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Alcohol misuse among women in Brazil: recent trends and associations with unprotected sex, early pregnancy and abortion

Running title: Alcohol misuse among women in Brazil

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Abstract

Objective: This study compared the rates of binge drinking and alcohol use disorder reported for 2006 with those reported for 2012, exploring their associations with unprotected sex, early pregnancy and abortion, in a representative sample of women within the Brazilian household.

Methods This was a descriptive analysis of data from a cross-sectional study involving randomised multistage cluster sampling of the population \geq 14 years of age. Weighted prevalence rates and odds ratios were estimated, and serial mediation analysis was performed.

Results 4,256 women were analysed. The prevalence of binge drinking was 35.1% and 47.1% in 2006 and 2012, respectively, the increase being significant, especially among women 40–59 years of age. There was no significant difference in terms of the prevalence of alcohol use disorder. Binge drinking (without alcohol use disorder) was found to increase the odds of unprotected sex and abortion. The path analysis showed that early pregnancy was a mediator of the relationship between alcohol consumption and abortion.

Conclusion Among women in Brazil, the harmful use of alcohol is increasing, which has an impact on female reproductive health and exposure to risks. There is a need for specific prevention initiatives focussing on alcohol-related behaviours in women.

Keywords: Brazil, Alcohol Abuse, Binge Drinking, Female, Abortion

INTRODUCTION

Among women, alcohol consumption is responsible for 2.3% of the global burden of disease and injury, 4% of all deaths among women being attributed to the use of alcohol in 2012.¹ An increase in alcohol consumption among women, due to harmful drinking patterns, has frequently been reported for low- and middle-income countries (LMICs), where gender-specific social roles and the economic status of women have changed drastically, narrowing the cultural gaps between men and women.^{2 3}

Clinical studies have shown that once substance use has been initiated, the rates of alcohol, cannabis, opioid and cocaine consumption tend to increase more rapidly in women than in men, and that women may progress to the development of drug-use disorders and dependence more quickly than do men.⁴ In addition, there is a large body of evidence suggesting an association between alcohol misuse and a variety of risk behaviours, which can have a negative impact on the biopsychosocial well-being of women in particular. ⁵ ⁶ Examples of negative outcomes commonly associated with the misuse of alcohol by women include unprotected sex, early unplanned pregnancies, and abortions.^{7–9} Such risk behaviours are already quite prevalent among Brazilian women ¹⁰, and can be considered public health issues regardless of the chances of being magnified by alcohol misuse.

The aim of this study was to respond to an urgent demand for up-to-date information regarding trends in alcohol consumption among women in Brazil, as well as to investigate the rates of unprotected sex, early pregnancy and abortion, evaluating their associations with alcohol consumption. We also examine the effect of alcohol misuse on abortion, analysing the potential mediating roles of unprotected sex and early pregnancy. A deeper understanding of such associations will be of great value for developing tailored prevention strategies and providing individualized health care.

MATERIAL AND METHODS

This was a descriptive, cross-sectional analytical study. Data were obtained from the Brazilian National Alcohol and Drugs Survey (BNADS), a serial cross-sectional study conducted in 2006 and 2012.

Sampling and procedures

The BNADS, which was conducted by the research firm Ipsos Public Affairs, used randomised multistage cluster sampling to select 3007 and 4607 individuals, respectively, in 2006 and 2012. This technique was used to guarantee that the sample represents specific sub-groups or strata with higher statistical precision. This is because the variability within each subgroup is lower when compared to the variability within the entire population. As this technique has high statistical precision, it also allows for smaller sample sizes as would be otherwise required.

The sample comprised individuals \geq 14 years of age, including an oversampling of adolescents (14–17 years of age), and were selected from the household population of Brazil. Residents of Brazil who do not speak Portuguese (native Brazilians living in the Amazon rainforest) were excluded, as were individuals with cognitive impairment or intellectual disability. The overall response rates in 2006 and 2012 were 66% and 77%, respectively. The sampling process was conducted in three steps: the selection of 149 counties using probability proportional to size methods, the selection, using those same methods, of two census sectors within each county, totalling 298 census sectors, and the selection, by simple random sampling, of eight households within each census sector, followed by the selection of a household member to be interviewed, using the "the closest upcoming birthday" technique. One-hour, face-to-face interviews were conducted, in the home of the respondent, by trained interviewers using a standardised fully structured questionnaire. In the present study, we analysed the female subsample, which comprised 1,719 respondents in 2006 and 2,537 respondents in 2012, for a collective total of 4,256 women.

Ethics

This study was approved by the Research Ethics Committee of the Federal University of São Paulo, in the city of São Paulo, Brazil. All respondents gave written informed consent.

Socioeconomic and demographic characteristics

The variables of interest were evaluated in relation to the main socioeconomic and demographic characteristics (sex, age, level of education, marital status and socioeconomic status). We also evaluated those variables by the principal geographic regions of Brazil, which include the northern, northeastern, central-west, southeastern and southern regions.

