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Substance dependence among those without symptoms of substance abuse in the World Mental Health Survey

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Abstract

The World Health Organization (WHO) World Mental Health (WMH) Survey Initiative uses the Composite International Diagnostic Interview (CIDI). The first 13 surveys only assessed substance dependence among respondents with a history of substance abuse; later surveys also assessed substance dependence without symptoms of abuse. We compared results across the two sets of surveys to assess implications of the revised logic and develop an imputation model for missing values of lifetime dependence in the earlier surveys. Lifetime dependence without symptoms of abuse was low in the second set of surveys (0.3% alcohol, 0.2% drugs). Regression-based imputation models were built in random half-samples of the new surveys and validated in the other half. There were minimal differences for imputed and actual reported cases in the validation dataset for age, gender and quantity; more mental disorders and days out of role were found in the imputed cases. Concordance between imputed and observed dependence cases in the full sample was high for alcohol [sensitivity 88.0%, specificity 99.8%, total classification accuracy (TCA) 99.5%, area under the curve (AUC) 0.94] and drug dependence (sensitivity 100.0%, specificity 99.8%, TCA 99.8%, AUC 1.00). This provides cross-national evidence of the small degree to which lifetime dependence occurs without symptoms of abuse. Imputation of substance dependence in the earlier WMH surveys improved estimates of dependence.

Keywords

health, substance, among, dependence, those, survey, without, symptoms, abuse, world, mental

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Substance Dependence among those without symptoms of Substance Abuse in the World Mental Health Survey

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Declaration of interest:

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Abstract

The WHO World Mental Health (WMH) Survey Initiative uses the Composite International Diagnostic Interview (CIDI) for data collection and operationalizes diagnoses using DSM-IV criteria. The first 13 WMH surveys used CIDI version 3.0, which only assessed substance dependence among respondents with a history of substance abuse, while subsequent surveys also assessed substance dependence without symptoms of abuse. The aim of the current report is to compare results across the two sets of surveys to assess the implications of the revised skip logic and develop an imputation model for missing values of lifetime dependence without symptoms of abuse in the earlier surveys. Prevalence of lifetime dependence without symptoms of abuse was low in the second set of WMH surveys (0.3% for alcohol and 0.2% for drugs). Regression-based imputation models were built in random half-samples of the new surveys and validated in the other half-samples. There were minimal difference in the distributions of imputed and reported cases in the validation dataset for important correlates such as age, gender and quantity though higher numbers of additional mental disorders and number of days out of role were found in the imputed than reported cases. Concordance between imputed and observed estimates of total lifetime dependence in the full sample was high both for alcohol dependence (sensitivity 88.0%, specificity 99.8%, TCA 99.5% and AUC 0.94) and drug dependence (sensitivity 100.0%, specificity 99.8%, TCA 99.8% and AUC 1.00). This study provides cross-national evidence of the degree to which each of lifetime alcohol dependence and lifetime drug dependence occur without symptoms of abuse. Additionally imputation of substance dependence without symptoms of abuse in the earlier WMH surveys will result in improved estimates of lifetime prevalence for comparison with other epidemiological studies both cross-nationally and over time.

Key words: DSM-IV alcohol dependence, DSM-IV alcohol abuse, World Mental Health Survey, Imputation, Substance Use Disorder

Introduction

Alcohol and drug use are estimated to be responsible for around 5% of global disease burden and are among the biggest risk factors for burden of disease (Lim et al. 2012). However major challenges exist in accurately estimating the population prevalence of substance use and substance use disorders, particularly for illicit drugs (Degenhardt and Hall 2012). Where estimates do exist, they can vary substantially depending on the conceptualisation and classification of use disorder (Lago et al. 2016), limitations from balancing the needs of comparability and cultural specificity (Beals et al. 2003), interviewer mode (Turner et al. 2005) and the survey instrument (Grant et al. 2007). Epidemiological surveys such as the World Health Organization (WHO) World Mental Health (WMH) surveys provide valid, in-depth, data on the prevalence and correlates of mental disorders in the general population (Kessler and Üstün 2004), with the data collected in a consistent way across countries to allow cross-national comparison (Harkness et al. 2008). The WMH surveys individually are also a rich source of information for within country research (Kessler et al. 2003, Alonso et al. 2004, Kawakami et al. 2005, Slade et al. 2009).

