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# The Intricate Interactions between Maternal Smoking and Drinking During Pregnancy and Birthweight Z-Scores of Preterm Births

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## Abstract

**Background:** The extent to which smoking and drinking in a local community is associated with nutrition and Z-scores of infants from spontaneous preterm deliveries, is uncertain.

**Aim:** To investigate associations of different levels of maternal smoking and drinking in spontaneous preterm birth with infant birthweight Z-scores.

**Methods:** Information, including gestational age (determined by earliest ultrasound), maternal arm circumference (measured at enrolment), smoking-drinking data (obtained up to 4 occasions), birthweight data (obtained from medical records) and birthweight Z-scores (calculated from INTERGROWTH- 21st study), collected over a period of nine years was used to compare 407 spontaneous preterm births with 3 493 spontaneous term births Analyses of variance, correlations and multiple regression were performed in STATISTICA.

**Results:** Women with spontaneous preterm birth, had significantly higher gravidity and smaller arm circumference when compared to women with spontaneous birth at term.. Women with spontaneous preterm birth drank more and heavier during pregnancy, and more smoked. Gestational age at birth was significantly longer in heavy-smokers-heavy-drinkers compared to heavy-smokers-no-drinkers (7.1 days) and in no-smokers-heavy-drinkers when compared to no-smokers-no-drinkers (11.2 days). Birthweight was significantly lower in low-smokers-heavy-drinkers when compared to low-smokers-no-drinkers (240g) and in heavy-smokers-low-drinkers when compared to no-smokers-low-drinkers (273g). Birthweight Z-scores were significantly lower in low-smokers-heavy-drinkers when compared to low-smokers-low-drinkers and low-smokers-no-drinkers; and, also significantly lower in heavy-smokers-low-drinkers when compared to low-smokers-low-drinkers and no-smokers-low-drinkers.

**Conclusion:** Alcohol aggravates the detrimental effect of smoking on birthweight and birthweight Z-scores but seems to counteract the negative association of smoking with gestational age.

**Keywords:** Spontaneous preterm birth; Pregnancy; Cigarette smoking; Alcohol drinking; Gestational age; Birthweight; Birthweight Z-Scores

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## Introduction

Preterm birth is a critical global health problem and a major challenge in perinatal health care because of its high morbidity and mortality [1]. It does not only affect infants and their families but also increases costs of health care [2,3]. Perinatal outcome is particularly susceptible to socio-economic conditions affecting lifestyle choices and behavioural factors [4].

Substance use during pregnancy, including cigarette smoking and alcohol consumption [5-7], has been linked to adverse birth outcomes such as preterm birth, low birth weight, and fetal growth restriction [8-10]. Smoking during pregnancy increased the risk of preterm birth nearly two-fold with a dose response further increasing the risk [7]. Worldwide, significant numbers of women still drink heavily during pregnancy despite public health advisories, psychosocial interventions [11], and detailed information on the adverse effects of smoking and drinking [12]. South Africa has one of the highest levels of alcohol consumption, heavy binging as well as heavy smoking in certain communities [13,14].

Birthweight and duration of gestation are important predictors of health and survival of new-borns [15] with birthweight the best marker of optimal fetal growth and development [16]. Nutritional status, reflected by the maternal mid-upper arm circumference, is an important contributor to infant birthweight [17], is an indicator of the progress of pregnancy and its outcome [16], and is significantly associated with preterm births [15,18].

The Safe Passage Study (SPS) by the PASS Network was a large prospective multidisciplinary study to investigate the associations of smoking and drinking during pregnancy with stillbirths and infant deaths [19]. Detailed information on various aspects of pregnancy, labour and neonatal outcome was collected within geographically defined communities. Analysis of the South African part of the data demonstrated a high preterm birth rate of 13.8% [20], in sharp contrast to the rate of 5.4%-8.9% for 24 European countries in 2010 [21].

Synergistic interactions between smoking and drinking lead to higher rates of preterm birth than predicted by their additive effects [22,23]. As the co-occurrence between tobacco and alcohol use is well established [24], the South African SPS data presented an ideal opportunity to investigate the association of smoking and drinking with maternal arm circumference, gestational age, birthweight, and their combined effect on infant birthweight Z-scores in spontaneous preterm birth.

## Methods

In the Western Cape province of South Africa, pregnant women, ≥16 years-old, attending antenatal clinics of midwife obstetric units near Tygerberg Hospital, were enrolled between August 2007 and January 2015 and their infants followed up to the age of one year (August 2016). Of the 7060 women recruited, only 3900 women with 407 (10%) who had a spontaneous preterm birth, remained in the study after exclusions for non-spontaneous births (17%), multiple enrolments (14%), drug use (9%), withdrawals (2%), twin pregnancies (1%), missing data (1%) and minor exclusions (1%) (Figure 1).

