Drinking or Not Drinking in Pregnancy: The Multiplicity of Confounding Influences

Janni Niclasen*

Department of Psychology, University of Copenhagen, Øster Farimagsgade 2A, Copenhagen K 1353, Denmark

*Corresponding author: Tel.: +45-40817776; E-mail: janni.niclasen@psy.ku.dk

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Abstract — Aims: Studies investigating associations between prenatal exposure to low-moderate doses of alcohol and mental health development in childhood are inconsistent. The aim of the present study was to compare women who drink and who do not drink alcohol in pregnancy on a number of potential confounding variables, and to investigate whether any latent variables could be identified among these. Methods: Data were obtained from the Danish National Birth Cohort. Exposure: cumulated alcohol intake in full pregnancy (n = 63,464). The women were subdivided into intake groups 0, >0–10, >10–30, >30–90 and >90 units of alcohol in full pregnancy. Hereafter, the abstainers were subdivided into an all-time and a pregnancy-abstaining group, and the high intakers (>90) were subdivided into a high (>90–180) and a very high (>180) intake group. Outcome: self-reported and register-based information on socio-demographic and lifestyle factors, and latent variables from an exploratory factor analysis. Results: Significant differences were observed between the intake groups on virtually all parameters. Significant differences were observed between the abstaining groups and the high-intake groups. The exploratory factor analyses identified a number of latent variables between the potential confounding variables. Conclusion: Differences on confounding factors may in part explain the lack of consistency in the literature investigating prenatal exposure to low-moderate doses of alcohol and mental health development. It is cautiously concluded that the failure to control for these factors introduces residual and/or unmeasured confounding into the analyses, and thus masks the potential (small) effect of being exposed to low doses of alcohol in pregnancy. It is recommended that future studies control for factor scores rather than for the observed variables as is practice today.

INTRODUCTION

Forty years ago the Lancet published Jones and Smith’s now legendary article on ‘Recognition of the Fetal Alcohol Syndrome in Early Infancy’, describing the first eight identified clinical cases of fetal alcohol syndrome (FAS) (Jones and Smith, 1973). The focus in the early years was on identifying effects of large doses of alcohol on mental health outcomes. Since then, much research has been carried out investigating associations between exposure to more moderate doses of alcohol, typically <1 unit/week, and binge drinking on the one hand and mental health outcomes in childhood on the other (Gray and Henderson, 2007; Henderson et al., 2007; Sayal et al., 2007, 2009, 2013). Thus, the focus today is largely on establishing whether there is a ‘safe’ lower threshold below which drinking alcohol in pregnancy is not associated with any damages to the developing foetus. The findings from these observational studies are somewhat contradictory. Some studies have concluded that prenatal exposure to lower doses of alcohol is indeed negatively associated with mental health development in childhood (Fried and Watkinson, 1988; Streissguth et al., 1990; Olson et al., 1997; Larroque and Kaminski, 1998; NIAAA: National Institute of Alcohol Abuse and Alcoholism, 2000; Sood et al., 2001; Sayal, 2007; Testa et al., 2007), whereas others have found no such associations (O’Leary et al., 2009; Rodriguez et al., 2009; Skogerbo et al., 2012; Underbjerg et al., 2012; Sayal et al., 2013). Many studies even report on a J-shaped association between alcohol exposure and mental health outcomes in childhood, such that exposure to low doses of alcohol has an apparently protective effect on the foetus (Kelly et al., 2009, 2012; Robinson et al., 2010). Observational studies today generally apply multivariante research designs and control for what are considered the most relevant confounding factors. However, other confounding factors that may be relevant for mental health development are not controlled for, and the examination of potential childhood mediating factors is virtually absent.

The primary aim of the present study was to thoroughly describe women who drink and who do not drink alcohol in pregnancy on a large number of background characteristics, these being potential confounding factors, including socio-demographic and lifestyle factors. All-time abstainers and pregnancy abstainers were then compared separately as were high intakers and very high intakers. It was hypothesized that if large variations were observed between exposure groups, and such variables were not controlled for in the statistical analyses, this could introduce residual and/or unmeasured confounding. This residual and/or unmeasured confounding could in turn mask potential effects of exposure to lower doses of alcohol, and thus explain the lack of consistency in studies hitherto concerned with prenatal exposure to low doses of alcohol and mental health development in childhood. The secondary aim was to carry out exploratory factor analyses in order to identify possible subtle latent variables underlying the reported background characteristics.

METHODS

Sample

Data were derived from the population-based, large-scale birth cohort, the Danish National Birth Cohort (DNBC), that comprises information on 100,418 pregnancies (Olsen et al., 2001). The intention of the DNBC was to examine associations between diverse forms of exposures early in pre- and postnatal life and the health and development of the children from a life-course perspective. Between 1996 and 2002 pregnant women were enrolled nationwide at their first antenatal visit. The women were approached twice in pregnancy at approximately Weeks 16 and 30 regarding their lifestyle in the early and middle part of pregnancy and then again at age 6 months of their child regarding their lifestyle in the last part of pregnancy. The sample for the present study was restricted to women with full information on key alcohol variables.
Prenatal alcohol intake

In the three interviews the women answered separate questions regarding their weekly average intake of beer, wine and spirits. A standard drink in Denmark is defined by the National Board of Health as 12 g of absolute alcohol. In order to compute a single estimate for the cumulated intake of alcoholic drinks in the entire pregnancy the reported intake from each interview was multiplied by the number of weeks between each interview. Because the focus was to investigate the background characteristics of women with different estimates of cumulated alcohol intake in pregnancy, information from the three interviews was summed in order to obtain a total intake sum scores. The following categories of cumulated alcohol intake were adopted: 0, >0–10, >10–30, >30–90, >90. These categories were selected in order to be able to distinguish between intake groups with what can be considered very low intakes of alcohol, and further to include a fairly large number of women in each of the intake groups.