Substance-related disorders are defined in DSM-IV as "disorders related to the taking of a drug of abuse (including alcohol), to the side effects of a medication, and to toxin exposure" (American Psychiatric Association 1994). The DSM-IV divides substance-related disorders into two groups, substance use disorders (substance dependence and substance abuse) and substance-induced disorders. Substance dependence requires a cluster of cognitive, behavioural and physiological symptoms resulting in continued use despite significant problems that can involve tolerance, withdrawal and compulsive behaviour. Substance abuse is defined as a maladaptive pattern of use, with recurrent and significant adverse consequences. Although symptoms of abuse commonly occur prior to those of dependence (Kessler and Merikangas 2007), abuse is often neither mild nor prodromal to dependence (Hasin et al. 2013). Furthermore, a prominent U.S. survey found that a substantial proportion of persons with dependence never had prior symptoms of abuse (Hasin and Grant 2004) and that this was especially true for women and minorities, leading to the conclusion that failure to assess dependence among people without symptoms of abuse would not only lead to under-detection of dependence but would do so selectively in vulnerable segments of the population. Based on these observations, a consensus view emerged that symptoms of dependence should be assessed among substance users whether or not they have symptoms of abuse (Cottler 2007, Grant et al. 2007).

Prior to the time this consensus emerged, the WHO WMH Survey Initiative (Kessler and Üstün 2008) carried out a number of large national epidemiological surveys using a version of the WMH–Composite International Diagnostic Interview (CIDI) (Kessler and Üstün 2004) that only assessed symptoms of substance dependence among respondents with a history of symptoms of abuse. The WMH investigators subsequently revised the CIDI to also include assessments of dependence among respondents without symptoms of abuse in future WMH surveys. In an effort to evaluate the implications of this change and to develop an imputation model for missing values in the first 13 WMH surveys, an analysis of the prevalence and predictors of DSM-IV lifetime dependence without symptoms of abuse among non-abusing lifetime users was carried out in the nine more recent WMH surveys. The results of that analysis are presented in the current report. Imputation of dependence without symptoms of abuse in the earlier WMH surveys will improve the cross-national comparability of estimates of substance dependence (Degenhardt et al. 2008) and related measures such as global burden of disease (Degenhardt et al. 2013), improve comparisons with other epidemiological studies (Grant et al. 2004) and provide improved evidence when assessing changes in the prevalence of substance use disorders over time(Blanco et al. 2007, McCabe et al. 2008).

Methods

Samples

The study was carried out using data from nine recent WMH surveys with the revised skip logic. One of these surveys was carried out in a country classified by the World Bank (The World Bank 2015) as lower-middle income (a national survey in Iraq), three in countries classified upper-middle income (a national survey in Romania and regional surveys in Sao Paulo Brazil and Medellin Colombia), and five in countries classified high income (national surveys in Australia, Northern Ireland, Portugal, and Poland and a regional survey in Murcia Spain). As Portugal did not assess drug dependence, their data was used only to study alcohol dependence. Most surveys were based on a multi-stage clustered area probability sampling design of adult (ages 18 and over) household residents. One randomly-selected resident was interviewed in each sampled household. The average response rate across surveys was 64.7% and the total sample size was 44,341. A detailed description of WMH sampling procedures is presented elsewhere (Heeringa et al. 2008).

Insert Table 1 here

Field procedures

Interviews were carried out face-to-face in the homes of respondents after obtaining informed consent using procedures approved by local Institutional Review Boards. The interview schedule was developed in English and translated into other languages using a standardized WHO translation, back-translation, and harmonisation protocol (Harkness et al. 2008). Bilingual supervisors from each country were trained and supervised by the WMH Data Collection Coordination Centre to guarantee cross-national consistency in training and field procedures (Harkness et al. 2008). The interviews were administered by trained lay interviewers.

