affiliates has been published previously (Kessler & Ustun, 2008).

Figure 1. Histogram representing the final Part I weights

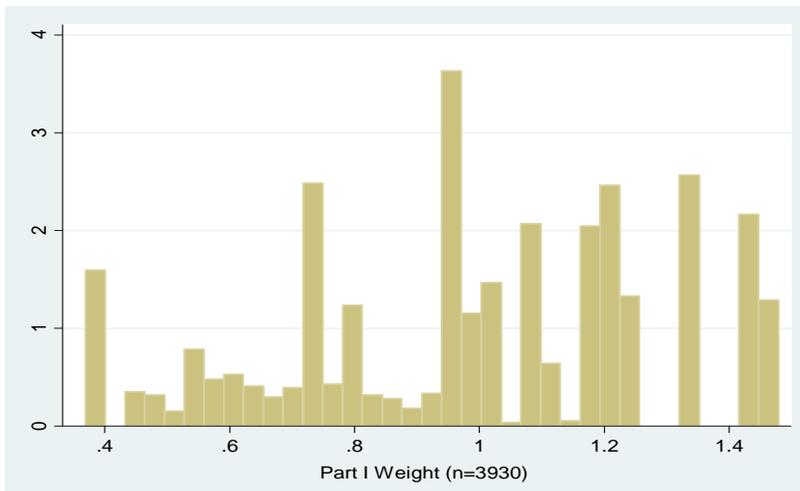
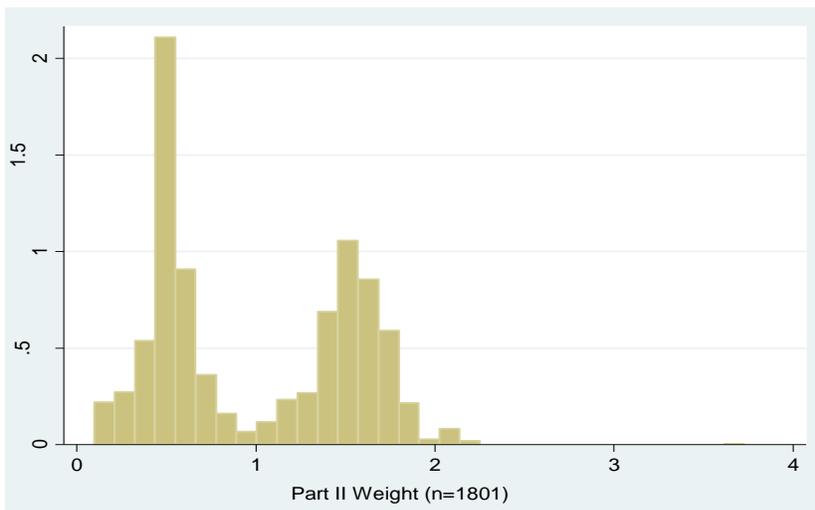


Figure 2. Histogram representing the final Part II weights



Variables

Outcome variables, such as Major Depressive Episode (MDE), Alcohol Abuse and Alcohol Dependence were assessed during the interview and based on DSM-IV criteria (Appendix B). MDE is defined by DSM-IV criteria as a period of two or more weeks during which there is depressed mood or loss of interest or pleasure in nearly all activities. The individual must also report four or more additional symptoms (i.e., changes in appetite or weight; sleep; psychomotor activity; decreased energy; feelings of worthlessness or guilt; difficulty thinking, concentrating, or making decisions; or recurrent thoughts of death or suicide) (American Psychiatric Association, 1994). Major Depressive Disorder (MDD) is defined by those individuals that have had one or more episodes of MDE and no history of Manic, Mixed, or Hypomanic Episodes. Thus, this analysis includes those who have had one or more MDE, whether they may ultimately meet the diagnostic criteria for unipolar or bipolar depression.

As defined by the American Psychiatric Association, substance abuse is a maladaptive pattern of substance use characterized by recurrent and significant adverse consequences (American Psychiatric Association, 1994). Substance dependence is characterized by cognitive, behavioral and physiological symptoms related to continued substance use by the individual despite significant substance-related problems (American Psychiatric Association, 1994). Because alcohol abuse and dependence can represent a spectrum and one can transition from abuse to dependence and vice versa during a lifetime. In the current analysis, AUDs included alcohol abuse with or without dependence.

Data Management

The Institutional Review Board of the Peru (Facultad de Salud Publica y Admistracion) approved and monitored compliance with procedures for obtaining informed consent and protecting human subjects for the data collection completed in Peru. Additionally, Oregon

Health and Sciences University Institutional Review Board determined that the secondary analysis met criteria for exemption from full review because the data were de-identified.

De-identified data files were provided in STATA format. Though the data analysis focused on those with lifetime MDE and AUDs, all respondent records were kept in the master dataset as required by STATA for correct variance estimation of complex survey data. Analysis was completed using STATA version 13 (Stata/IC 13.1, College Station, TX, USA). Variance was estimated using the jackknife repeated replication method. Data management included recoding and creating new variables, including creating context-appropriate categorization of the variables.

Statistical Analysis

Data analysis accounted for the complex sample design and weighting. Independent variables were coded as shown in Table 2. Weights were applied to adjust for the stratified multistage sampling procedure and associated clustering (as described in *Survey Weights*

Table 2. Summary of Independent Variables			
Variable	Question / Additional information	Possible Responses	Coding for analysis
Gender	What is your sex?	1. Male 2. Female	1 = Male 0 = Female
Age	How old are you?	0. ... 120. 998. Refused 999. Don't know	1 = ≥18 - <30 2 = ≥30 - <40 3 = ≥40 - <50 4 = ≥50+
City	(Recorded by interviewers)	1. Iquitos 2. Arequipa 3. Lima 4. Huancayo 5. Chiclayo	1 = Iquitos 2 = Arequipa 3 = Lima 4 = Huancayo 5 = Chiclayo
Marital Status	Are you currently married?	1. Married 2. Separated 3. Divorced 4. Widowed 5. Never married 8. Refused 9. Don't know	1 = Married / marriage-like relationship 2 = Previously married 3 = Never married
	Are you currently living with someone in a marriage-like relationship?	1. Yes 5. No 8. Refused 9. Don't know	
Educational Attainment	What is the highest grade of school or year of college you completed?	0. None 1. One 2. Two 3. Three ... 17. Seventeen or more 98. Refused 99. Don't know	1 = 0 - Up to one year of secondary 2 = Some secondary 3 = Completed secondary 4 = Some university 5 = Completed university level to post-graduate

section above). The prevalence data were examined by sociodemographic variables, including gender, age, city, educational attainment, and marital status by cross-tabulation.

Univariate Logistic Regression Analysis

Univariate logistic regression models examined patterns in sociodemographic variables within both disease outcomes and assessed odds ratios (ORs) and corresponding confidence intervals. Wald test results and corresponding p-values were used to assess statistical significance. Associations were expressed as unadjusted ORs with their corresponding 95% confidence intervals.