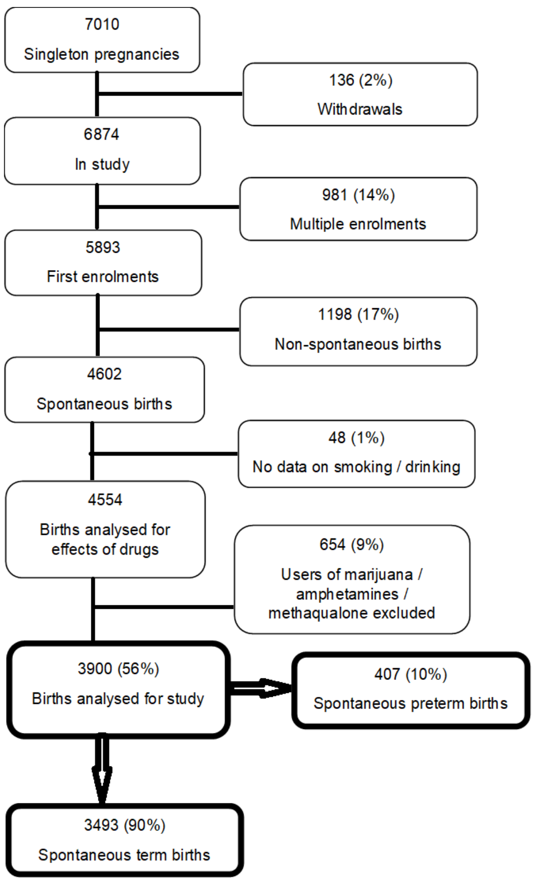


**Figure 1:** Study profile.

Gestational age was determined by earliest ultrasound before the second antenatal visit. Depending on the gestational age at enrolment, women had up to three further antenatal visits at Tygerberg Hospital at 20-24, 28-32, and at 34-38 weeks of gestation. Demographic and anthropometric information were obtained at enrolment and/or first antenatal visit. For the mid-upper arm circumference, the midpoint of the upper arm was first determined and then the circumference measured twice. If measurements differed by more than 2 mm, a third measurement was taken, and the mean of the closest two measurements used.

The validated Timeline-Follow-Back method [19], used at up to four occasions, obtained detailed information on drinking, cigarette smoking and drug use during pregnancy. To examine combinations of dual exposure, nine categories of smoking and drinking were created: no-smoking-no-drinking, low-smoking-no-drinking, heavy-smoking-no-drinking, no-smoking-low-drinking, no-smoking-heavy-drinking, low-smoking-low-drinking, heavy-smoking-low-drinking, low-smoking-heavy-drinking, and heavy-smoking-heavy-drinking. Smoking six and a half cigarettes (+- 80$^{th}$ centile) or more per day was categorized as heavy-smoking, as nine cigarettes (often used in literature) left a paucity in the heavy-smoking category. The drinking groups were categorized according to binge drinking (four or more standard drinks at one sitting) and total standard drinks (total grams of alcohol consumed per drink was calculated and converted into standard drinks using the National Institute on Alcohol Abuse and Alcoholism definition of one standard drink equals 14 g of pure alcohol) [25]. Drinking was divided into heavy-drinking with ≥4 binge-drinking episodes and ≥ 32 total standard drinks during pregnancy, and low-drinking.

Other information collected included preterm delivery, fetal sex, and birthweight Z-scores, calculated from the international standards of the INTERGROWTH-21$^{st}$ study (available for gestational ages from 168-299 days, excluding twins) [26].

A nutritionist calculated the calories per standard drink, and thereafter the total added calories per alcohol intake during pregnancy were calculated for each drinking category. The calorie content (kcals) of a standard drink of the most popular brands was 219 for liqueur, 160 for beer, 128 for cider and coolers, 107 for wine and 97 for rum, whisk(e)y and brandy. The mean calories per standard drink was 137.83 kilocalories.

Statistical analyses on data entered in Excel 365 (Microsoft, USA) were performed using SAS/STAT® software, Version 9.3, Copyright© 2011 and STATISTICA (Dell Inc. (2016) Dell Statistica® (data analysis software system), version 13. software.dell.com). Continuous variables were compared between groups with analysis of variance (ANOVA). Bonferroni or least significant difference (LSD) multiple comparisons identified significant differences between the means in the ANOVA. Two-way ANOVAs and LSD multiple comparisons were used to compare means of one factor relative to another factor. The Mann-Whitney U test compared differences between two groups where responses were not normally distributed. The Chi-square test was used with contingency tables to determine significances in categorical data. Spearman correlations measured correlations between ordinal response variables. A p-value<0.05 was regarded as statistically significant. Seven covariates were used in a multiple regression to determine which covariates had the most significant effect on birthweight Z-scores and to determine the underlying effect of smoking and drinking on these variables and birthweight Z-scores. Therefore, all spontaneous births were subdivided: smoking yes drinking no; smoking no drinking yes;

smoking yes drinking yes; and smoking no drinking no. A best subsets regression was used to determine the three best covariates for predicting birthweight Z-scores, selected such that their inter-correlations do not exceed 0.7 for each of the four subdivisions.

Ethics approval for the study was obtained from the Health Research Ethics Committee of Stellenbosch University (approval number: N06/10/210 and S19/07/119), as well as from the Western Cape Department of Health.

## Results

Table 1 demonstrates the significant differences between the spontaneous preterm and spontaneous term birth groups with regard to gravidity, education, maternal mid-upper arm circumference, as well as smoking and drinking.

Only 4-5% of no-smoking women drank heavily whereas 25-28% of heavy-smoking women also drank heavily ($p<0.0001$). Regarding specific alcohol consumption, beer was consumed most frequently (44.3%) followed by coolers or ciders (31.6%), spirits (14.6%), wine (6.3%), liqueur (2.0%), and others (1.2%).