Interviews were carried out in two parts in all surveys other than Australia, Romania and Iraq, where the full interview was administered to all respondents. Part I, which was completed by all respondents, assessed core mental disorders. Part II, which was administered to 100% of Part I respondents with any lifetime disorder and a probability subsample of other respondents, assessed correlates and disorders of secondary interest. Data from Part II were weighted to account for the under-representation of Part I non-cases, and to make the weighted Part II sample equivalent to the Part I sample in prevalence and correlates of disorders. The Part II data, which are used here, were also weighted to adjust for differences in within-household probabilities of selection and discrepancies between the sample and population on a cross-classification of Census socio-demographic and geographic variables. A more detailed description of the WMH weighting procedures is available elsewhere (Heeringa et al. 2008).

Diagnostic Instrument

In the nine surveys used in this study, DSM-IV disorders were assessed using the WHO CIDI Version 3.0. The substance use disorders assessed were alcohol abuse, alcohol dependence, drug abuse and drug dependence. The anxiety disorders assessed were panic disorder (with or without agoraphobia), agoraphobia without a history of panic disorder, generalized anxiety disorder, posttraumatic stress disorder, separation anxiety disorder, social phobia, specific phobia, and obsessive compulsive disorder. The mood disorders assessed were major depressive disorder, dysthymic disorder, and bipolar disorder. As detailed elsewhere (Haro et al. 2006), generally good concordance was found between diagnoses based on the CIDI and diagnoses based on blinded clinical reappraisal interviews with the Structured Clinical Interview for DSM-IV, research version (SCID) (First et al. 2002). A series of 5 questions was used to operationalize the symptom criteria for alcohol abuse and a further 11 questions to assess the symptom criteria for alcohol dependence. These 16

questions were asked of people who, in the year they drank most, consumed alcohol at or above a quantity/frequency threshold of one or more drinks per week or, if drinking less often, three or more drinks per day on the days they drank. This threshold was set slightly higher in the Australian survey (drinking at least one drink three or more days per week or, if drinking less often, three or more drinks per day on the days they drank). A further 15 questions were used to assess criteria for Drug Use Disorders (DUD), 4 questions assessing drug abuse and 11 questions operationalizing drug dependence. These questions were asked of respondents who had ever used medicines for non-medical reasons or had ever used illicit drugs (henceforth referred to 'used drugs'). A diagnosis of substance abuse or substance dependence requires the cluster of symptoms to occur within the same 12 month period, and the resulting diagnoses are defined for both past 12 months and lifetime. There were some slight variations in the assessment of DUDs across surveys because respondents were asked about their use of a list of drugs that varied slightly across surveys, although most had an 'any other drug' category. The Australian and Polish surveys included additional detail, assessing DUD separately for each drug/drug type; however this information was generalizable to any DUD.

Statistical Analysis

Statistical modelling was carried out in SAS v9.3 and SUDAAN v11.0 using logistic regression to predict lifetime alcohol dependence among respondents who met the drinking threshold described above but had no symptoms of abuse, and lifetime drug dependence among respondents who had used drugs without symptoms of abuse. Part II respondents in each of the nine WMH surveys that assessed dependence without symptoms of abuse were divided into two random halves then pooled: the first half a pooled 'training dataset' for building the imputation model and the second half a pooled 'validation dataset' for independent assessment of predictive accuracy.

A broad set of potential predictors was considered for alcohol dependence without symptoms of abuse, including age, sex, other mental and drug use disorders, age of first use, age of first regular use (drinking at least 12 standard drinks per year), frequency of drinking at least one standard drink in the one year in life when drinking most, lifetime and current smoking status, history of drug use, and high income country. Several variables were investigated as predictors of lifetime drug dependence without abuse: number of drug used, drug types, number of mental health diagnoses, alcohol abuse and dependence, age, sex, age of onset of first drug use, days out of role, education and high income country. We focused largely on survey items available in all surveys, the exception being drug use variables that were available in all surveys other than Portugal. A full list of variables is included in Appendix 1, Table A1 (for alcohol) and Appendix 2 Table A3 (for drugs).