Multivariate Logistic Regression Analysis

Multiple logistic regression analysis examined the effect of multiple co-variables on the disease states of interest (lifetime MDE and lifetime AUD). Covariates were included in the model based on their clinical utility and statistical significance if univariate analysis suggested a potential relationship (i.e., p-value < 0.25). Variables were included in the model based on the Pearson residual (higher value of Pearson Chi-Square statistic suggests model fits well), Deviance residual, Hosmer-Lemeshow test, Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) (Akaike, 1974; Schwarz, 1978). The AIC and BIC were helpful in building the most parsimonious model because the sample size is relatively large and both the AIC and BIC penalize the model for having too many parameters (Hosmer, Lemeshow, & Sturdivant, 2013). Once this preliminary model was built, interactions were assessed between independent variables.

We sought to identify risk factors related to comorbid MDD and AUDs, but were limited by the small sample size of those who met criteria for having both of these diseases in their lifetime (n = 25). To identify covariate patterns that were poorly fit or influential the analysis examined Pearson Chi-Square Statistic, Deviance and Hosmer-Lemeshow statistics (Hosmer,

Lemeshow, & Sturdivant, 2013). These methods measure the difference between the observed and fitted values and were assessed visually by graphics created using STATA.

Results

The demographic distribution of the weighted and unweighted surveyed population is shown in Table 3. The population was weighted based on a combination of the non-response weight and 2005 census data related to city, age and gender. The unweighted sample was more likely to be female and older in age. A majority of the respondents were inhabitants of Lima (70.7% of unweighted, 80.6% of weighted), which represents the relative population density of Lima compared to the other cities. A majority of the population was never married (58.3% of weighted) and completed secondary education (57.1% of weighted).

Table 3. Demographic distribution of respondents, weighted and unweighted *		
	Weighted sample (%)*	Unweighted sample (%)
Gender		
Male	48.4	44.8
Female	51.6	55.2
Age		
Mean (SE)	36.0 (0.25)	37.4 (0.20)
≥18 - <30	37.8	31.9
≥30 - <40	25.3	26.1
≥40 - <50	18.6	22.7
50 +	18.3	19.4
City		
Arequipa	8.2	11.6
Chiclayo	4.9	6.4
Huancayo	3.0	5.5
Iquitos	3.4	5.9
Lima	80.6	70.7
Marital Status		
Married	32.9	35.4
Never married	58.3	54.9
Married before		
Separated	5.3	5.9
Divorced	1.2	1.4
Widowed	2.2	2.4
Other		
Refused	0.03	0.03
Don't Know	0.03	0.03
Education		
Primary	13.2	14.8
Some Secondary	12.2	11.8
Completed Secondary	29.3	28.1
Some University	27.6	26.8
Completed University	17.6	18.5
Employment Status (n = 2129)		
Employed	33.6	33.2
Self-employed	29.8	30.0
Looking/unemployed	5.4	4.9
Temporarily...	2.1	1.7
Retired	1.6	2.0
Illness	0.1	0.1
Disabled	0.3	0.2
Student	8.0	7.1
Homemaker	18.1	19.7

*Sample size was 3930 unless otherwise noted.

Prevalence of DSM-IV Mental and Substance Use Disorders

The lifetime prevalence of a major depressive episode was 6.9%, alcohol abuse with and without dependence was 5.6%, alcohol dependence was 1.3% and comorbid major depressive episode and alcohol use disorder was 0.8% (Table 4). The prevalence of a lifetime

major depressive episode was lower in men (5.7%) than women (8.0%). In contrast, lifetime alcohol abuse and dependence were more common among men (10.7% = abuse with and without dependence; 2.6% = dependence) than women (0.8% = abuse with and without dependence; 0.1% = dependence). Overall the prevalence of lifetime comorbid major depressive episode and alcohol use disorder was 0.8%, but when evaluated by gender, lifetime comorbid major depressive episode was more common in men (1.2%) compared to women (0.3%). However, this outcome was relatively rare (n = 25) and most with comorbid disorder were from Lima (n = 24/25 or 96%).

	Total (n = 3930)			Men (n = 1759)			Women (n = 2171)		
	Lifetime	12-month	1-month	Lifetime	12-month	1-month	Lifetime	12-month	1-month
Major Depressive Episode	6.9 (0.38)	2.9 (0.26)	0.7 (0.13)	5.7 (0.63)	2.4 (0.33)	0.6 (0.17)	8.0 (0.40)	3.4 (0.36)	0.9 (0.21)
Alcohol Use Disorder**	5.6 (0.33)	1.5 (0.17)	0.4 (0.10)	10.7 (0.65)	2.7 (0.33)	0.8 (0.21)	0.8 (0.20)	0.3 (0.13)	0 (0)
Alcohol Dependence	1.3 (0.13)	0.5 (0.11)	0.2 (0.07)	2.6 (0.28)	1.0 (0.22)	0.4 (0.15)	0.1 (0.06)	0 (0)	0 (0)
MDD and AUD	0.8 (0.15)			1.2 (0.28)			0.3 (0.13)		

*Values are given as % (SE)

**Defined as alcohol abuse with and without dependence

Demographic correlates of lifetime DSM-IV MDE, AUD and comorbid MDE and AUD

Men were significantly less likely to have lifetime MDE compared to women (unadjusted OR 0.69, 95% CI 0.53 – 0.90) (Table 5). Age was not associated with lifetime MDE, as demonstrated by the lack of trend or significant differences between age categories (p-value 0.76). Populations surveyed in different cities varied. Respondents from Arequipa, Chiclayo and Iquitos were significantly less likely to have lifetime MDE compared to individuals in Lima. Level of education was not a predictor of lifetime major depressive episode, though respondents with higher education tended to have lower lifetime MDE (p-value 0.03). Those that were married previously (unadjusted OR 2.5) or never married (unadjusted OR 1.4) were significantly more likely to have MDE; marriage appeared to be protective for MDE.

Men were significantly more likely to be diagnosed with an AUD in their lifetime compared to women (unadjusted OR 14.3, 95% CI 8.46 – 24.29). Age was not associated with a lifetime diagnosis of an alcohol use disorder. When compared to Lima, living in Arequipa and Chiclayo was protective against a lifetime AUD (unadjusted ORs 0.35 and 0.50, respectively). Those living in Huancayo were more likely than those living in Lima to have a lifetime AUD (OR 1.4, 95% CI 1.08 – 1.86). When examined by education category, respondents with some secondary education and those that completed secondary education were more likely than those with university education to have an AUD (unadjusted ORs 3.4 and 1.9, respectively). Additionally, there was a significant trend between education and lifetime alcohol use disorder (p-value 0.002).