In the spontaneous preterm birth group, the mean (median; standard deviation) number of total drinks during pregnancy in the three heavy-drinking categories were 146.9 (101.5; 177), 124.7 (108; 84) and 106 (93.9; 56) for heavy-smoking, low-smoking and no-smoking respectively. Mean total drinks in three low-drinking categories ranged from 8.2-11.7. The mean (standard deviation) number of cigarettes smoked per day in the three heavy-smoking categories were 10.5 (4), 9.7 (3), and 9.7 (3) for no-drinking, low-drinking and heavy-drinking respectively. Mean daily cigarettes in the three low-smoking categories ranged from 2.9-3.3. The mean total calories (kcal) in the three heavy-drinking categories were 20,247, 17,187, and 14,610 per pregnancy for heavy-smoking, low-smoking and no-smoking respectively. Mean total calories (kcal) in the three low-drinking categories ranged from 1130-1613 per pregnancy.

**Table 1:** Comparison between spontaneous preterm and spontaneous term birth.

| **Continuous variables** | **SPTB (407)** | **STB (3 493)** | **p-value** |
|---|---|---|---|
| | **mean (sd)** | **mean (sd)** | |
| Maternal age | 24.9 (6.0) | 24.7 (5.9) | 0.45 |
| Gravidity | 2.4 (1.4) | 2.1 (1.3) | **< 0.01** |
| Education (years) | 9.7 (1.7) | 10.1 (1.7) | **0.02** |
| Maternal mid-upper arm circumference (mm) | 265.0 (45.6) | 275.7 (44.6) | **< 0.01** |
| Edinburgh depression score | 13.1 (6.1) | 12.6 (5.9) | 0.61 |
| Household income (ZAR/month) | 855.9 (620.4) | 882.5 (604.7) | 0.54 |
| Gestational age at delivery (days) | 241.7 (20.4) | 276.8 (8.4) | **< 0.01 *** |
| Birthweight (g) | 2 268.5 (635.9) | 3 116.8 (454.0) | **< 0.01 *** |
| Birthweight Z-score | -0.23 (1.0) | -0.36 (1.0) | 0.42 |
| Cigarettes smoked per day | 3.4 (3.9) | 2.6 (3.5) | 0.24 |
| Total drinks during pregnancy | 22.4 (62.4) | 17.2 (42.0) | **< 0.01** |
| Total binges during pregnancy | 3.5 (7.2) | 2.7 (5.1) | **< 0.01** |
| **Nominal variables** | **SPTB (407)** | **STB (3 493)** | **p-value** |
| | **n (%)** | **n (%)** | |
| Number of smokers | 301 (74%) | 2 245 (64%) | **< 0.01** |
| Number of heavy smokers | 76 (25%) | 450 (20%) | **0.02** |
| Number of drinkers | 265 (65%) | 2 264 (65%) | 0.91 |
| Number of heavy drinkers | 52 (20%) | 406 (18%) | 0.25 |

* = as expected, due to selection of two groups.

sd = standard deviation.

Bold p-value if significant ($p<0.05$).

SPTB = spontaneous preterm birth; STB = spontaneous term birth.

1$ = 15.2 ZAR or 1 EURO = 18.5 ZAR.

In the spontaneous term birth group, the mean (median; standard deviation) number of total drinks during pregnancy in the three heavy-drinking categories were 115.1 (73.9; 105), 95.4 (72.1; 74) and 84.5 (64.7; 52) for heavy-smoking, low-smoking and no-smoking respectively. Mean total drinks in the three low-drinking categories ranged from 8.2-14.1. The mean (standard deviation) number of cigarettes smoked per day in the three heavy-smoking categories were 10.0 (4), 9.5 (4), and 9.1 (3) for no-drinking, low-drinking and heavy-drinking respectively. Mean daily cigarettes in the three low-smoking categories ranged from 2.7-3.3. The mean total calories (kcal) in the three heavy-drinking categories were 15,864, 13,149, and 11,647 per pregnancy for heavy-smoking, low-smoking and no-smoking respectively. Mean total calories (kcal) in the three low-drinking categories ranged from 1130 - 1943 per pregnancy.

Smoking-drinking exposure categories in the spontaneous preterm birth group and their associations with gestational age, birthweight and birthweight Z-scores are summarized in Table 2. Data in top half of table paired according to heavy, low and no smoking, while data in bottom half of table paired according to heavy, low and no drinking. For gestational age, the lowest (33 weeks 6 days) and highest (36 weeks) mean gestational ages were found in the heavy-smoking-no-drinking and no-smoking-heavy-drinking categories, respectively. For birthweight, the lowest and highest mean birthweights were found in the low-smoking-heavy-drinking and no-smoking-heavy-drinking categories, respectively. For birthweight Z-scores, the lowest and highest mean birthweight Z-scores were found in the low-smoking-heavy-drinking and no-smoking-low-drinking categories, respectively.

The nine exposure categories in the spontaneous preterm birth and spontaneous term birth groups and their associations with birthweight Z-scores are shown in Figure 2 where some of the significant differences between exposure categories are circled and lowest / highest mean of each variable is indicated in the spontaneous preterm birth group only.

Figure 3 illustrates the associations of the smoking-drinking categories in spontaneous preterm birth and spontaneous term birth groups with mid-upper arm circumference. In the spontaneous preterm birth group, no-smoking as compared to low-smoking or heavy-smoking was associated with a significantly larger mean mid-upper arm circumference. The smallest and largest mean mid-upper arm circumferences were found in the heavy-smoking-no-drinking and no-smoking-no-drinking categories, respectively.