Associated variables

Alcohol use disorder

Alcohol use disorder (AUD) was assessed with the Portuguese-language version of the Composite International Diagnostic Interview (CIDI 2.1), adapted for use in Brazil.¹¹ Although the 2006 and 2012 BNADS series both pre-dated the issuance of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), the questionnaire included questions related to craving, which allowed AUD to be diagnosed on the basis of the eleven corresponding DSM-5 criteria. Individuals who had met two or more of those criteria in the past 12 months were classified as having AUD.

Binge drinking

We defined binge drinking (BD) as proposed in 2004 by the National Advisory Council to the National Institute on Alcohol Abuse and Alcoholism, which considers it a pattern of drinking that brings the blood alcohol concentration to 0.08 g/dl or above. For the typical adult, this pattern corresponds to women consuming ≥ 4 drinks over a period of approximately 2 hours.¹² The questionnaire addressed this subject with the following yes-no question: "In the last 12 months, have you drunk four or more shots of any alcoholic beverage, on any given occasion, over a period of approximately 2 hours?".

In the statistical models, we tested the alcohol use status (AUS) variable. The AUS score combines AUD and BD, as follows: 0 = moderate drinker (no BD or AUD), 1 = binge drinker (BD without AUD), and 2 = problem drinker (BD+AUD).

Abortion

The history of abortion was assessed by a yes/no question: "Have you ever aborted a pregnancy?".

Unprotected sex

The frequency of unprotected sex was assessed by the question: "*How often did you wear condom when you have sex?*". The responses included *never*, *almost never*, *almost always* and *always*, coded 0, 1, 2 and 3, respectively.

Early pregnancy

Early pregnancy was defined as that occurring in females under 20 years of age.¹³ It was assessed by the following yes/no question: "*Have you ever been pregnant?*".

Statistical analysis

All preliminary findings were analysed using the Stata statistical software package, version 13.0.¹⁴ Prevalence rates were estimated using data weighted to correct for unequal probabilities of selection into the sample, and post-stratification weights were applied to correct for non-responses and to adjust the 2006 and 2012 samples to known population distributions of selected socioeconomic and demographic variables (age, level of education, marital status, socioeconomic status and region of the country), according to the Brazilian Census of 2010.¹⁵ Cross-tabulations were used in order to examine alcohol consumption by socioeconomic and demographic characteristics.

We used multinomial regression to assess the unconditional associations between the AUS (moderate drinker, binge drinker or problem drinker) and three possible outcomes (unprotected sex, early pregnancy and abortion). All multinomial models were adjusted for age and level of education.

Serial mediation analysis

Serial mediation analysis was performed using Mplus software, version 7.4 (Muthén & Muthén, 1998–2015), as depicted in Figure 1. Two potential mediators were analysed—unprotected sex (as an ordinal variable) and early pregnancy (as a dichotomous variable: 0 = no early pregnancy, and 1 = early pregnancy). Abortion was also analysed as a dichotomous variable. The control variables were age and years of schooling, which were regressed on unprotected sex, early pregnancy and abortion.

The parameterisation and the weighted least squares mean- and variance-adjusted (WLSMV) estimator, employing a diagonal weight matrix with standard errors, were employed as suggested by Muthén *et al.*¹⁶ Under WLSMV estimation, the indirect effect is determined by analysing the latent response variables underlying the categorical variables (the two mediators), rather than the categorical variables themselves.¹⁷ In addition, the indirect effects were calculated based on bootstrap resampling (with 10 000 replicates). Thus, 95% bootstrap confidence intervals are estimated, and when those confidence intervals encompass zero, the null hypothesis (of no indirect effect) is accepted. Due to the theta parameterisation, the estimations of the indirect effects are given in probit regression. Because no effect size is estimated for the indirect effect, the results are interpreted only in terms of their significance and direction regarding increasing or decreasing probabilities. Positive values indicate an increase in the probability of abortion, whereas negative values indicate a reduction in that probability.

RESULTS

BD

Among women, the prevalence of BD increased by 34.2% (from 35.1% to 47.1%) between 2006 and 2012 (Table 1). With the exception of the northern region, all regions of the country showed an increase in BD. The increase was largest (68.4%) in the central-west region and smallest (10.2%) in the southern region. Among women 40–59 years of age, the prevalence of BD increased by 88.4% (from 26.8% to 50.5%), and there was also a significantly greater increase in that prevalence among women with a lower level of education (70.7% among those with \leq 9 years of schooling vs. 24.5% among those with \leq 12 years of schooling).

AUD

In the sample of women as a whole, the prevalence of AUD did not change significantly between 2006 (5.9%) and 2012 (6.1%) (Table 1). As for regional differences, only the southern region presented a significant reduction in the prevalence of AUD (from 7.6% to 5.2%). However, there were significant reductions in that prevalence in two age groups: women 14–17 years of age, among whom it decreased by 33.3% (from 6.0% to 4.0%), and women 18–28 years of age, among whom it decreased by 15.5% (from 10.3% to 8.7%).