	Depression		Alcohol Use Disorder		Depression and Alcohol Use Disorder	
	% (SE)	OR (95% CI)	% (SE)	OR (95% CI)	% (SE)	OR (95% CI)
Sex						
Male	5.7 (0.63)	0.69 (0.53-0.90)	10.7 (0.65)	14.3 (8.46-24.29)	1.2 (0.28)	4.4 (1.41-13.57)
Female	8.0 (0.40)	referent	0.83 (0.20)	referent	0.29 (0.13)	referent
Age						
≥18 - <30	6.7 (0.78)	referent	5.8 (0.57)	referent	1.1 (0.25)	referent
≥30 - <40	7.3 (0.96)	1.1 (0.72 – 1.70)	5.5 (0.59)	0.94 (0.70-1.26)	0.46 (0.23)	0.43 (0.16-1.13)
≥40 - <50	7.2 (0.77)	1.1 (0.75-1.59)	6.0 (1.00)	1.0 (0.66-1.63)	0.92 (0.36)	0.86 (0.30-2.43)
50 +	6.4 (0.84)	0.96 (0.69-1.35)	4.9 (0.95)	0.83 (0.51-1.35)	0.34 (0.24)	0.31 (0.06-1.54)
Trend test		0.76		0.29		0.25
City						
Arequipa	1.4 (0.41)	0.16 (0.08-0.31)	2.2 (0.09)	0.35 (0.30-0.42)	0	--*
Chiclayo	2.1 (0.83)	0.25(0.10-0.61)	3.1 (0.73)	0.50 (0.29-0.86)	0	--*
Huancayo	6.7 (1.34)	0.83(0.52-1.34)	8.2 (0.82)	1.4 (1.08-1.86)	0	--*
Iquitos	3.6 (0.23)	0.43 (0.36-0.53)	7.0 (1.83)	1.2 (0.64-2.22)	0.43	--*
Lima	7.9 (0.46)	referent	5.9 (0.39)	referent	0.86	--*
Education						
Primary	8.8 (1.11)	1.6 (0.96-2.71)	4.0 (0.59)	1.1 (0.59-1.98)	0.70 (0.37)	0.8 (0.15-4.66)
Some secondary	6.5 (1.21)	1.2 (0.73-1.81)	11.4 (1.11)	3.4 (1.96-5.75)	0.5 (0.36)	0.6 (0.07-5.70)
Complete secondary	7.3 (1.00)	1.3 (0.77-2.25)	6.8 (0.88)	1.9 (1.10-3.29)	1.1 (0.32)	1.3 (0.29-6.01)
Some University	6.5 (0.69)	1.1 (0.72-1.83)	3.7 (0.66)	1.0 (0.49-2.03)	0.4 (0.22)	0.58 (0.09-3.59)
Completed University	5.7 (1.03)	referent	3.7 (0.79)	referent	0.8 (0.46)	referent
Trend test		0.03		0.002		0.93
Marital Status						

Married / marriage-like relationship	5.6 (0.41)	referent	5.8 (0.52)	referent	0.55 (0.13)	referent
Married previously	12.5 (2.11)	2.5 (1.71-3.61)	7.3 (1.62)	1.2 (0.75-1.95)	1.7 (0.92)	3.2 (1.09 – 9.18)
Never married	7.8 (0.69)	1.4 (1.07-1.85)	4.9 (0.36)	0.88 (0.64-1.20)	0.84 (0.31)	1.4 (0.58 – 3.42)

*Insufficient data for analysis

Comorbid MDE and AUD were more common in men compared to women (unadjusted OR 4.4, 95% CI 1.41 – 13.56). Age and education were not correlated with lifetime comorbid MDE and AUD (Table 5). Those who were previously married were significantly more likely to have comorbid MDE and AUDs in their lifetime compared to those who were married or never married (OR = 3.2; 95% CI 1.09 – 9.18). Overall, 96% of comorbid MDE and AUD was found in Lima (24/25 total). This limited the analysis of the correlates based on city.

Sociodemographic characteristics of those with lifetime MDE and lifetime AUDs were examined by gender (Table 6). The prevalence of MDE was lowest in women between the ages of 18 and 30 years (6.2%) and increased to 9.1% in those 30 to 40 years of age. Conversely, in men, the prevalence of MDE was highest in the youngest age group (7.2%) and decreased to 3.7% among men 50 years of age and older.

	Major Depressive Episode		Alcohol Use Disorder	
	Men	Women	Men	Women
Total	5.7 (0.63)	8.0 (0.40)	10.7 (0.65)	0.83 (0.20)
Age				
≥18 - <30	7.2 (1.07)	6.2 (0.84)	10.7 (1.07)	1.2 (0.51)
≥30 - <40	5.5 (1.12)	9.1 (1.18)	10.8 (1.14)	0.48 (0.38)
≥40 - <50	4.8 (1.14)	9.5 (1.28)	11.1 (1.86)	1.28 (0.61)
50 +	3.7 (1.35)	9.0 (1.41)	9.9 (1.98)	0.15 (0.15)
City				
Arequipa	0.52 (0.50)	2.1 (0.68)	4.2 (0.32)	0.33 (0.34)
Chiclayo	0.93 (0.88)	3.2 (0.90)	6.5 (1.15)	0
Huancayo	5.0 (0.21)	8.2 (2.34)	14.2 (0.01)	2.7 (1.45)
Iquitos	1.8 (1.92)	5.4 (1.64)	14.2 (2.78)	0
Lima	6.7 (0.78)	9.1 (0.47)	11.3 (0.80)	0.89 (0.24)
Marital Status				
Married / Marriage-like relationship	4.3 (0.79)	6.8 (0.67)	11.5 (1.17)	0.58 (0.13)
Previously married	9.6 (3.52)	14.2 (2.56)	17.0 (3.19)	1.9 (0.85)
Never married	7.1 (0.93)	8.5 (0.85)	8.5 (0.66)	1.0 (0.49)
Education				
Primary	5.4 (0.38)	10.2 (1.47)	11.6 (1.68)	0.4 (0.26)
Some Secondary	3.9 (1.03)	9.0 (2.13)	21.4 (2.10)	1.5 (0.87)
Complete Secondary	7.4 (1.53)	7.3 (0.81)	12.3 (1.56)	1.0 (0.57)
Some University	4.3 (0.87)	8.5 (1.22)	6.7 (1.15)	0.8 (0.30)
Completed University	5.9 (1.40)	5.4 (1.58)	6.3 (1.41)	0.5 (0.38)

*Values are given as % (SE)

Men and women living in Lima had the highest prevalence of MDE (6.7% and 9.1%, respectively). Those living in Huancayo also had a relatively high prevalence of MDE (8.2% = women; 5.0% = men). Previously married men and women had a high prevalence of MDE (9.6% and 14.2%, respectively). In women, those with lower educational attainment had a higher prevalence of MDE than those who have completed secondary or university level. This trend was not seen in men.

Prevalence trends of lifetime AUD based on age were not evident. Men living in Huancayo, Iquitos and Lima had a relatively high prevalence of AUD (14.2%, 14.2% and 11.3%, respectively). Trends were difficult to determine in women based on the low prevalence of lifetime AUDs. Previously married men and those who have only had some secondary education had the highest prevalence of AUDs (17% and 24%, respectively).

Logistic Regression Analysis: Lifetime Major Depressive Episode

Univariate logistic regression suggested that gender, city, marital status and education were associated with lifetime MDE (p-values < 0.20) (Table 7). Weighted percentages and unadjusted odds ratios are reported in Table 7.