Multiple regression analyses of best three covariates that influenced birthweight Z-scores were selected for the four exposure subdivisions. Of the seven variables (daily cigarettes, total standard drinks, mid-upper arm circumference, education years, the Edinburgh depression score, gravidity, and household income), mid-upper arm circumference was found to have the largest significant effect on birthweight Z-scores in all subdivisions ($p<0.001$). In the joint exposure subdivision (n=1788, 49%), total standard drinks ($p<0.001$) followed by daily cigarettes ($p<0.005$), had the second and third largest significant effect on birthweight Z-scores. In the drinking only subdivision (n=516, 14%), a high household income was associated with a low birthweight Z-scores ($p<0.05$). In the smoking only subdivision (n=693, 19%), only mid-upper arm circumference was positively associated with birthweight Z-scores, while in the no smoking no drinking subdivision (n=628, 17%), high gravidity ($p<0.02$) and low Edinburgh depression score ($p<0.05$) were associated with high birthweight Z-scores.

## Discussion

To the best of our knowledge, this is the first study to examine

**Table 2:** Association of exposure categories in spontaneous preterm birth with gestational age at birth, birthweight and birthweight Z-scores.

| Spontaneous preterm birth | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Gestational age at birth (days)** | | | **Birthweight (gram)** | | | **Birthweight Z-scores** | | |
| **High Smoking (HS)** | | | | | | | | | |
| Exposure category | HSND* | HSLD | HSHD | HSND | HSLD | HSHD | HSND | HSLD | HSHD |
| n | 16 | 39 | 21 | 16 | 39 | 21 | 15 | 39 | 21 |
| Mean (sd) | 237.5 (26.6) [b^] | 241.3 (16.5) | 244.6 (12.5) [b^] | 2182 (751) | 2101 (586) | 2131 (447) | -0.17 (0.94) | -0.57 (1.13) | 0.66 (G61.04) |
| **Low Smoking (LS)** | | | | | | | | | |
| Exposure category | LSND | LSLD | LSHD | LSND | LSLD | LSHD* | LSND | LSLD | LSHD* |
| n | 76 | 123 | 26 | 76 | 122 | 25 | 75 | 120 | 24 |
| Mean (sd) | 241.5 (21.4) | 241.0 (20.5) | 245 (19.4) | 2315 (669) [b^] | 2291 (605) [c^] | 2075 (556) [b^c^] | -0.08 (0.86)[b^^] | -0.11 (1.00)[c^^] | -0.97 (0.95)[b^^c^^] |
| **No Smoking (NS)** | | | | | | | | | |
| Exposure category | NSND | NSLD | NSHD# | NSND | NSLD | NSHD | NSND | NSLD | NSHD |
| n | 50 | 51 | 5 | 49 | 51 | 5 | 48 | 51 | 5 |
| Mean (sd) | 240.8 (25.2) [b^] | 242.6 (18.7) | 252 (2.9) [b^] | 2320 (703) | 2374 (698) | 2572 (276) | -0.15 (1.07) | -0.00 (0.96) | 0.3 (0.77) |
| **High Drinking (HD)** | | | | | | | | | |
| Exposure category | NSHD | LSHD | HSHD | NSHD# | LSHD* | HSHD | NSHD | LSHD | HSHD |
| n | 5 | 26 | 21 | 5 | 25 | 21 | 5 | 24 | 21 |
| Mean (sd) | 252.0 (2.9) | 245.0 (19.4) | 244.6 (12.5) | 2572 (276)[a^] | 2075 (556) [a^] | 2131 (447) | -0.30 (0.77) | -0.97 (0.95) | 0.66 (1.04) |
| **Low Drinking (LD)** | | | | | | | | | |
| Exposure category | NSLD | LSLD | HSLD | NSLD | LSLD | HSLD | NSLD# | LSLD | HSLD |
| n | 51 | 123 | 39 | 51 | 122 | 39 | 51 | 120 | 39 |
| Mean (sd) | 242.6 (18.7) | 241.0 (20.5) | 241.3 (16.5) | 2374 (698) [b^] | 2291 (605)[c^] | 2101 (586) [b^c^] | -0.00 (0.96) [b^] | -0.11 (1.00)[c^] | 0.57 (1.13) [b^c^] |
| **No Drinking (ND)** | | | | | | | | | |
| Exposure category | NSND | LSND | HSND | NSND | LSND | HSND | NSND | LSND | HSND |
| n | 50 | 76 | 16 | 49 | 76 | 16 | 48 | 75 | 15 |
| Mean (sd) | 240.8 (25.2) | 241.5 (21.4) | 237.5 (26.6) | 2320 (703) | 2315 (669) | 2182 (751) | -0.15 (1.07) | -0.08 (0.86) | 0.17 (0.94) |

[a] = difference between category column 1 and 2.
[b] = difference between category column 1 and 3.
[c] = difference between category column 2 and 3.
^ = $p < 0.05$, ^^ = $p < 0.01$.
* = smoking-drinking category with lowest/smallest mean of variable.
# = smoking-drinking category with highest/largest mean of variable.
N=no; L=low; H=heavy; S=smoking; D=drinking.
sd= standard deviation.