Table 1

Risk behaviours

Table 2 shows the prevalence rates and associations for the 2012 dataset only. Methodological improvements in comparison with the BNADS I were made in order to avoid underreporting in the assessment of risk behaviours. That change confounds comparisons between the two waves (2006 and 2012) regarding risk behaviours rates. Unprotected sex was reported by 36.1% of the women in the sample, and 11.3% of the women \leq 20 years of age reported having been pregnant at least once. Abortion was reported by 16.3% of those women. When estimated for the three AUS categories— moderate drinker, binge drinker, and problem drinker—those rates increased in a dose-response pattern. Approximately half of the women who reported BD also reported having had unprotected sex, BD increasing the chances of engaging in unprotected sex by 1.5 times. Among women \leq 20 years of age who reported BD, more than one in every ten were or had been pregnant and the chances of having an abortion were almost double that calculated for those who did not report BD. Among the women classified as problem drinkers, the abortion rate was nearly 25%. Those same women were also 3.0 times more likely to have had an early pregnancy and 2.5 times more likely to have had an abortion than were those classified as moderate drinkers.

Table 2

Path analysis

As indicated in Figure 1, regarding the indirect specific effects, only one specific path was statistically significant (AUS \rightarrow early pregnancy \rightarrow abortion [indirect effect = 0.267, 95% bootstrap confidence interval = 0.051 to 0.483]), indicating that higher scores for alcohol dependence or BD (i.e. higher AUS scores) translate to a higher probability of abortion, the conditional path passing through early pregnancy, independent of the frequency of unprotected sex. There was no evidence that the following specific indirect effects (paths) were significant: AUS \rightarrow unprotected sex \rightarrow abortion (indirect effect =

-0.002, 95% bootstrap confidence interval = -0.034 to 0.031), and AUS \rightarrow unprotected sex \rightarrow early pregnancy \rightarrow abortion (indirect effect = 0.011, 95% bootstrap confidence interval = -0.015 to 0.037). In addition, when early pregnancy was excluded from the analysis, there was no evidence that AUS had a direct effect on abortion probabilities (direct effect = 0.142, 95% confidence interval = -0.103 to 0.386).

Figure 1

DISCUSSION

Our findings show that, among women in Brazil, there was an increase in BD between 2006 and 2012. This increase was significant among some subpopulations, such as women 40–59 years of age, poorly educated, and of low socioeconomic status. Increasing drinking and alcohol-related problems among women have been reported in various studies and have been brought to public attention by several organisations.¹ In Brazil, there is a lack of focussed, effective public health policies to limit the activities of the alcohol industry, as it is common in LMICs,¹⁸ which is partially responsible for this scenario. The impact of that shortcoming is augmented by the scarcity of women-centred health care services,^{19 20} which is attributable to the combination of a disjointed health care network and the use of treatment protocols focussing on men.^{3 5}

We did not detect any significant changes in AUD during the period under study, the rates actually decreasing significantly among specific subpopulations, such as younger women and women living in the southern region of the country. Although the rates of BD increased between 2006 and 2012, that increase was more moderate in the southern region. It should be borne in mind that previous studies had shown the rates of alcohol consumption among adolescents to be highest in the southern region,^{21 22} which led to several regional initiatives for environmental prevention.^{23 24} Our findings suggest that such strategies might have succeeded in changing harmful drinking behaviours in that population.²⁵ The concentration of prevention programs limited to school settings, ²⁶ combined with the lack of universal and selected prevention initiatives for the population as a whole, could explain the significant decrease among women 14–28 years of age, whereas there was a 45% increase among women 40–59 years of age. However, such speculation contradicts evidence that school prevention initiatives are ineffective in contexts with a lack of environmental prevention.²⁷

The current rates of AUD in Brazil are still a matter of concern, as it affects more than 6% of the female population. This rate is well above the 3.2% observed among women in the Americas, as well as being higher than the 2.9% observed among women in Europe.¹ The stable but consistently elevated rates of AUD among females in Brazil should be the focus of more detailed investigation in the future.

There is a large body of evidence suggesting that abusive alcohol consumption is closely related to a range of risk behaviours and negative events, especially in LMICs such as Brazil.²⁸ A previous study with a population sample from a south-eastern Brazilian capital evaluated sexual practices and showed that 14%, 23% of drug-use adolescents reported unprotected sex and abortion respectively, with nearly one third of them reporting early pregnancy.²⁹ Our findings show that the rates of unprotected sex, early pregnancy and abortion are worryingly high in Brazil, and that those events are significantly associated with AUD. The results suggested a dose-response relationship between the AUS and the outcomes investigated, in which AUD alone was sufficient to predict unprotected sex and abortion, as was BD alone.