Table 7. Summary of Unadjusted Associations between Independent Variables and Lifetime MDE							
	Lifetime MDE	Coefficient	Constant	Standard Error	Odds Ratio	95% CI	p
Gender*			-2.44				
Male	5.7 (0.63)	-0.38		0.13	0.69	0.53-0.90	0.009
Female	8.0 (0.40)				referent		
City*			-2.46				
Arequipa	1.4 (0.41)	-1.83		0.32	0.16	0.08-0.31	0.00
Chiclayo	2.1 (0.83)	-1.39		0.43	0.25	0.10-0.61	0.004
Huancayo	6.7 (1.34)	-0.19		0.23	0.83	0.52-1.34	0.42
Iquitos	3.6 (0.23)	-0.83		0.09	0.44	0.36-0.53	0.00
Lima	7.9 (0.46)	--			referent		
Age			-2.64				0.90
≥18 - <30	6.7 (0.78)	--			referent		
≥30 - <40	7.3 (0.96)	0.10		0.21	1.11	0.72-1.70	0.63
≥40 - <50	7.2 (0.77)	0.09		0.18	1.10	0.75-1.59	0.62
50 +	6.4 (0.84)	-0.04		0.16	0.96	0.69-1.35	0.82
Marital Status*			-2.83	0.08			
Married/Marriage-like relationship	5.6 (0.41)	--		--	referent	--	
Separated	12.5 (2.11)	0.89	0.21		2.44	1.59 – 3.75	0.00
Never married	7.8 (0.69)	0.36	0.13		1.43	1.10 – 1.86	0.01
Education*			-2.81	0.19			
Primary	8.8 (1.11)	0.48		0.25	1.61	0.96 – 2.71	0.07
Some secondary	6.5 (1.21)	0.14		0.22	1.15	0.72 – 1.81	0.54
Completed	7.3 (1.00)	0.28		0.26	1.32	0.77 – 2.25	0.30

secondary							
Some University	6.5 (0.69)	0.14		0.22	1.14	0.72 – 1.83	0.55
Completed University	5.7 (1.03)	--		--	referent	--	--

*Highly associated with outcome in univariate logistic regression models (p<0.20)

A main effects multivariate logistic regression model for lifetime MDE included gender, city and marital status (Table 8) and provided a relatively good fit (HL Ward F=1.84, p = 0.87). Adding the education variable did not improve the fit so it was excluded from the final regression model.

Table 8. Multivariate Logistic Regression Models for Lifetime Major Depressive Episode		
	Final Model	
	OR [95% CI]	p-value
Gender		
Men	0.63 (0.49 – 0.83)	0.001
Women	referent	
City		
Arequipa	0.17 (0.08 – 0.37)	0.00
Chiclayo	0.36 (0.18 – 0.75)	0.006
Huancayo	0.91 (0.53 – 1.54)	0.72
Iquitos	0.46 (0.23 – 0.91)	0.03
Lima	referent	--
Marital Status		
Married	referent	--
Previously married	2.48 (1.70 – 3.62)	0.00
Never married	1.48 (1.12 – 1.95)	0.005

Preliminary analysis for potential interactions revealed no significant interactions between the variables comprising the main effects model. Furthermore, when marital status was recoded from a categorical variable (married / marriage like relationship, previously married and never married) to a dichotomist variable (married / married like relationship, not married) there were no interactions between gender and marital status.

Logistic Regression Analysis: Lifetime Alcohol Use Disorder

Univariate logistic regression suggested that gender, city, marital status and education were associated with lifetime AUD (p-values < 0.20) (Table 9). Weighted percentages and unadjusted odds ratios are reported in Table 9 for all variables considered. A main effects

model for lifetime AUD included gender, city, marital status and education (Table 10). This model provided a relatively good fit of the data (HL Ward $F=10.1$, $p = 0.26$).

Table 9. Demographic correlates of Lifetime DSM-IV Alcohol Use Disorders: Summary of Unadjusted Associations							
	Lifetime AUD	Coefficient	Constant	Standard Error	Odds Ratio	95% CI	p
Gender*			-4.79				
Men		2.66		0.25	14.3	8.46 – 24.29	0.00
Women		--			referent		
City*			-2.76				
Arequipa		-1.04		0.08	0.35	0.30 – 0.42	0.00
Chiclayo		-0.69		0.26	0.50	0.29 – 0.86	0.02
Huancayo		0.35		0.26	1.41	1.08 – 1.86	0.02
Iquitos		0.18		0.30	1.19	0.64 – 2.22	0.56
Lima		--			referent		
Age			-2.79				
≥18 - <30		--	--		referent		
≥30 - <40		-0.06		0.14	0.94	0.70 – 1.26	0.66
≥40 - <50		0.03		0.22	1.04	0.66 – 1.63	0.86
50 +		-0.19		0.23	0.83	0.51 – 1.35	0.43
Marital Status*			-2.78				
Married/Marriage-like relationship		--		--	referent	--	
Previously married		0.24		0.29	1.27	0.69 – 2.33	0.42
Never married		-0.19		0.11	0.83	0.66 – 1.03	0.09
Education*			-3.26				
Primary		0.08			1.08	0.59 – 1.98	0.80
Some Secondary		1.21			3.36	1.96 – 5.75	0.00
Completed Secondary		0.64			1.90	1.10 – 3.29	0.02
Some University		-0.005			1.00	0.49 – 2.03	0.99
Completed University		--		--	referent	--	--

*Highly associated with outcome in univariate logistic regression models (p<0.20)

Table 10. Multivariate Logistic Regression Models for Lifetime Alcohol Use Disorder		
	Final Model	
	OR [95% CI]	p-value
Gender		
Men	15.6 (9.50 – 25.59)	<0.001
Women	referent	--
City		
Arequipa	0.36 (0.18 – 0.73)	0.004
Chiclayo	0.44 (0.20 – 0.96)	0.04
Huancayo	1.62 (0.92 – 2.84)	0.09
Iquitos	1.32 (0.77 – 2.29)	0.31
Lima	referent	--
Marital Status		
Married	referent	--
Previously married	1.90 (1.14 – 3.17)	0.01
Never married	0.80 (0.58 – 1.11)	0.19
Education		
Primary	2.06 (1.12 – 3.79)	0.02
Some Secondary	4.05 (2.39 – 6.88)	<0.001
Completed Secondary	2.35 (1.43 – 3.84)	0.001
Some University	1.34 (0.78 – 2.29)	0.29
Completed University	referent	--

Discussion

This secondary analysis examined the epidemiology of DSM-IV lifetime major depressive episode and alcohol use disorders (including alcohol abuse and alcohol abuse with dependence) among respondents living in urban Peru.