Exploratory analysis of the training dataset showed that drinkers who either drank rarely or who drank relatively small quantities on the days they drank were highly unlikely to have alcohol dependence, leading us to exclude these respondents from further analysis and code them as not having dependence without symptoms of abuse in the imputation. These 'light drinkers' represented 71.3% of all lifetime drinkers and 12.0% of respondents with lifetime alcohol dependence.

Once these light drinkers were removed from the training dataset, four alternate models were estimated. Model A included substance use variables (see Appendix 1Table A1) and sex as predictors. Predictors related to age-of-onset and consumption were treated as continuous. Model B added to Model A an adjustment to the intercept for surveys from high income countries. Model C then dichotomized the age and consumption variables. Model D, finally, used forward stepwise regression with a .05-level entry criterion to select the subset of variables in Model C that was significantly associated with the outcome.

Individual-level imputes of lifetime dependence without abuse based on each of the above models were made in the validation sample and compared to reported diagnoses. This was done as follows. The model coefficients developed using the training dataset were applied to data in the validation dataset to generate predicted probabilities of dependence without symptoms of abuse. For alcohol, this was done among those who met the minimum alcohol consumption threshold described previously, while for drugs it was done in the subsample of respondents who reported lifetime drug use. We used a pseudo-benchmark by assuming the ratio of prevalence of dependence without symptoms of abuse to dependence with abuse for alcohol, and similarly for drugs, would be the same across countries. We calculated this ratio across the nine surveys without the skip error and used it to generate an expected number of cases of dependence without symptoms of abuse in these same surveys. Within each country, respondents were imputed to a diagnosis of dependence without symptoms of abuse when the predicted probability was above the threshold required to achieve this ratio.

Multiple Imputation (MI) (Rubin 1987) is an approach to imputation which can improve statistical inference by incorporating uncertainty into the imputed data through the creation of several imputed values. No missing data technique is optimal for every missing data situation, and MI is not the only principled method and isn't necessarily the best for any given problem (Schafer 1999). The improvement in variance estimation of parameters due to missing data is dependent on the amount of missing data (Rubin 1987). The nine surveys used in this study provide an estimate of the size of the missing data, that is an estimated 0.3% population prevalence of lifetime alcohol dependence without abuse and a corresponding figure of 0.2% for drugs. As the number of imputed values was very small, we used a single imputation method rather than multiple imputation. This also reduces the complexity of analysis for future use of the datasets.

We assessed the relative performance of the predictive models in the validation dataset using McNemar's chi-square test, and the Akaike and Bayesian Information Criterion (AIC and BIC respectively). The best performing model was further assessed by comparing imputed and reported cases of dependence without symptoms of abuse in the validation dataset on a set of covariates including age, gender, consumption, and comorbidities.

Lastly, the diagnostic accuracy resulting from imputed data was reported on the complete pooled dataset of nine surveys (eight surveys for drug dependence). The classification of lifetime substance dependence, that is reported cases of dependence with symptoms of abuse in combination with imputed cases of dependence without symptoms of abuse, was assessed for re-production of reported population prevalence, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), Total Classification Accuracy (TCA) and Area Under the Curve (AUC). These calculations are not able to be performed on the 13 imputed surveys where dependence without symptoms of abuse was not assessed.