Our results show that, in Brazil, more than one in ten women ≤ 20 years of age have been pregnant. Teenage pregnancy is a serious public health issue in LMICs, including Brazil, due to the short- and long-term negative consequences for mother and child.³⁰ Our findings also show that more than 16% of the female population ≥ 14 years of age reported having had at least one pregnancy terminated, a rate well above the 9% previously estimated.¹⁰ Abortion is currently prohibited in Brazil, (except in cases in which the life of the mother is at immediate risk, cases of rape and cases of anencephaly).³¹ That discrepancy may be attributed to the discretion method used in drug use surveys such as this one. In addition to increasing public health care costs in the country,³² unsafe abortion is one of the main causes of maternal mortality, death resulting from physical complications and psychosocial factors.³³ Although some interventions can be safe, simple and effective, it is estimated that nearly 22 million unsafe abortions take place every year worldwide, significantly contributing to the global burden of maternal mortality and morbidity.³⁴ In a recent survey, it was estimated that nearly 17 million unsafe abortion services per year.³⁵ Current restricted abortion legislation in Brazil leads women faced with unwanted pregnancies to practice self-induced abortion or to undergo the procedure at clandestine abortion clinics, putting their lives at risk. Policy and regulatory barriers also limit access to post-abortion services, resulting in missed opportunities for educational and therapeutic interventions that could prevent future abortions.³⁴

The serial mediation model confirmed that a harmful AUS (BD or BD+AUD) increases the probability of abortion via early pregnancy, although that relationship was not found to be dependent on the frequency of unprotected sex. To our knowledge, the proposed path from AUS to abortion has not previously been explored. However, our hypothesis is in line with previous evidence showing an association between AUS and early pregnancy,^{36–38} as well as between AUS and abortion.^{9 39} The association between harmful drinking patterns and unprotected sex has been quite well established in the literature.^{38 40} Contrary to our hypothesis, we did not find unprotected sex to be a mediator of the association between AUS and abortion. We can speculate that, even though the rates of unprotected sex were high (being reported by more than one third of the female population), that event does not necessarily lead to pregnancy, a necessary condition for the abortion

outcome. Therefore, unprotected sex was not found to play a role in that relationship. Due to the cross-sectional design of the study, a causal chain cannot be established, since it is not possible to known if women abort because they drink more and, therefore, expose themselves to unprotected sex, or they drink more after the traumatic experience of abortion and previously, already had a pattern of carelessness in sexual exposure. Although we cannot make inferences regarding causal influences, the associations presented here are strong enough to indicate the need for the development of future longitudinal studies of alcohol use in order to explore causal mechanisms related to the impacts of alcohol use on risk exposure and female reproductive health.

The intrinsic limitations of this study should be mentioned. Due to methodological changes in the data collection between 2006 and 2012, it was not possible to analyse the trends of risk behaviours between the two waves of the survey. Further, the use of crossectional design demands a very careful interpretation of path analysis models, which should avoid, at all means, any assumption regarding causal relationships between the studied variables.

Finally, this study provides sufficient evidence of a recent increase in the harmful consumption of alcohol among women in Brazil. Our results also call attention to a series of risk behaviours associated with alcohol misuse, and we have proposed a model to explain those associations, in which the predictor alcohol misuse has a direct effect on abortion, that effect being mediated by early pregnancy. Because the harmful use of alcohol is avoidable, it is of utmost importance that universal and selective prevention initiatives focussing on alcohol-related behaviours be implemented among women in Brazil.

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Conflict of interest

None

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Table 1 Prevalence of binge drinking and alcohol use disorder among women (N = 4256) in 2006 and 2012, by socioeconomic

and demographic characteristics.