Lifetime Prevalence

Major Depressive Episode

The estimated prevalence of lifetime major depressive episode in Peru (6.9%) was similar to the burden of depression found in Central and South America with WMHSI methodology (4.6% - 16.9%) (Medina-Mora, et al., 2008; Viana & Andrade, 2012). Interestingly, the prevalence in the United States and other high income countries is consistently higher (Kessler & Bromet, 2013; Kessler, et al., 2007). Using DSM-IV criteria and WMHSI methodology, the average estimated prevalence of depression in high-income countries is 14.6% versus 11.1% in low- and middle-income countries (Kessler & Bromet, 2013). These cross-national differences can be partially attributed to the methodology and diagnostic questions used to detect clinical cases of depression. The countries that had the highest prevalence of depression generally report less impairment from the condition (Simon, Goldberg, Von Korff, & Ustun, 2002). Thus, the DSM-IV depression criteria may capture different levels of severity in different countries (Simon, Goldberg, Von Korff, & Ustun, 2002).

A study completed in Peru, Mexico and Venezuela used different depression criteria to identify the prevalence of late-life depression and found the prevalence of depression differed comparing DSM-IV criteria versus two geriatric depression scoring scales: the Geriatric Mental State – Automated Geriatric Examination for Computer Assisted Taxonomy (GMS-AGECAT) and the EURO-D depression scoring criteria (Guerra, et al., 2009). Sub-syndromal depression was independently associated with disability in this study, which may indicate that by using the DSM-IV criteria this analysis is missing a portion of severely disabling, yet sub-syndromal depression.

Furthermore, it is possible that the low prevalence of lifetime MDE is the result of non-response bias; individuals with more severe mental health conditions are less likely to respond positively to a survey. This type of bias might be marked in countries like Peru where mental health conditions are widely untreated on the community level.

Alcohol Use Disorders

The lifetime prevalence of alcohol abuse in Peru was 10.7% in men and 0.83% in women and is lower than the prevalence of alcohol abuse in other Central and South American countries. Using the WMHSI methodology in Mexico, the prevalence of alcohol abuse was higher than Peru among men (14.5%) and women (1.3%) (Medina-Mora, et al., 2006). The same was also found when comparing the lifetime prevalence of alcohol abuse in Sao Paulo, Brazil where it is also higher in men (16.4%) and women (4.0%) (Viana & Andrade, 2012).

The relatively low prevalence of lifetime AUDs in Peru is likely an underrepresentation of the true burden of disease. One of the possible explanations is that troublesome behaviors that are the cultural norm in Peru (i.e. heavy episodic drinking or binge drinking) are not captured by the DSM-IV definitions of alcohol abuse and dependence. Secondly, it is unclear how well the WMH-CIDI questions conformed to the cultural context of those interviewed in Peru. Questions that are components of the DSM-IV alcohol abuse definition, such as “Did drinking result in problems with the police?” or “Did you jeopardize your safety or drank when you could get hurt?” depend on an individuals’ perception and possible consequences of their own risk-taking behaviors. However, this may be obscured by the cultural context or acceptability of these pathologic behaviors.

Lifetime Comorbid Major Depressive Episode and Alcohol Use Disorders

The overall lifetime prevalence of comorbid MDE and AUDs was low in this analysis (0.75%). Based on a cross-national study looking at the comorbidity between MDD and AUDs, 20% of individuals with alcohol problems and 26% of those with alcohol dependence also had a lifetime history of any mood disorder (Merikangas, et al., 1998). Based on these estimates, the

low overall lifetime prevalence of alcohol dependence (1.3%) found in Peru compared to other countries, probably resulted in the low estimates of lifetime comorbid MDE and AUDs.

Existing epidemiological data suggest that these conditions are linked in a casual manner (Boden & Fergusson, 2010). In the United States, the association between MDD and alcohol dependence is strong and this has been attributed to genetic factors and psychotropic effects of alcohol (Kendler, Heath, Neale, Kessler, & Eaves, 1993; Grant & Harford, 1995). Interestingly, the association between MDD and AUDs is especially strong among women in the United States (Grant & Harford, 1995). This may have implications in Peru related to the cultural acceptability of using alcohol and reporting alcohol problems among women. It is possible that the cultural norms in Peru are protective for women and reduce their predilection to using alcohol in the setting of mood disorders.

Lifetime Major Depressive Episode: Gender Differences

There were significant differences in the burden of depression in men (5.7%) compared to women (8.0%) in this study. Peruvian men were, on average, 37% less likely to suffer from lifetime major depressive episodes (adjusted OR 0.63, 95% CI 0.48 – 0.83). This is consistent with the relatively higher prevalence of depression among women globally. Several hypotheses have been generated to explain these differences. The *differential exposure* hypothesis proposes that women report poorer health compared to men because they have more obligations and demands in their social roles and fewer resources to cope with these demands (Walters, McDonough, & Strohschein, 2002). *Differential vulnerability* relates to women's greater "reactivity" or responsiveness to ongoing life stressors compared to men (Walters, McDonough, & Strohschein, 2002). The *differential exposure* theory was supported by a study completed in Latin America which found that women are more exposed to social and material disadvantages during their life compared to men (Alvarado, Zunzunegui, Beland, Sicotte, & Tellechea, 2007). These disadvantages related to marital status (increased widowhood

compared to men), socioeconomic resources and levels of physical functioning (Alvarado, Zunzunegui, Beland, Sicotte, & Tellechea, 2007).

The gender gap between the prevalence of lifetime MDE in women compared to men becomes obvious at the transition from the youngest age category (18 - 29 years) to the slightly older age category (30 – 39 years). The prevalence of lifetime MDE in the youngest category of women is 6.2%, increases to 9.1% in the next category and remains approximately stable throughout the other age categories (Table 3). This increase occurs at the time of the emergence of gender differences in social roles, and this trend has been highlighted by other studies (Wilhelm & Parker, 1994; Wilhelm, Parker, & Hadzi-Pavlovic, 1997). Anxiety disorders were positively and significantly associated with more episodes of major depression for women and the association may be modified by other comorbid mental health disorders, including anxiety (Wilhelm, Parker, & Hadzi-Pavlovic, 1997). If there is a differential in the prevalence of another mental health condition in women, like anxiety, this could impact the reporting of depressive symptoms. The result would be an artificially high prevalence of depression.

Interestingly, more studies have examined the less tangible entities associated with common mental health disorders (CMDs) like depression. Social capital, defined as the norms, networks and associations that facilitate cooperative action, appears to be a protective factor for CMDs (Putnam, 1993). In a small study looking at the social capital of mothers in various low-income countries, those in Peru had less cognitive social capital compared to mothers in Vietnam, India and Ethiopia (De Silva, Huttly, Harpham, & Kenward, 2007). Based on these results and the inverse relationship between cognitive social capital and CMDs, women in Peru may be at a higher risk of developing lifetime MDE (De Silva, McKenzie, Harpham, & Huttly, 2005).

Alcohol Use Disorders: Gender Differences

In contrast to MDE, lifetime AUDs were found to be much more prevalent in men (10.7%) compared to women (0.8%). The higher prevalence found among men is consistent

with other Central and South American countries based on the WMHSI methodology (Medina-Mora, et al., 2006; Viana & Andrade, 2012).