Results

Prevalence of lifetime alcohol and drug dependence

Estimates of lifetime prevalence of alcohol dependence with a history of abuse ranged from 0.1 to 4.2% and averaged 2.2% in the nine surveys with the updated skip logic. Prevalence of lifetime alcohol dependence with or without a history of abuse was in the range 0.2-4.8% and averaged 2.5% (Table 2). The proportion of respondents without a lifetime history of abuse among those meeting lifetime criteria for alcohol dependence was in the range 4.4-73.9% and averaged 13.5% over all surveys. Pairwise comparisons showed this proportion differed between Iraq (which had a very small number of cases, less than 10

dependence cases in total), and all other surveys (p-values ranged from 0.0% to 1.2%). No statistically significant differences were found in pairwise comparisons amongst the other surveys (p-values ranged from 5.7% to 98.2%). Even though the number of people who used drugs was much smaller than the number who used alcohol, the proportion of respondents with lifetime drug dependence who had never met criteria for abuse (0.2% dependence without symptoms of abuse out of 1.3% dependence with or without symptoms of abuse) was similar to the proportion of respondents with alcohol dependence who never had symptoms of alcohol abuse.

Insert Table 2 here

Validation of the imputation models

The final model for predicting alcohol dependence without symptoms of abuse included the following covariates: sex, four or more mental health diagnoses, at least one day out of role, and survey in high income country (AIC=229.4, BIC = 251.4) (see Table 3). The model for predicting drug dependence without symptoms of abuse consisted of the following covariates: sex, four or more mental health diagnoses, alcohol dependence with or without abuse, used four or more different drugs, and high income country (AIC=205.2, BIC=239.3) compared to the model containing all predictors (AIC=210.0, BIC=289.4).

Insert Table 3 here

The imputation method was also evaluated for bias in the validation dataset by comparing various attributes of reported cases of alcohol dependence without symptoms of abuse with imputed cases. As there was an overlap between the groups (true positives) violating independence assumptions for standard significance testing methods, we present the mean and 95% CI for each characteristic to determine if there are any non-overlapping CIs that might raise concerns. The distributions were generally consistent, with overlap in the CIs for age, gender, average drinks per day and proportion who used drugs, although the imputed cases had higher rates of mental disorders (2.9 in imputed cases compared to 1.5 for reported cases) and mean days out of role (5.4 for imputed cases compared to 1.6 for reported cases).

Insert Table 4 here

The finals models were then used to predict dependence without symptoms of abuse in the pooled data from surveys with the revised skip logic (pooled sample details shown in Table 2). The resulting lifetime alcohol dependence Total Classification Accuracy (TCA) was very high (99.5%), as were sensitivity (88.0%), specificity (99.8%), and AUC (0.94). Lifetime drug dependence was also found to have excellent concordance with reported diagnoses (TCA = 98.1%, sensitivity = 27.5%, specificity = 98.9%, AUC = 0.63) (individual models not shown)

Insert Table 5 here

Discussion

Contrary to the conclusions in the U.S. survey which found that 33.7% of respondents did not additionally meet criteria for abuse (Hasin and Grant 2004), and led to the changes in the CIDI skip rules, the nine recent WMH surveys that assessed alcohol and drug dependence without symptoms of abuse found that such cases were quite rare in comparison to the prevalence of dependence with a history of abuse. Analysis of the data patterns in these nine countries demonstrated that an imputation model could be developed for the small proportion of respondents who met criteria for lifetime alcohol dependence without symptoms of abuse (0.3%) compared to all respondents with lifetime alcohol dependence (2.5%), and similarly for those who met criteria for lifetime drug dependence without symptoms of abuse (0.2%) compared to all respondents with lifetime drug dependence (1.3%). The imputation models resulted in consistent estimates of prevalence of lifetime dependence in the full samples of these nine surveys both for alcohol dependence (2.5% pooled survey estimate, 2.4% using

imputed data) and drug dependence in the eight surveys where this was assessed (1.3% pooled survey estimate, 1.5% using imputed data), with strong individual-level classification accuracy metrics and similar distributions of important correlates such as age, gender and quantity, though higher numbers of additional mental disorders and number of days out of role were found in the imputed than reported cases. The U.S. study (Hasin and Grant 2004) also presented percentages of alcohol dependence with and without symptoms of abuse by sex, race and age and concluded that the proportion of cases without symptoms of abuse varied by gender and race. In contrast this study developed a predictive model, finding gender and other variables to be predictive of alcohol dependence without symptoms of abuse. These results strongly suggest that these imputation models can be used to adjust for the absence of information about substance dependence without symptoms of abuse in early WMH surveys. In some surveys this will result in slightly higher estimates of the prevalence of lifetime drug or alcohol dependence