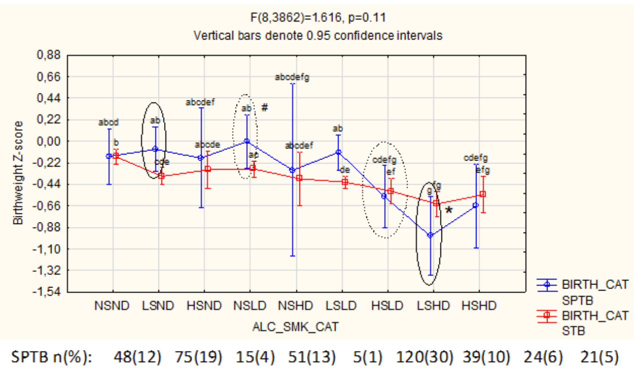


**Figure 2:** Associations of exposure categories with birthweight Z-scores.

Legend: Vertical bars denote 95% confidence intervals.
Duplicated differentials (letters) above vertical bars indicate absence of significant difference.
N=no; L=low; H=heavy; S=smoking; D=drinking.
SPTB = spontaneous preterm birth; STB = spontaneous term birth.
…….. Low-drinking categories that differed significantly.
------- Low-smoking categories that differed significantly.
# Category with highest mean birthweight Z-score in spontaneous preterm birth.
* Category with lowest mean birthweight Z-score in spontaneous preterm birth.

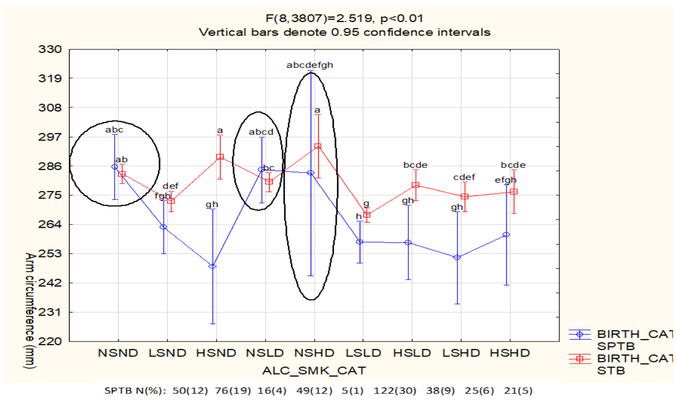


**Figure 3:** Maternal mid-upper arm circumference and the nine-level smoking and drinking categories in spontaneous preterm and term births.

Legend: Vertical bars denote 95% confidence intervals.
Duplicated differentials (letters) above vertical bars indicate absence of significant difference.
N=no; L=low; H=heavy; S=smoking; D=drinking.
SPTB = spontaneous preterm birth; STB = spontaneous term birth.
Circled are the no-smoking categories in spontaneous preterm birth.

various levels of concurrent smoking and drinking in women who had spontaneous preterm births. We found significant differences of the various smoking-drinking exposures on gestational age at delivery, birthweight, and birthweight Z-scores. Maternal mid-upper arm circumference, a proxy for nutritional status, was also found to differ significantly, especially in the smoking categories.

Causes of spontaneous preterm birth are multiple, complex and uncertain, but smoking and alcohol have been associated with preterm birth. Although significantly more women in the spontaneous preterm birth group smoked, the low number of cigarettes smoked in the community may be a reason for the poor association of smoking with spontaneous preterm birth in our study. This finding is supported by Salihu HM, et al. (2007) [7], who found a dose effect of cigarettes, on the increased risk of preterm birth. This differed from Räisänen S, et al. (2013) [27], who found smoking to be the largest contributor to preterm birth, concurring with other studies that tobacco use increases the risk of preterm birth [2,28, and 29].

Women in the spontaneous preterm birth group drank and binged significantly more. This confirms the finding of O'Leary CM, et al. (2009) [30], that higher alcohol intake is associated with increased risk of preterm birth [30]. Our finding that significantly more pregnant smokers engaged in heavy alcohol consumption than pregnant non-smokers, is supported by Okah FA, et al. (2005) [30], who found that pregnant smokers were seven times more likely than non-smokers to consume alcohol [31].

In the spontaneous preterm birth group, heavy drinking in combination with no or heavy smoking was associated with an increased gestational age (Table 2). Heavy drinking seems to limit the reduction of gestational age by heavy-smoking, but the categories where this played a role were small with large confidence intervals. It is unlikely that a direct effect of alcohol on uterine activity could have played a role, as the tocolytic properties of alcohol are unconvincing [32].

Women who experienced spontaneous preterm birth, appeared to comprise a vulnerable group, sensitive to the effects of heavy-smoking and heavy-drinking on birthweight. Heavy drinking without smoking was associated with an increased birthweight**.** Most other studies confirmed alcohol consumption to be associated with a decreased birthweight [33,34]. However, Henderson J, et al. (2007) [35], suggested that low amounts of alcohol seem to have a small protective effect on birthweight [35]. Our results showed synergistic interaction between alcohol consumption and smoking regarding a decreased birthweight.