AUDs are more prevalent in men not just in Central and South America, but globally (Durrant & Thakker, 2003; Wilsnack, Wilsnack, Kristjanson, Vogeltanz-Holm, & Gmel, 2009). Alcohol consumption by women is generally less acceptable and this reflects the concept that drinking does not align with the traditional female roles associated with home and family (Durrant & Thakker, 2003). Gender disparities in the lifetime prevalence of AUDs varies significantly between countries and in one study, several Central and South American countries were among the countries with male/female ratios greater than 1.5 (Wilsnack, Wilsnack, Kristjanson, Vogeltanz-Holm, & Gmel, 2009).

The marked gender disparity in Peru found in this analysis (adjusted OR 15.6, 95% CI 9.50—25.60) is comparable to older and more limited studies of alcohol abuse in Peru. Using a revised translated form of the DIS based on DSM-III criteria in a district of Lima, men were much more likely to have alcohol abuse or dependence compared to women (relative risk 13.6) (Yamamoto, Silva, Sasao, Wang, & Nguyen, 1993). Future population-based surveys that include epidemiological trends in urban and rural settings in Peru will help understand the existing trends and how they evolve in the wake of economic and sociocultural transitions. The reasons behind the higher alcohol consumption in men are likely multifactorial and entrenched in complex social and cultural mores (Wilsnack, Wilsnack, Kristjanson, Vogeltanz-Holm, & Gmel, 2009).

Lifetime major depressive episode: Geographic variation

There were significant trends in the prevalence of MDE by city – Arequipa (1.4%), Chiclayo (2.1%) and Iquitos (3.6%) had the lowest prevalence. Most notably, those surveyed in Arequipa were 83% less likely to have a lifetime major depressive episode compared to those in Lima (adjusted OR 0.17, 95% CI 0.08-0.37). The cities with the lowest prevalence of depression were not clustered in one region; Arequipa is in the highland region of Peru, while

Chiclayo is coastal and Iquitos is in the rainforest. Nor was there a trend found by increasing or decreasing population size (Peru: Instituto Nacional de Estadística e Informática).

These findings align with other studies which reported variation in the prevalence of depression among older adults living in Latin American cities (Alvarado, Zunzunegui, Beland, Sicotte, & Tellechea, 2007). In this study, the variation in the prevalence of depression between cities was attributed to “context-specific exposures” and characteristics related to social networking in cities. Also, individuals in lower social positions, such as manual workers, were more vulnerable to depression compared to non-manual workers (Alvarado, Zunzunegui, Beland, Sicotte, & Tellechea, 2007). If there is relative variance in the population of manual workers between cities, this could affect the prevalence of depression.

Geographic variability in the prevalence of MDE could also be attributed to internal migration, patterns of political violence and armed conflict in Peru in the past several decades. Those living in the Huanta region of the highlands experienced a radical guerrilla movement during the early 1980s to the late 1990s. During this time period, hundreds of thousands of people were internally displaced from this region of the highlands to coastal towns, including Lima. Many of these people experienced torture, murder and other atrocities, all of which have been associated with poor mental health (Pedersen, Tremblay, Errazuriz, & Gamarra, 2008). These types of demographic changes may result in the variation that is seen between cities in this analysis.

Lifetime Alcohol Use Disorder: Geographic variation

Like the prevalence of MDE, AUDs varied significantly among cities. Those living in Arequipa and Chiclayo were significantly less likely to have a lifetime AUD compared to Lima (adjusted ORs 0.36 and 0.44, respectively). A univariate analysis suggested that those living in Huancayo tended to be more likely to have a lifetime AUD than those in Lima, but this was not statistically significant after adjusting for other covariates (adjusted OR 1.62, 95% CI 0.92 –

2.84). These geographic differences can be attributed to sociocultural factors that impact alcohol use in different geographic areas.

For example, it has been documented that men living in the Andean foothills drink excessively, but this is understood as fraternal bonding among men. In contrast, the pattern of drinking in urban settings of Peru is more likely to represent patterns of drinking in developed countries (Giesbrecht, et al., 2003). Therefore, behaviors surrounding alcohol use in Peru may be highly variable depending on individuals' cultural identity and background.

Lifetime Major Depressive Episode: Marital Status

Marital status was predictive of lifetime MDE in this sub-analysis. Those that were previously married (separated, divorced, widowed) and never married were at significantly higher risk of a lifetime major depressive episode compared to those who were married, regardless of gender (adjusted OR 2.48 and 1.48, respectively). The relationship between marital status and depression has been researched extensively and this association has been consistently replicated in many countries. The directionality is not completely clear, though the casual direction is often assumed to be depression leading to lower levels of marital quality (Gagnon, Hersen, Kabacoff, & Van Hasselt, 1999). The converse, where high levels of marital dissatisfaction are associated with increased incidence of MDE, has also been demonstrated in some populations (Whisman & Bruce, 1999).

A relatively small proportion of the previously married category were divorced (1.2%) compared to the percentage of those who are separated (5.3%). Relative to other countries, even those in Latin America, a low proportion of marriages in Peru end in divorce (Goode, 1993). The prevalence of divorce and separation, however, is rising in Peru and this trend is expected to continue given the association between increasing female education, decreasing mortality rates and other demographic trends (Heaton & Forste, 1998). Furthermore, in 2008, a new law was implemented which allows divorce by one party without the other present (*ley de divorcio rápido* N 29227) (Heredia, Ureta, & Vargas, 2013). These trends may influence the

prevalence of depression in the future, as divorced women and men experience less stigma.

Lifetime Alcohol Use Disorders: Marital Status

Lifetime AUD was associated with being previously married in this population (adjusted OR 1.90, 95% CI 1.14-3.17). The association between lifetime marital dissolution and lifetime AUD has been found in other populations as well, including in prospective longitudinal studies in the United States (Cranford, 2014). This relationship is complex and alcohol use disorders have been known to impact several factors associated with marital satisfaction (Cranford, 2014).

Lifetime Alcohol Use Disorder: Education

Level of education was associated with lifetime AUD and was incorporated in the final regression model. The association between educational attainment and alcohol use disorders has been reported in populations worldwide. In Russia, several studies reported an inverse association between alcohol intake and level of education and this relationship is especially prominent in males (Malyutina, Bobak, Kurilovitch, Nikitin, & Marmot, 2004; Carlson & Vagero, 1998). In men and women surveyed in The Netherlands, excessive alcohol consumption occurred more frequently in those with the lowest educational group (Droomers, Schrijvers, Stronks, van de Mheen, & Mackenbach, 1999). In this population, material stressors, like financial problems, deprivation and income, were related to part of the educational gradient observed in alcohol consumption (Droomers, Schrijvers, Stronks, van de Mheen, & Mackenbach, 1999).

In the United States, individuals who dropped out of high school or college were significantly more likely to develop alcohol abuse or dependence compared to individuals with a college degree (ORs 6.34 and 3.01, respectively) (Crum, Helzer, & Anthony, 1993).