Limitations

As with most real-world missing data problems, we were unable to assess the accuracy of the imputed values in the original 13 WMH surveys even though we were able to do so in the validation dataset of the more recent surveys. However, an advantage of having the WMH Survey Initiative is that a consistent method of data collection has been employed across a large number of countries representing varied income levels. This gives us confidence that we are using a broad set of data to develop and assess an imputation method that is applied to a small number of cases of missing data across a large number of countries. As imputed values are appropriately flagged in the dataset, sensitivity analysis may be carried out in future substantive analyses to determine the impact of imputation on any statistical modelling. However, based on the small number of missing values, we anticipate that in most cases this impact will be small. The small number of cases of dependence and dependence without abuse lead to confidence intervals of width 20-30% when estimating the proportion of respondents with dependence who do not have symptoms of abuse by survey (excluding Iraq), however the pooled survey estimate across the nine surveys has an interval with width less than 10% for both alcohol and drugs.

Some of the earlier WMH surveys were carried out 15 years ago. Data from older surveys may not be as precise for estimating current prevalence as later surveys, but this does not diminish the value of the rich data source for understanding phenomenon related to substance use. This includes differential patterns of use across countries, and understanding and predicting transitions between use and use disorders/remission among those who use alcohol and/or drugs.

The list of drugs asked about varied slightly across surveys but in most cases a catch all category was included. We did not impute drug dependence for specific drugs, only lifetime dependence among those who use drugs, so anticipate no major impact.

Conclusion

These results strongly suggest that these imputation models can be used to adjust for the absence of information about lifetime DSM-IV alcohol and drug dependence without symptoms of abuse in early WMH surveys.

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Table 1: WMH sample characteristics by World Bank income categories[a]

Country by income category	Survey[b]	Sample characteristics[c]	Field dates	Age range	Sample Size		Response rate[d]
					Part I	Part II	
I. Low and lower middle income countries							
Iraq	IMHS	Nationally representative.	2006-7	18-96	4,332	4,332	95.2
TOTAL					**(4,332)**	**(4,332)**	**95.2**
II. Upper-middle income countries							
Brazil - São Paulo	São Paulo Megacity	São Paulo metropolitan area.	2005-8	18-93	5,037	2,942	81.3
Colombia – Medellin[f]	MMHHS	Medellin metropolitan area	2011-12	19-65	3,261	1,673	97.2
Romania	RMHS	Nationally representative.	2005-6	18-96	2,357	2,357	70.9
TOTAL					**(10,655)**	**(6,972)**	**82.8**
III. High-income countries							
Australia[e]	NSMHWB	Nationally representative.	2007	18-85	8,463	8,463	60.0
Northern Ireland	NISHS	Nationally representative.	2005-8	18-97	4,340	1,986	68.4
Poland	EZOP	Nationally representative	2010-11	18-65	10,081	4,000	50.4
Portugal	NMHS	Nationally representative.	2008-9	18-81	3,849	2,060	57.3
Spain - Murcia	PEGASUS- Murcia	Murcia region	2010-12	18-96	2,621	1,459	67.4
TOTAL					**(29,354)**	**(17,968)**	**57.5**
IV. TOTAL					**(44,341)**	**(29,272)**	**64.7**

[a] The World Bank (2012) Data. Accessed May 12, 2012 at: http://data.worldbank.org/country. Some of the WMH countries have moved into new income categories since the surveys were conducted. The income groupings above reflect the status of each country at the time of data collection. The current income category of each country is available at the preceding URL.