	Binge drinking*			Alcohol use diso	order [†]	
			Relative			Relativ
	2006	2012	difference	2006	2012	differer
Characteristic	% (95% CI)	% (95% CI)	%	% (95% CI)	% (95% CI)	%
Sample as a whole	35.1 (30.2,40.2)	47.1 (42.4,51.8)	34.2 [‡]	5.9 (4.6,7.5)	6.1 (4.8,7.7)	3.39
Age, in years						
14–17	30.9 (21.8,41.8)	39.5 (28.9,51.2)	27.8	6.0 (3.5,10.2)	4.0 (2.4,6.7)	-33.3 [‡]
18–28	42.8 (35.2,50.8)	46.0 (38.4,53.7)	7.5	10.3 (7.2,14.5)	8.7 (5.8,13.0)	-15.5‡
29–39	38.0 (29.9,46.8)	52.3 (44.7,59.7)	37.6	6.8 (4.0,11.5)	8.3 (5.8,11.7)	22.1
40–59	26.8 (19.9,35.1)	50.5 (42.3,58.6)	88.4 [‡]	4.0 (2.6,6.1)	5.8 (3.8,8.8)	45.0
≥ 60	20.8 (9.7,39.0)	22.2 (9.6,43.2)	6.7	0.3 (0.0,2.1)	0.5 (0.1,1.8)	67.0
Education						
≥9	33.4 (26.5,41.0)	57.0 (49.5,64.2)	70.7 [‡]	5.1 (3.5,7.3)	6.1 (4.2,8.8)	19.6
≥12	38.7 (32.7,45.1)	48.2 (42.1,54.3)	24.5 [‡]	6.9 (5.1,9.4)	6.4 (4.7,8.7)	-7.2
> 12	23.7 (13.4,38.3)	32.4 (24.1,42.1)	36.7	4.6 (1.9,10.4)	5.0 (2.6,9.6)	8.7
Marital status						
Single	43.8 (36.1,51.7)	48.6 (40.5,56.7)	11.0	8.9 (6.3,12.6)	6.6 (4.4,9.8)	-25.8
Married	29.7 (23.7,36.5)	44.4 (38.9,50.0)	49.5	4.3 (2.9,6.3)	5.8 (4.1,8.1)	34.9
Widowed	32.0 (16.6,52.7)	57.6 (38.8,74.4)	80.0	5.2 (2.5,10.6}	3.2 (1.1,8.9)	-38.5
Divorced/separated	32.3 (20.3,47.1)	60.1 (45.5,73.0)	86.0	5.5 (2.8,10.4)	9.8 (5.8,16.3)	78.2
Socioeconomic class [§]						
А	27.7 (10.7,55.1)	23.7 (10.4,45.4)	-14.4	7.3 (2.1,22.4)	4.0 (0.9,16.7)	-45.2
В	31.6 (22.2,42.8)	40.6 (32.8,48.3)	28.5	5.7 (3.0,10.5)	5.3 (3.4,8.3)	-7.0
С	35.1 (28.0,42.9)	51.5 (45.1,57.9)	46.7	7.7 (5.5,10.8)	7.2 (5.2,9.8)	-6.5
D	35.7 (28.4,43.8)	52.5 (42.0,62.8)	47.1	4.4 (2.9,6.7)	4.6 (2.6,8.0)	4.5
Е	47.5 (24.4,71.7)	57.7 (42.1,72.0)	21.5 [‡]	6.7 (2.8,15.2)	6.0 (4.7,7.6)	-10
Region						
Northern	39.2 (24.1,56.6)	42.3 (27.5,58.6)	7.9	5.7 (2.3,13.4)	10.0 (6.0,16.4)	75.4
Northeastern	37.2 (27.6,47.9)	62.1 (53.9,69.7)	66.9 [‡]	3.5 (1.9,6.4)	3.5 (1.8,6.9)	0
Southeastern	33.1 (26.1,41.0)	42.3 (35.3,49.7)	27.8 [‡]	6.4 (4.5,9.0)	6.7 (4.6,9.6)	4.7
Southern	39.1 (28.0,51.4)	43.1 (30.7,56.6)	10.2 [‡]	7.6 (4.1,13.4)	5.2 (3.1,8.8)	-31.6‡

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Central-west	24.4 (14.9,37.3)	41.1 (28.3,55.2)	68.4 [‡]	9.0 (4.4,17.4)	9.5 (5.2,16.8)	5
Depressive disorder	38.6 (31.4,46.4)	52.8 (43.9,61.5)	36.8	9.3 (6.8,12.4)	9.3 (6.7,12.8)	
*Defined as the ingesti	ion of 4 units of alcoho	ol within 2 hours (calcul	ated among dr	inkers).		
[†] As defined in the fifth	edition of the Diagno	stic and Statistical Man	ual of Mental I	Disorders.		
[‡] p<0.05 for the compa	rison between 2006 an	d 2012 (chi-square test)				
Categories established	d by the Brazilian Mar	keting Research Associa	ation, class A b	being the most afflu	ent.	
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	nu	ups.//mc04.manuSci	ihreimar.co	out/unh-scielo		

 Table 2 Logistic regression, adjusted for age and education, of prevalence rates and odds ratios for

 unprotected sex, early pregnancy and abortion among women according to their alcohol use status, in 2012.