Furthermore, those who completed between one and eight years of education had a modestly increased risk of developing alcohol abuse or dependence relative to college graduates (Crum, Helzer, & Anthony, 1993). Similar patterns were found in our sub-analysis. Respondents with a primary level of education were found to have significantly higher risk of lifetime AUD compared

to those who completed their university degree or higher (adjusted OR 2.06; 95% CI 1.12 – 3.79). Respondents with some secondary education had the highest odds of developing a lifetime AUD compared to those with a university degree (adjusted OR 4.05; 95% CI 2.39 – 6.88). It is possible that those who fail to achieve their educational goals, such as starting but not completing secondary school, may be at increased risk for alcohol abuse or dependence (Crum, Helzer, & Anthony, 1993).

The significant association between educational attainment and lifetime alcohol use disorders in Peru is important to recognize because it may be a modifiable characteristic to target for intervention programs (Crum, Helzer, & Anthony, 1993). Further analyses should examine the patterns of alcohol use among different indicators of socioeconomic status, such as income and occupation, to see if these trends are consistent.

Limitations and Strengths

Despite the strength of the WHO-CIDI survey and internationally validated survey design methods, there are several limitations when estimating the burden of depression and alcohol use disorder in the Peruvian population. The first limitation is related to the sensitive nature of the interview and the cultural acceptability of the interview questions. The survey was translated to Spanish based on WHO protocols by a panel of experts from several Spanish-speaking countries, however, it may not account for the cultural nuances in Peru. For example, as a matter of courtesy, Peruvians frequently respond “no” when asked questions. The stigmatizing nature of mental health and substance use disorder makes self-reporting symptoms and episodes even more difficult. Under-reporting of symptoms or episodes may have a more significant role in Peru because treatment for these conditions is not widely available in primary care settings.

Also, self-reported data can be affected by differential recall bias. This is especially important to consider in a survey of this nature because those with comorbid disorders may not accurately recall the duration or symptomatology of previous episodes. It is also possible that

the respondent's mental state at the time of the survey affects the recollection of their symptoms and severity.

Another significant limitation of this survey is the use of DSM-IV criteria for the classification of depression and alcohol use disorder. These criteria may underestimate the true burden of these conditions. Evidence from a study of late-life depression (age >60 years) in Peru, Mexico and Venezuela, the DSM-IV definition had the most restrictive criterion when compared to ICD-10, GMS-AGECAT, EURO-D classification systems (Guerra, et al., 2009). With the transition to DSM-V criteria, where substance use is a spectrum of severity, there may be a shift in the prevalence of alcohol use disorders based on changes in the diagnostic threshold (Hasin D. , 2015).

Though the complex weighting scheme was designed to adjust for non-response bias, those with severe mental health conditions or substance use disorders are less likely to partake in an extensive survey like the WMH-CIDI. Thus, this population is probably under-represented in national survey data (Blazer, Kessler, McGonagle, & Swartz, 1994).

Furthermore, this analysis is not generalizable to all of Peru because it captures information about an exclusively urban, non-institutionalized population. Though a majority of the population of Peru is urban, there are significant cultural and sociodemographic differences between urban and rural settings. The cross-sectional nature of the survey also limits the inferences that can be made with these data.

Despite these limitations, this analysis has several strengths. International multicenter studies and several smaller center studies have determined that the WHO-CIDI survey was acceptable for most subjects and found to be appropriate for use in different kinds of settings and countries (Wittchen, 1994). Adequate inter-rater reliability, test-retest reliability and validity of earlier CIDI versions has been documented (Medina-Mora, et al., 2006). Furthermore, the World Health Survey Initiative includes data from 28 countries and represents all regions of the

world (Harvard Medical School, 2005). Thus, the survey and sampling design are internationally recognized and these data are useful in international comparisons.

Furthermore, no population-level prevalence data and regression models of this kind have been reported based on Peruvian samples. Understanding the epidemiologic distribution and trends in mental health and substance use disorders is vital when advocating for mental health infrastructure and policies.

Public Health Implications and Future Research

Though health was defined by the WHO in 1946 as the “state of complete physical, mental and social well-being and not merely the absence of disease or infirmity,” common mental health conditions are often not a priority for public health interventions (World Health Organization, 1946). From this analysis, it is clear that MDD and AUDs represent at least a sizeable public health concern for Peru. These conditions carry a high morbidity on the individual, family and societal level and it is important to address them by implementing comprehensive and thoughtful screening, treatment and care services.

Improving the training and capacity of human resources to provide screening, treatment management, cognitive behavioral therapy and social services should be of utmost priority. Recently launched strategies, such as the WHO Mental Health Gap Action Programme, seek to reduce the burden of mental health and substance use conditions by providing evidence-based recommendations related to interventions in low- and middle-income countries (World Health Organization, 2010). Implementation and strengthening of mental health and substance use treatment and care services at the country level should begin by organizing a national stakeholders meeting, conducting a needs assessment and the identification of the barriers to scaling up (World Health Organization, 2010). As a result, this should lead to a country-level action plan for scaling up mental health resources, advocacy, human resources allocation, budgeting issues and monitoring and evaluation (World Health Organization, 2010). Once a

country-level plan is in place, district-level interventions will be easier to implement and capacity-building can take place.

Another vital aspect of scaling-up mental health and substance use care and treatment services is increased investment in infrastructure and human resources related to graduate-level programs and advances in research on mental health, addiction and social science. In Latin American countries, there is extremely limited research and information related to the economic and cultural conditions that impact mental health (Razzouk, et al., 2008). Investment in this realm will inform policy makers about innovative ways to approach and address mental health in urban populations (De Silva, McKenzie, Harpham, & Huttly, 2005). Understanding the distribution of disease in urban Peru, such as the disparities between gender and geographic regions found in this analysis, will permit policy-makers to take gender differences into account when formulating interventions (Galvez-Buccollini, Paz-Soldan, Herrera, DeLea, & Gilman, 2009). Stable funding mechanisms, like those implemented in Brazil, will facilitate the training of high-level research professionals and boost research productivity in Peru (Razzouk, et al., 2008).

The WMHSI team in Peru focused on urban populations, however based on studies in Peru and elsewhere, it is possible that epidemiologic trends in MDE are different among rural populations. Rural populations are thought to have more social capital, which has been shown to be protective in reducing mental health risk (Loret de Mola, Stanojevic, Ruiz, Gilman, Smeeth, & Miranda, 2012). Furthering epidemiological and social science research related to the distribution of mental health conditions in rural communities of Peru will be beneficial in formulating action plans and policy. Understanding the different protective aspects of social capital may be integral into providing treatment on the individual and societal levels.