[b] IMHS (Iraq Mental Health Survey); MMHHS (Medellín Mental Health Household Study); RMHS (Romania Mental Health Survey); NSMHWB (National Survey of Mental Health and Wellbeing); NISHS (Northern Ireland Study of Health and Stress); EZOP (Epidemiology of Mental Disorders and Access to Care Survey); NMHS (Portugal National Mental Health Survey); PEGASUS-Murcia (Psychiatric Enquiry to General Population in Southeast Spain-Murcia).

[c] Most WMH surveys are based on stratified multistage clustered area probability household samples in which samples of areas equivalent to counties or municipalities in the U.S. were selected in the first stage followed by one or more subsequent stages of geographic sampling (e.g., towns within counties, blocks within towns, households within blocks) to arrive at a sample of households, in each of which a listing of household members was created and one or two people were selected from this listing to be interviewed. No substitution was allowed when the originally sampled household resident could not be interviewed. These household samples were selected from Census area data in all countries. 6 of the 9 surveys are based on nationally representative household samples. The Polish sample was not a household sample but a nationally representative sample of individuals sampled from the population register.

[d] The response rate is calculated as the ratio of the number of households/individuals in which an interview was completed to the number of households/individuals originally sampled, excluding from the denominator households known not to be eligible either because of being vacant at the time of initial contact or because the residents were unable to speak the designated languages of the survey. The weighted average response rate is 64.7%.

[e] For the purposes of cross-national comparisons we limit the sample to those 18+. The NSMHWB surveyed respondents aged 16-85 with a total sample size of 8841. The response rate reported here refers to the full survey sample response rate.

[f] Colombia moved from the "lower and lower-middle income" to the "upper-middle income" category between 2003 (when the Colombian National Study of Mental Health was conducted) and 2010 (when the Medellin Mental Health Household Study was conducted), hence Colombia's appearance in both income categories. For more information, please see footnote *a*.

Table 2: Lifetime dependence (with or without symptoms of abuse) and lifetime dependence without symptoms of abuse in surveys with the revised skip logic

		Alcohol (weighted lifetime estimates[a])			Drugs (weighted lifetime estimates[a])		
Survey	**N**	**Dependence with or without symptoms of abuse %(s.e.)**	**Dependence without symptoms of abuse % (s.e.)**	**Proportion of dependence without symptoms of abuse % (95% CI)**	**Dependence with or without symptoms of abuse % (s.e.)**	**Dependence without symptoms of abuse % (s.e.)**	**Proportion of dependence without symptoms of abuse % (95% CI)**
Iraq	4,332	0.2 (0.1)	0.2 (0.1)	73.9 (36.8,100.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0,0.0)
Brazil - São Paulo	5,037	3.6 (0.4)	0.5 (0.1)	13.0 (6.1, 19.9)	1.4 (0.2)	0.3 (0.1)	19.8 (7.3, 32.2)
Colombia – Medellin	1,673	4.8 (0.8)	0.6 (0.3)	12.6 (0.0, 25.7)	1.9 (0.4)	0.0 (0.0)	2.4 (0.0, 5.2)
Romania	2,357	0.7 (0.2)	0.1 (0.1)	8.8 (0.0, 25.1)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0, 0.0)
Australia	8,463	4.0 (0.3)	0.6 (0.1)	14.9 (9.1, 20.8)	2.9 (0.3)	0.0 (0.0)	10.7 (5.7, 15.6)
Spain - Murcia	1,459	1.5 (0.5)	0.1 (0.1)	4.4 (0.0, 13.0)	1.3 (0.5)	0.0 (0.0)	0.0 (0.0, 0.0)
Northern Ireland	1,986	2.5 (0.4)	0.2 (0.1)	7.5 (0.0, 15.3)	0.6 (0.2)	0.1 (0.1)	10.8 (0.0, 25.2)
Poland	4,000	2.2 (0.3)	0.2 (0.1)	7.6 (1.3, 14.0)	0.2 (0.1)	0.1 (0.1)	54.3 (22.3, 86.3)
Portugal	2,060	1.3 (0.3)	0.3 (0.2)	21.2 (3.6, 38.8)	-	-	- -
TOTAL	**31,367**	**2.5 (0.1)**	**0.3 (0.0)**	**13.5 (9.9, 17.1)**	**1.3 (0.1)**	**0.2 (0.0)**	**12.1 (8.0, 16.2)**

a. Part I sample weights used in Australia, Romania and Iraq (which did not include a Part II), and in Brazil - São Paulo where alcohol use disorders were assessed in Part I. Part II weights were used for all other surveys.