Dual exposure had an additive, negative effect on birthweight Z-scores, with the lowest mean in the low-smoking-heavy-drinking category in both groups. Compared to international standards, our cohort had much lower birthweight Z-scores. Sbrana M, et al. (2016) [36], reported that alcohol consumption did not increase the risk of preterm birth whereas a higher risk of preterm birth was observed among infants born to mothers who smoked in addition to consuming alcohol during pregnancy [36]. O'Leary CM, et al. (2009) [30], found that the proportion of SGA infants and preterm birth increased with higher levels of prenatal alcohol exposure; however, the association between alcohol intake and SGA infants was attenuated after adjustment for maternal smoking [30]. Mid-upper arm circumference had the strongest association with birthweight Z-scores in all four exposure subdivisions, suggesting that maternal nutrition plays an important role, but when pregnant women smoke and drink, total drinks followed by daily cigarettes had the second and third largest significant effect on birthweight Z-scores.

The use of cigarettes and alcohol probably influence nutritional status before pregnancy, continuing further into pregnancy. Smoking was associated with a significant reduction of mid-upper arm circumference, which in turn was associated with an increased risk of spontaneous preterm birth. Nicotine seems to suppress appetite, which may explain why smokers have smaller mid-upper arm circumferences than non-smokers do [37,38]. A small mid-upper arm circumference could also be an indicator of poor nutritional status [16,39], as corroborated by a Cape Town based study that found gestational weight gain and nutritional intake to be inadequate even though a mean mid-upper arm circumference of 27.7-28.8 cm was found [40]. In our study, mid-upper arm circumference was significantly smaller in the spontaneous preterm birth group. In a previous study, we found that a small mid-upper arm circumference was strongly associated with a higher risk of spontaneous preterm birth [41]. In addition, many other studies confirm that women who were underweight during pregnancy or had a small mid-upper arm circumference, had an increased risk of preterm birth [15,18,42, and 43], suggesting that maternal under nutrition contributes to preterm birth.

Our finding of small mid-upper arm circumferences in heavy drinking women (with spontaneous preterm birth) despite their additional intake of 14,610 to 20,247 kcals, might be explained by Carter RC, et al. (2017) [40], who found that heavy alcohol consumption was not associated with weight gain during pregnancy, suggesting that heavy drinkers replace calorie dense nutritious foods with alcohol [40]. However, in women who had spontaneous term births, the mid-upper arm circumference was significantly larger in heavy drinkers who did not smoke or smoked less. Adequate nutrition combined with added excess kcals from heavy drinking, greater than tenfold more than the kcals from light drinking, may play a role here. A significantly larger mid-upper arm circumference was associated with heavy smoking than with low smoking, which is confirmed by other studies [37,44-46].

Despite this being a large study with a high incidence of spontaneous preterm birth, the small numbers (and large confidence intervals) in certain smoking-drinking categories limit the strength of these findings. The prevalence rate of spontaneous preterm birth in this study was 10% in contrast to 14% in a previous study, where multiple enrolments, induced preterm birth and drug users were not excluded [20], indicating that there are also other associations with preterm birth.

## Conclusion

Interpretation of the effects of smoking and drinking on spontaneous preterm birth is difficult. Alcohol aggravates the reduction of birthweight and birthweight Z-scores associated with smoking but seemed to counteract the negative association of smoking with gestational age in this study. A small mid-upper arm circumference, probably indicating poor nutritional status, and cigarette smoking, was associated with an increased risk for spontaneous preterm birth. Interventions to help women quit smoking and drinking should be addressed before pregnancy.

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## Contribution to Authorship

LB responsible for extraction and quality control of data. Involved with planning and protocol of this study. Obtained ethical approval. Wrote the original manuscript. Assisted with editing, revising and controlled final manuscript. DN performed the statistical analyses and assisted with writing and editing the manuscript. DH assisted with writing, editing and revising of manuscript. HO, principal investigator at South African SPS site, initiated study and obtained ethical approval and funding. He assisted with conception, writing, editing, revising, and controlled final manuscript.

## Disclosure of Interests

All authors agree to submission and have nothing to declare.

## Details of Ethics Approval

Approval for the study was obtained from the Health Research Ethics Committee of Stellenbosch University (approval number: N06/10/210 and S19/07/119), as well as from the Western Cape Department of Health.

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## Availability of Data and Materials

Available upon request.