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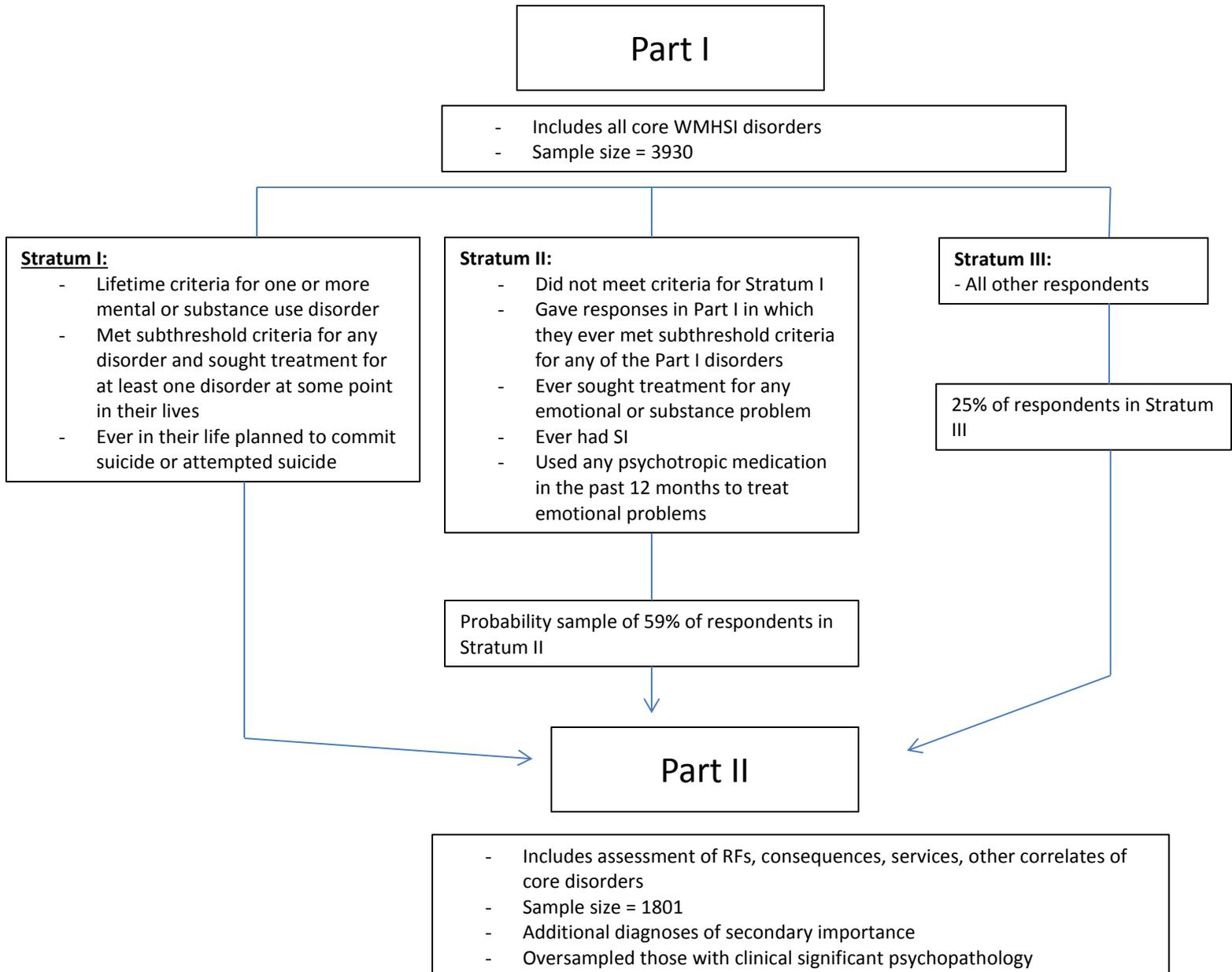
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APPENDIX A: Interview Flowsheet



APPENDIX B: Description of Variables

Major Depressive Episode		
	Response	Description
Duration		
D22b	>= 2 weeks	Length of worst episode
D22d	>= 2 weeks	Length of last bad episode
D39	>= 2 weeks	Longest episode
Symptoms (if >5 symptoms excluding mood)		
Mood		
D24a	Yes	Sad/depressed for 2 week period
D24b	Yes	Nothing could cheer you up
D24c	Yes	Discouraged about things going in life
D24d	Yes	Hopeless about the future
D24e	Yes	Lose interest in things do for fun
D24f	Yes	Lose ability to take pleasure in good things happen
Weight changes		
D26a	Yes	Significant weight loss when not dieting or weight gain (change of more than 5% of body weight in a month)
D26fm	>= 10lbs/4 kilos	Weight loss
D26b	Yes	Larger appetite
D26dm	>= 10 lbs/4 kilos	Weight gain
Insomnia or hypersomnia		
D26g	Yes	Trouble falling asleep/staying asleep, waking early
D26h	Yes	Sleep more than usual
Psychomotor agitation or retardation		
D26m	Yes	Anyone notice talking or moving slowly
D26o	Yes	Anyone notice restless or jittery
Fatigue or loss of energy nearly every day		
D26j	Yes	Feel tired/low in energy
Feelings of worthlessness or excessive or inappropriate guilt nearly every day		
D26v	Yes	Feel totally worthless
Diminished ability to think or concentrate, or indecisiveness, nearly every day		
D26p		Thoughts come slowly or mixed up
Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or suicide attempt or a specific plan for committing suicide		
D26aa	Yes	Think a lot about death
D26bb	Yes	Better off if you are dead
D26cc	Yes	Think about suicide
D26dd	Yes	Make suicide plan
D26ee	Yes	Make suicide attempt
Not due to direct physiological causes of a general medical condition		
D29b	No	Sadness/discouragement episodes always due to physical causes

Alcohol Abuse		
Variable	Response	Description
SU12	Yes	Drinking interfered with your work
SU12a	Yes	Drinking caused problems with family/friends/others
SU12b	Yes	Continue drinking cause problems with people
SU12c	Yes	Jeopardized safety or drank when you could get hurt
SU12d	Yes	Drinking resulted in problems with the police
Never met the criteria for alcohol dependence		
Dsm_ald	^= 1	Criteria for alcohol dependence are not fulfilled

Alcohol Dependence		
Variable	Response	Description
Symptoms (>= 3 need to be met occurring at any time during a 12-month period)		
Tolerance		
SU19a	Yes	Need larger amount of alcohol to get an effect
Withdrawal		
SU19b	Yes	Did not feel well when you stopped drinking
SU19c	Yes	Drank keep feeling physical/emotional problems
Larger amounts than intended		
SU19d	Yes	Drank when planned not to / drank more than planned
SU19e	Yes	Drank more frequently than intended
SU19f	Yes	Got drunk when you did not want to
Persistent desire or unsuccessful efforts to cut down or control alcohol use		
SU19g	Yes	Tried were not able to stop/cut down drinking
SU32	>= 3	Number of times you have made a serious attempt to quit drinking
Time spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects		
SU19h	Yes	Spent several days drinking / recovering
Important social, occupational, or recreational activities are given up or reduced because of alcohol		
SU19i	Yes	Gave up/reduced activities due to drinking
Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem		
SU19j	Yes	Caused/worsened physical/emotional problems
SU26	1.) past month 2.) 2-6 months ago 3.) 7-12 months ago	Recently had drinking problem
SU38a	1 – A lot	Physical health harmed drinking past year