Variable(N = 2537)No BD, no AUDBD, no AUDBD+AUDUnprotected sex $\[mathcal{W}(95\%\CI)\]$ 36.1 (33.2,39.1)32.7 (29.4,36.1)48.5 (39.9,57.2)54.8 (44.6,64.6) $\[mathcal{W}(95\%\CI)\]$ -11.5 (1.0,2.2)*2.1 (1.3,3.2)^{+}Early pregnancy-11.2 (0.4,3.3)25.8 (15.1,40.6) $\[mathcal{W}(95\%\CI)\]$ 11.3 (8.8,14.5)10.4 (8.0,13.6)10.6 (4.4,23.5)25.8 (15.1,40.6) $\[mathcal{W}(95\%\CI)\]$ -11.2 (0.4,3.3)3.1 (1.5,6.4)*Abortion $\[mathcal{W}(95\%\CI)\]$ 16.3 (14.5,18.3)15 (13.2,17.0)20.4 (15.3,26.7)24.9 (16.3,36.2) $\[mathcal{W}(95\%\CI)\]$ -11.9 (1.3,2.8)^{+}2.5 (1.5,4.4)^{+}* p<0.05, ⁺ p<0.01* p<0.05, ⁺ p<0.01* p<0.05, ⁺ p<0.01	Variable (N = 2537) No BD, no AUD BD, no AUD BD+AUD Unprotected sex 36.1 (33.2,39.1) 32.7 (29.4,36.1) 48.5 (39.9,57.2) 54.8 (44.6,64.6) OR (95% CI) 6.1 (33.2,39.1) 32.7 (29.4,36.1) 48.5 (39.9,57.2) 54.8 (44.6,64.6) OR (95% CI) - 1 1.5 (1.0,2.2)* 2.1 (1.3,3.2) [†] Early pregnancy - - - 25.8 (15.1,40.6) OR (95% CI) 1.3 (8.8,14.5) 10.4 (8.0,13.6) 10.6 (4.4,23.5) 25.8 (15.1,40.6) OR (95% CI) 6.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 25 (1.5,4.4) [†] *p<∪0.5, [†] p<0.01 - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†]		Sample as a whole				
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% (95% CI) 36.1 (33.2,39.1) 32.7 (29.4,36.1) 48.5 (39.9,57.2) 54.8 (44.6,64.6) OR (95% CI) - 1 1.5 (1.0,2.2)* 2.1 (1.3,3.2) [†] Early pregnancy % (95% CI) 11.3 (8.8,14.5) 10.4 (8.0,13.6) 10.6 (4.4,23.5) 25.8 (15.1,40.6) OR (95% CI) - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4)* Abortion - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4)* % (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†] * p<0.05, [†] p<0.01	% (95% CI) 36.1 (33.2,39.1) 32.7 (29.4,36.1) 48.5 (39.9,57.2) 54.8 (44.6,64.6) OR (95% CI) - 1 1.5 (1.0,2.2)* 2.1 (1.3,3.2) [↑] Early pregnancy * * 54.8 (44.6,64.6) 0.1 (1.3,2.2)* 2.1 (1.3,3.2) [↑] Early pregnancy * * 1.3 (8.8,14.5) 10.4 (8.0,13.6) 10.6 (4.4,23.5) 25.8 (15.1,40.6) OR (95% CI) - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4)* Abortion * * * 24.9 (16.3,36.2) OR (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [↑] 2.5 (1.5,4.4) [↑] * p<0.05, [†] p<0.01	Unprotected sex					
OR (95% CI) - 1 $1.5 (1.0,2.2)^*$ $2.1 (1.3,3.2)^\dagger$ Early pregnancy % (95% CI) 11.3 (8.8,14.5) 10.4 (8.0,13.6) 10.6 (4.4,23.5) 25.8 (15.1,40.6) OR (95% CI) - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4) * Abortion - - 1 1.9 (1.3,2.6.7) 24.9 (16.3,36.2) OR (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8)^† 2.5 (1.5,4.4)^† * p<0.05, *p<0.01	OR (95% CI) - 1 1.5 (1.0,2.2)* 2.1 (1.3,3.2) [†] Early pregnancy % (95% CI) 11.3 (8.8,14.5) 10.4 (8.0,13.6) 10.6 (4.4,23.5) 25.8 (15.1,40.6) OR (95% CI) - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4)* Abortion - - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4)* OR (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†] *p<0.05, ⁺ p<0.01	% (95% CI)	36.1 (33.2,39.1)	32.7 (29.4,36.1)	48.5 (39.9,57.2)	54.8 (44.6,64.6)	
Early pregnancy % (95% CI) 11.3 (8.8,14.5) 10.4 (8.0,13.6) 10.6 (4.4,23.5) 25.8 (15.1,40.6) OR (95% CI) - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4)* Abortion % (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [↑] 2.5 (1.5,4.4) [↑] * p<0.05, [†] p<0.01 BD - binge drinking; AUD - alcohol use disorder.	Early pregnancy % (95% CI) 11.3 (8.8,14.5) 10.4 (8.0,13.6) 10.6 (4.4,23.5) 25.8 (15.1,40.6) OR (95% CI) - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4)* Abortion % (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†] * p<0.05, [†] p<0.01 BD - binge drinking; AUD - alcohol use disorder.	OR (95% CI)	-	1	1.5 (1.0,2.2) *	2.1 (1.3,3.2) [†]	
$\begin{tabular}{lllllllllllllllllllllllllllllllllll$	% (95% CI) 11.3 (8.8,14.5) 10.4 (8.0,13.6) 10.6 (4.4,23.5) 25.8 (15.1,40.6) OR (95% CI) - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4) * Abortion % (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [↑] 2.5 (1.5,4.4) [↑] * p<0.05, [†] p<0.01 BD - binge drinking; AUD - alcohol use disorder.	Early pregnancy					
OR (95% CI) - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4) * Abortion % (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†] * $p<0.05$, $^{+}p<0.01$ BD - binge drinking; AUD - alcohol use disorder.	OR (95% CI) - 1 1.2 (0.4,3.3) 3.1 (1.5,6.4) * Abortion * * * * % (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†] * p<0.05, [†] p<0.01	% (95% CI)	11.3 (8.8,14.5)	10.4 (8.0,13.6)	10.6 (4.4,23.5)	25.8 (15.1,40.6)	
Abortion % (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†] * p<0.05, [†] p<0.01 BD - binge drinking; AUD - alcohol use disorder.	Abortion % (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†] * p<0.05, [†] p<0.01 BD - binge drinking; AUD - alcohol use disorder.	OR (95% CI)	-	1	1.2 (0.4,3.3)	3.1 (1.5,6.4) *	
% (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†] * p<0.05, [†] p<0.01	% (95% CI) 16.3 (14.5,18.3) 15 (13.2,17.0) 20.4 (15.3,26.7) 24.9 (16.3,36.2) OR (95% CI) - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†] *p<0.05, [†] p<0.01 BD - binge drinking; AUD - alcohol use disorder.	Abortion					
OR (95% CI) - 1 $1.9 (1.3, 2.8)^{\dagger} 2.5 (1.5, 4.4)^{\dagger}$ * p<0.05, [†] p<0.01 BD - binge drinking; AUD - alcohol use disorder.	OR (95% CI) - 1 1.9 (1.3,2.8) [†] 2.5 (1.5,4.4) [†] *p<0.05, [†] p<0.01 BD - binge drinking; AUD - alcohol use disorder.	% (95% CI)	16.3 (14.5,18.3)	15 (13.2,17.0)	20.4 (15.3,26.7)	24.9 (16.3,36.2)	
* p<0.05, [†] p<0.01 BD - binge drinking; AUD - alcohol use disorder.	* p<0.05, [†] p<0.01 BD - binge drinking; AUD - alcohol use disorder.	OR (95% CI)	-	1	1.9 (1.3,2.8) [†]	2.5 (1.5,4.4) [†]	
BD - binge drinking; AUD - alcohol use disorder.	BD - binge drinking; AUD - alcohol use disorder.	* p<0.05, [†] p<0.01					