### References

1. Harrison MS, Goldenberg RL (2016) Global burden of prematurity. Semin Fetal Neonatal Med 21: 74-79. http://dx.doi.org/10.1016/j.siny.2015.12.007
2. Tucker J, Mcguire W (2004) Epidemiology of preterm birth. BMJ 329: 675-678. https://doi.org/10.1136/bmj.329.7467.675
3. Moore E, Blatt K, Chen A, Van Hook J, Defranco EA (2016) Relationship of trimester-specific smoking patterns and risk of preterm birth. Am J Obstet Gynecol 215: 109.e1-109.e6. https://doi.org/10.1016/j.ajog.2016.01.167
4. Joseph KS, Liston RM, Dodds L, Dahlgren L, Allen AC (2007) Socioeconomic status and perinatal outcomes in a setting with universal access to essential health care services. C Can Med Assoc J 177: 583-590. https://doi.org/10.1503/cmaj.061198
5. Abraham M, Alramadhan S, Iniguez C, Duijts L, Jaddoe VWV, et al. (2017) A systematic review of maternal smoking during pregnancy and fetal measurements with meta-analysis. PLoS One 12: 1-13. https://doi.org/10.1371/journal.pone.0170946
6. Lin YJ (2014) Low birth weight, preterm births, and intrauterine growth retardation in relation to parental smoking during pregnancy. Pediatr Neonatol 55: 3-4. http://dx.doi.org/10.1016/j.pedneo.2013.09.014
7. Salihu HM, Wilson RE (2007) Epidemiology of prenatal smoking and perinatal outcomes. Early Hum Dev 83: 713-720. https://doi.org/10.1016/j.earlhumdev.2007.08.002
8. Mullally A, Cleary BJ, Barry J, Fahey TP, Murphy DJ (2011) Prevalence, predictors and perinatal outcomes of peri-conceptional alcohol exposure - retrospective cohort study in an urban obstetric population in Ireland. BMC Pregnancy Childbirth 11: 1-7. https://doi.org/10.1186/1471-2393-11-27
9. Patra J, Bakker R, Irving H, Jaddoe VWV, Malini S, et al. (2011) Dose-response relationship between alcohol consumption before and during pregnancy and the risks of low birthweight, preterm birth and small for gestational age (SGA)-a systematic review and meta-analyses. Int J Obstet Gynaecol 118: 1411-1421. https://doi.org/10.1111/j.1471-0528.2011.03050.x
10. Pfinder M, Kunst AE, Feldmann R, van Eijsden M, Vrijkotte TGM (2013) Preterm birth and small for gestational age in relation to alcohol consumption during pregnancy: Stronger associations among vulnerable women? Results from two large Western-European studies. BMC Pregnancy Childbirth 13: 1-10. https://doi.org/10.1186/1471-2393-13-49
11. American College of Obstetricians and Gynecologists (2011) At-risk drinking and alcohol dependence: obstetric and gynecologic implications. Committee Opinion 496: 1-6.
12. Odendaal HJ, Brink LT, Nel DG, Carstens E, De Jager M, et al. (2020) Prevalence of drinking and smoking in successive pregnancies. S Afr Med J 110: 1100-1104. https://dx.doi.org/10.7196/SAMJ.2020.v110i11.14667
13. Myers B, Koen N, Donald KA, Nhapi RT, Workman L, et al. (2018) Effect of hazardous alcohol use during pregnancy on growth outcomes at birth: findings from a South African cohort study. Alcohol Clin Exp Res 42: 369-377. https://doi.org/10.1111/acer.13566
14. Steyn K, Yach D, Stander I (1997) Smoking in urban pregnant women in South Africa. S Afr Med J 87: 460-463.
15. Sebayang SK, Dibley MJ, Kelly PJ, Shankar AV, Shankar AH, et al. (2012) Determinants of low birthweight, small-for-gestational-age and preterm birth in Lombok, Indonesia: Analyses of the birthweight cohort of the SUMMIT trial. Trop Med Int Heal 17: 938-950. https://doi.org/10.1111/j.1365-3156.2012.03039.x
16. Rani DN, Phuljhele DS, Beck DP (2017) Correlation between maternal mid upper arm circumference and neonatal anthropometry. Int J Med Res Rev 5: 717-724. https://doi.org/10.17511/ijmrr.2017.i07.10
17. Ramlal RT, Tembo M, Soko A, Chigwenembe M, Ellington S, et al. (2012) Maternal mid-upper arm circumference is associated with birth weight among HIV-infected Malawians. Nutr Clin Pr 27: 416-421. https://doi.org/10.1177/0884533611435991
18. Berhe T, Gebreyesus H, Desta H (2019) Determinants of preterm birth among mothers delivered in Central Zone Hospitals, Tigray, Northern Ethiopia. BMC Res Notes 12: 10-15. https://doi.org/10.1186/s13104-019-4307-z
19. Dukes KA, Burd L, Elliott AJ, Fifer WP, Folkerth RD, et al. (2014) The safe passage study: Design, methods, recruitment, and follow-up approach. Paediatr Perinat Epidemiol 28: 455-465. https://doi.org/10.1111/ppe.12136
20. Brink LT, Gebhardt GS, Mason D, Groenewald CA, Odendaal HJ (2019) The association between preterm labour, perinatal mortality and infant death (during the first year) in Bishop Lavis, Cape Town, South Africa. South African Med J 109: 102-106. https://doi.org/10.7196/SAMJ.2019.v109i2.13438
21. Zeitlin J, Mortensen L, Cuttini M, Lack N, Nijhuis J, et al. (2016) Declines in stillbirth and neonatal mortality rates in Europe between 2004 and 2010: Results from the Euro-Peristat project. J Epidemiol Community Health 70: 609-615. http://dx.doi.org/10.1136/jech-2015-207013
22. Dew PC, Guillory VJ, Okah FA, Cai J, Hoff GL (2007) The effect of health compromising behaviors on preterm births. Matern Child Health J 11: 227-233. https://doi.org/10.1007/s10995-006-0164-1
23. Odendaal HJ, Steyn DW, Elliott A, Burd L (2009) Combined effects of cigarette smoking and alcohol consumption on perinatal outcome. Gynecol Obstet Invest 67: 1-8. https://doi.org/10.1159/000150597
24. Peltzer K, Pengpid S (2019) Maternal alcohol use during pregnancy in a general national population in South Africa. South African J Psychiatry 25: 1-5. https://doi.org/10.4102/sajpsychiatry.v25i0.1236
25. National Institute on Alcohol Abuse and Alcoholism (2017) What is a standard drink?. United States.
26. Villar J, Papageorghiou AT, Pang R, Ohuma EO, Ismail LC, et al. (2014) The likeness of fetal growth and newborn size across non-isolated populations in the INTERGROWTH-21st project: The fetal growth longitudinal study and newborn cross-sectional study. Lancet Diabetes Endocrinol 2: 781-792. https://doi.org/10.1016/S2213-8587(14)70121-4
27. Räisänen S, Gissler M, Saari J, Kramer M, Heinonen S (2013) Contribution of risk factors to extremely, very and moderately preterm births - register-based analysis of 1,390,742 singleton births. PLoS One 8: 1-7. https://doi.org/10.1371/journal.pone.0060660
28. Baba S, Wikström AK, Stephansson O, Cnattingius S (2012) Influence of smoking and snuff cessation on risk of preterm birth. Eur J Epidemiol 27: 297-304. https://doi.org/10.1007/s10654-012-9676-8
29. Janisse JJ, Bailey BA, Ager J, Sokol RJ (2014) Alcohol, tobacco, cocaine, and marijuana use: Relative contributions to preterm delivery and fetal growth restriction. Subst Abus 35: 60-67. https://doi.org/10.1080/08897077.2013.804483