Table 3: Model fit in validation dataset for imputation of alcohol dependence without symptoms of abuse (N=1,805)

Model	**McNemar χ^2**	**AIC[e]**	**BIC[f]**
model A[a]	0.7 (p=0.42)	254.7	293.1
model B[b]$_2$	0.6 (p=0.43)	239.1	310.5
model C[c]$_3$	0.7 (p=0.40)	246.5	311.8
model D[d]$_4$	0.7 (p=0.40)	231.4	258.9

a. Model A included substance use variables (Appendix 1 Table A1) and sex as predictors. Predictors related to age and consumption were treated as continuous.
b. Model B included substance use variables as in Model A but also included an adjustment to the intercept for surveys from high income countries.
c. Model C included the same predictors as Model A, however the age and consumption variables were dichotomised.
d. Model D was a stepwise regression using the full set of covariates in Model C.
e. Akaike Information criterion
f. Bayesian information criterion

Table 4: Comparison of imputed vs known cases of alcohol dependence without symptoms of abuse in validation dataset - Model D

Statistic	**Reported DWOA distribution weighted[a] mean/proportion (95% CI) (N=90)**		**Imputed DWOA Distribution weighted[a] mean/proportion (N=89)**	
Mean age (95% CI)	40.8	(38.0, 43.7)	42.9	(40.0, 45.7)
Proportion Males (95% CI)	0.6	(0.5, 0.8)	0.6	(0.5, 0.7)
Mean drinks per day (95% CI)	10.3	(4.4, 16.2)	12.6	(8.5, 16.7)
Mean additional mental disorders (95% CI)	1.5	(1.1, 1.8)	2.9	(2.5, 3.3)
Mean days out of role[b] (95% CI)	1.6	(1.0, 2.1)	5.4	(4.7, 6.2)
Proportion used drugs (95% CI)	0.4	(0.3, 0.5)	0.3	(0.2, 0.5)

a. Part I sample weights used in Australia, Romania and Iraq (which did not include a Part II), and in São Paulo - Brazil where alcohol use disorders were assessed in Part I. Part II weights used for all other surveys.

b. Respondents were asked "Beginning yesterday and going back 30 days, how many days out of the past 30 were you totally unable to work or carry out your normal activities because of problems with either your physical health, your mental health, or your use of alcohol or drugs"

Table 5: Final model performance for imputation of alcohol dependence without symptoms of abuse in pooled sample[a] of surveys with revised skip logic

Criteria	**Alcohol dependence Estimate[b] (s.e.) (N=31,367)**	**Drug dependence Estimate[b] (s.e.) (N=29.307)**
Prevalence dependence (%, weighted, reported data)	2.5 (0.1)	1.3 (0.2)
Prevalence dependence (%, weighted, imputed data)	2.4 (0.1)	1.5 (0.2)
Sensitivity (s.e.)	88.0 (1.2)	100.0 (0.0)
Specificity (s.e.)	99.8 (0.0)	99.8 (0.0)
Positive Predicted Value (s.e.)	92.3 (0.7)	89.3 (1.0)
Negative Predicted Value (s.e.)	99.7 (0.0)	100.0 (0.0)
Total Classification Accuracy (s.e.)	99.5 (0.1)	99.8 (0.1)
AUC	0.94	1.00

a. Surveys included in pooled sample were Iraq, Colombia - Medellin, Spain - Murcia, Portugal (alcohol only), Poland, Australia, Northern Ireland and Romania

b. Sample weighted estimates for prevalence and all operator characteristics