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Figure 1 Serial Mediation Model - The higher the value of AUS the higher the probability of abortion through early pregnancy, independent of protected sex frequency.

Fig. 1.



Path statistically significant - (AUS > Early Pregnancy > Abortion)

Supplementary Information for manuscript entitled: *Alcohol misuse among women in Brazil: recent trends and associations with unprotected sex, early pregnancy and abortion.* Luciana T. S. Massaro BSc,^{1,2} Renata Rigacci Abdalla MD,^{1,2} Ronaldo Laranjeira PhD MD,^{1,2} Raul Caetano PhD MD,³ Ilana Pinsky PhD,¹ Clarice S. Madruga PhD^{1,2}

Supplementary Information:

Clarifications regarding the use of Path Analysis in crossectional database.

The authors would like to include, to the reviewers perusal, some extra information regarding our use of a path analysis model, once we are dealing with data from a crossectional study and enquiries regarding this procedure are common and frequently mentioned by reviewers. The use of mediation modeling in crossectional datasets is a sensitive subject and it has raised concerns regarding the possibility of indirect and direct effects be given a causal interpretation.

Firstly, it must be highlighted that recent works on causality inference have pointed out that even a study longitudinally designed with random assignment of the X predictor does not guarantee causal interpretation^{1,2}. The assumption succinctly summarized in the following quote from Valeri and VanderWeele³, elucidates that: "controlled direct effects require (a) no unmeasured treat-outcome confounding, and (b) no unmeasured mediator-outcome confounding. Natural direct and indirect effects require these assumptions, and also (c) no unmeasured treat-mediator confounding, as well as (d) no mediator-outcome confounder affected by treatment". Such assumptions have posed a new way of thinking on causality based on counterfactuals, even when the study is not longitudinal, in which the unidirectionality is not an assumption^{4,5,6,7}.

However, regarding these assumptions, we agree with other issues mentioned by the authors, for instance, that maybe the indirect and direct effect might be biased due to, say, interactions between (X and the two mediators) and non-linearities, as described by Valeri and VanderWeele⁸.

It is important to state that in the present study analysis, we have based our arguments under the works of Andrew Hayes's references as, for example, his 2013 book titled Introduction to mediation, moderation and conditional analysis. Such approach reflects a laissez-faire attitude about the role of data analysis in science (see Hayes, 2013, pp. 15-18, for a more extended discussion)⁹. Here, we do not dwell on some of the philosophical debates that can be found in the methodology literature about what cause-effect means, the limitations of various research designs for entertaining cause-effect questions, and the boundaries of the value of regression analysis and statistical control. As recently posed by the own Hayes et al^{10,11}, such regression-based

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approach seeks to use data analysis as a tool, only one of many in a researcher's arsenal, and ultimately secondary to theory, knowledge of the literature in one's substantive area, and with a logical argument in terms of clinical/psychological conduction of the phenomenon in hand. It also should be mentioned that MACROs for SAS for such analysis are discussed in Valeri and VanderWeele⁸ and broadly implemented in Mplus version 7.4 Muthén et al¹². Further, in a commentary on Mediation Analysis, Causal Process, and Cross-Sectional Data¹³, Shrout, encourages the detailed exploration of alternate causal models in psychology beyond the autoregressive model considered by Maxwell et al.