30. O'Leary CM, Nassar N, Kurinczuk JJ, Bower C (2009) The effect of maternal alcohol consumption on fetal growth and preterm birth. BJOG An Int J Obstet Gynaecol 116: 390-400. https://doi.org/10.1111/j.1471-0528.2008.02058.x

31. Okah FA, Cai J, Hoff GL (2005) Term-gestation low birth weight and health-compromising behaviors during pregnancy. Obstet Gynecol 105: 543-550. https://doi.org/10.1097/01.AOG.0000148267.23099.b7

32. Haas DM, Morgan AM, Deans SJ, Schubert FP (2014) Ethanol for preventing preterm birth in threatened preterm labor. Cochrane Database Syst Rev 2014. https://doi.org/10.1002/14651858.CD011445.pub2

33. Nykjaer C, Alwan NA, Greenwood DC, Simpson NAB, Hay AWM, et al. (2014) Maternal alcohol intake prior to and during pregnancy and risk of adverse birth outcomes: Evidence from a british cohort. J Epidemiol Community Health 68: 542-549. http://dx.doi.org/10.1136/jech-2013-202934

34. Virji SK (1991) The relationship between alcohol consumption during pregnancy and infant birthweight: An epidemiologic study. Acta Obstet Gynecol Scand 70: 303-308. https://doi.org/10.3109/00016349109007877

35. Henderson J, Gray R, Brocklehurst P (2007) Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome. BJOG An Int J Obstet Gynaecol 114: 243-252. https://doi.org/10.1111/j.1471-0528.2006.01163.x

36. Sbrana M, Grandi C, Brazan M, Junquera N, Nascimento MS, et al. (2016) Alcohol consumption during pregnancy and perinatal results: a cohort study. Sao Paulo Med J 134: 146-152. http://dx.doi.org/10.1590/1516-3180.2015.02040211

37. Chiolero A, Faeh D, Paccaud F, Cornuz J (2008) Consequences of smoking for body weight, body fat distribution, and insulin resistance. Am J Clin Nutr 87: 801-809. https://doi.org/10.1093/ajcn/87.4.801

38. Williams SCP (2011) Why smokers are skinny. AAAS.

39. Ricalde AE, Velásquez-Meléndez G, Tanaka AC, de Siqueira AA (1998) Mid-upper arm circumference in pregnant women and its relation to birth weight. Rev Saude Publica 32: 112-117.

40. Carter RC, Senekal M, Dodge NC, Bechard LJ, Meintjes EM, et al. (2017) Maternal alcohol use and nutrition during pregnancy: diet and anthropometry. Alcohol Clin Exp Res 41: 2114-2127. https://doi.org/10.1111/acer.13504

41. Brink LT, Nel DG, Hall DR, Odendaal HJ (2020) Association of socioeconomic status and clinical and demographic conditions with the prevalence of preterm birth. Int J Gynecol Obstet 149: 359-369. https://doi.org/10.1002/ijgo.13143

42. Davies HR, Visser J, Tomlinson M, Rotherham-Borus MJ, LeRoux I, et al. (2012) An investigation into the influence of socioeconomic variables on gestational body mass index in pregnant women living in a peri-urban settlement, South Africa. Matern Child Heal J 16: 1732-1741. https://doi.org/10.1007/s10995-011-0869-7

43. Shin D, Song WO (2015) Prepregnancy body mass index is an independent risk factor for gestational hypertension, gestational diabetes, preterm labor, and small- and large-for-gestational-age infants. J Matern Neonatal Med 28: 1679-1686. https://doi.org/10.3109/14767058.2014.964675

44. Bamia C, Trichopoulou A, Lenas D, Trichopoulos D (2004) Tobacco smoking in relation to body fat mass and distribution in a general population sample. Int J Obes 28: 1091-1096. https://doi.org/10.1038/sj.ijo.0802697

45. John U, Hanke M, Rumpf HJ, Thyrian JR (2005) Smoking status, cigarettes per day, and their relationship to overweight and obesity among former and current smokers in a national adult general population sample. Int J Obes 29: 1289-1294. https://doi.org/10.1038/sj.ijo.0803028

46. Chiolero A, Jacot-Sadowski I, Faeh D, Paccaud F, Cornuz J (2007) Association of cigarettes smoked daily with obesity in a general adult population. Obesity 15: 1311-1318. https://doi.org/10.1038/oby.2007.153