Further, according to Mueller¹⁴, "one cannot lose sight of the fact that establishing isolated causal relationships is not the only goal of SEM". In this publication the author suggests that the idea of cause and effect should be abandoned in the interpretation of SEM data, adopting the idea of predictors and outcomes instead. Therefore, we consider that the approach on SEM used in this manuscript is even more conservative when it comes to causal relationships.

Based on the above, and in order to state our point of view (and scientific position) regarding the analytical approach methods applied by us, we have added in the limitation subheading what follows:

"...Although we cannot make inferences regarding causal influences, the associations presented here are strong enough to indicate the need for the development of future longitudinal studies of alcohol use in order to explore causal mechanisms related to the impacts of alcohol use on risk exposure and female reproductive health." (Discussion section, page 12).

The audience interested in this new approach to data structuring might consider the mediation based on counterfactual–defined causal effects as an innovative way to structure the hypothesis tested, allowing to clarify the direct effect in the presence of the interaction mediator-predictor as well non-linearities.

Taking into consideration all the above stated, we emphasise that the use of Structural Equation Models to explore the effect of multiple and concomitant variables from crossectional data has been widely accepted by statisticians and epidemiologists and has been extensively published.

A few examples of the use of these models in crossectional data:

Supplementary Information for manuscript entitled: *Alcohol misuse among women in Brazil: recent trends and associations with unprotected sex, early pregnancy and abortion.* Luciana T. S. Massaro BSc,^{1,2} Renata Rigacci Abdalla MD,^{1,2} Ronaldo Laranjeira PhD MD,^{1,2} Raul Caetano PhD MD,³ Ilana Pinsky PhD,¹ Clarice S. Madruga PhD^{1,2}

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Dear Editor and Reviewer,

Thank you and your editors for the thoughtful review of our manuscript entitled Alcohol misuse among women in Brazil: recent trends and associations with unprotected sex, early pregnancy and abortion (RBP- 2017 - 0024), submitted on December 29, 2017.

It follows file with requested revisions on March 2, 2018.

We believe our manuscript improved greatly after these contributions.

We have responded to a reviewer's comment and have made the corresponding

alteration in the text. Below we display the comments followed by our response in red.

?₩. We look forward to your review.

Sincerely,

Luciana Massaro

Clarice Madruga

Reviewer: 1

Recommendation: Accept

Comments:

A paper addressing alcohol use among women in Brazil and the associations with unprotected sex, early pregnancy and abortion. The data provides up to date information regarding trends in alcohol consumption among Brazilian women to inform prevention strategies and individualized health care. The paper makes a meaningful contribution to Brazilian public health initiatives, of which the reader body would be interested. Grammar and punctuation was excellent.

Additional Questions:

Does the manuscript contain new and significant information to justify publication?: Yes

Does the Abstract (Summary) clearly and accurately describe the content of the article?: Yes

Is the problem significant and concisely stated?: Yes

Are the methods described comprehensively?: Yes

Are the interpretations and conclusions justified by the results?: Yes

Is adequate reference made to other work in the field?: Yes

Length of article is: Adequate

Are all the tables and figures necessary/adequate?: Yes

If not, please inform which tables and/or figures you think should be deleted:

Please state any conflict(s) of interest that you have in relation to the review of this paper (state "none" if this is not applicable) .: No.

Rating:

Interest: 2. Good

Quality: 2. Good

Originality: 2. Good

Overall: 2. Good

Please rate the quality of the language used in the paper (i.e., scientific English writing).: 2. Good

Are there issues with statistics? Do you think the paper should be checked by our statistical advisor?: No

Reviewer: 2

Recommendation: Minor Revision

Comments:

A very relevant study, with a theme of social impact in Brazil and this is well described and characterized in the introduction.

Although the authors have added a paragraph pondering this aspect in the discussion, it is worth emphasizing that, due to the transversal model, a causal chain cannot be established as proposed in the results.

It is not possible to known if women abort because they drink more and therefore expose themselves to unprotected sex, or they drink more (pattern of binge) after the traumatic experience of abortion and previously already had a pattern of carelessness in sexual exposure.

R: Altered as requested. Page 9

Additional Questions:

Does the manuscript contain new and significant information to justify publication?: Yes

Does the Abstract (Summary) clearly and accurately describe the content of the article?: Yes

Is the problem significant and concisely stated?: Yes

Are the methods described comprehensively?: Yes

Are the interpretations and conclusions justified by the results?: Yes

Is adequate reference made to other work in the field?: Yes

Length of article is: Adequate

Are all the tables and figures necessary/adequate?: Yes

If not, please inform which tables and/or figures you think should be deleted:

Please state any conflict(s) of interest that you have in relation to the review of this paper (state "none" if this is not applicable).: none

Rating:

- Interest: 1. Excellent
- Quality: 2. Good
- Originality: 2. Good
- Overall: 2. Good

Please rate the quality of the language used in the paper (i.e., scientific English writing).: 2. Good

Are there issues with statistics? Do you think the paper should be checked by our statistical advisor?: No