Outcome measure: background characteristics

The outcomes included both self-reported and register-based information on background characteristics including socio-demographic and lifestyle factors. Variables were included if they were a priori identified as possible confounders of the association between prenatal exposure to low-moderate doses of alcohol and mental health development. The socio-demographic factors included information on: maternal and paternal age, marriage, owning one’s own house, maternal and paternal education, and a number of variables on self-reported and register-based psychological problems and psychiatric diagnoses. The lifestyle factors included prior-to-pregnancy and in-pregnancy information on average alcohol consumption and binge drinking, pre-pregnancy BMI, in-pregnancy information on maternal and paternal smoking, in-pregnancy information on maternal intake of coffee, cola, vitamins, iron, fish oil, fish, analgesics and sleep medication, in-pregnancy maternal habits of TV watching and exercise, as well as in-pregnancy occurrences of maternal diabetes, asthma and anaemia.

Statistical analyses

The analyses were carried out using SPSS version 9.2 and SPSS version 19. By means of SAS, the data were analysed using ANOVA (for continuous variables) and Chi Square (for categorical variables) tests to test for differences between intake groups and LR tests for linear trends. In order to identify possible latent factors between the observed variables (i.e. the background characteristics), exploratory factor analyses (EFA) with Varimax rotation were carried out using SPSS.

RESULTS

Of the 63,464 women included in the sample a total of 56,258 (88.7%) women reported drinking average doses of alcohol on at least one occasion in the recognized or unrecognized part of pregnancy (Table 1). The majority of women reported drinking prior to pregnancy (87.2%), whereas similar percentages of women reported drinking average quantities of alcohol in early (44.8%), middle (49.5%) and late (46.9%) pregnancy.

Background characteristics of women who drink and do not drink alcohol in pregnancy

ANOVA and Chi Square tests between the intake groups revealed significant inter-group differences on most variables (Table 1). Socio-demographic factors: significant differences between the groups were observed for all variables. Significant linear trends were further observed for most variables. Maternal and paternal ages were positively associated with alcohol intake, as was university education. Housing (owning your own house), on the other hand, was negatively associated with cumulated alcohol intake. For the remaining variables a J-shape or reversed J-shape curve appeared, i.e. a linear trend was observed for four intake groups, whereas the fifth group (the abstaining or the high-intake group) had lower or higher estimates forming the curve on the J-shaped association between intake groups. This was observed for the married, mandatory education, and all of the psychological problems/psychiatric diagnoses variables. Compared with the high-intake group (>90 alcohol containing units, hereafter units), three times as many abstainers (0 units) had mandatory education only. The opposite was true for university education. For the psychological problems/psychiatric diagnoses variables the highest percentages were observed for the abstainers (0 units) and the high intakers (>90 units), and this was true for the self-reported as well as for the register-based variables. Lifestyle factors: apart from the fish oil variable significant differences were observed between the intake groups for all variables and linear trends were also observed for virtually all variables. The cumulated alcohol intake variable was found to be linearly associated (positively or negatively) with coffee, all alcohol variables, fish eating, BMI, TV, diabetes and asthma. For the remaining variables, namely smoking variables, vitamin, iron, analgesics and anaemia variables, a J-shape trend appeared, i.e. the low and high-intake groups had similar highest or lowest estimates, whereas the three remaining mid-intake groups revealed linear trends. For example, the abstaining (0 units) and high-intake (>90 units) groups had mean cumulated cigarettes estimates of 99 and 78 (total number of cigarettes in full pregnancy), respectively, whereas the means for the remaining groups were 62, 54 and 50 cigarettes in full pregnancy.

To further investigate the curve in the shape function observed for many of the variables, the abstaining groups were subdivided into an all-time abstaining group and a group of women ceasing to drink alcohol once recognizing their pregnancy. Correspondingly, the high-intake group (>90 units) was subdivided into a high (>90–180 units) and a very high (>180 units) intake group.

Differences in background characteristics between all-time abstainers and pregnancy-only abstainers

The abstaining (0 units) group was subdivided into a group of all-time abstainers (n = 7206) and a group of women drinking prior to pregnancy but ceasing once recognizing their pregnancy (n = 16,563) (Supplementary material, Table S1). The groups differed significantly on a large number of variables, and the means and percentages for the two groups were often
### Table 1. Background characteristics across levels of cumulated alcohol intake in pregnancy (number of units in full pregnancy including the early unrecognized part of pregnancy)

<table>
<thead>
<tr>
<th>Alcohol group</th>
<th>Full sample</th>
<th>0</th>
<th>&gt;0–10</th>
<th>&gt;10–30</th>
<th>&gt;30–90</th>
<th>&gt;90</th>
<th>P</th>
<th>Linear trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>63,464</td>
<td>7204</td>
<td>19,111</td>
<td>15,054</td>
<td>16,619</td>
<td>5476</td>
<td></td>
<td></td>
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<tr>
<td><strong>Socio-demographic factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (M)1,2</td>
<td>30.5</td>
<td>29.5</td>
<td>29.8</td>
<td>30.5</td>
<td>31.1</td>
<td>32.5</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age (P)1,3</td>
<td>32.3</td>
<td>31.5</td>
<td>31.6</td>
<td>32.2</td>
<td>32.9</td>
<td>34.6</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Married (no)4</td>
<td>2.3%</td>
<td>3.5%</td>
<td>2.5%</td>
<td>2.1%</td>
<td>1.9%</td>
<td>2.4%</td>
<td>****</td>
<td>0.75, NS</td>
</tr>
<tr>
<td>Tenant5</td>
<td>26.7%</td>
<td>30.6%</td>
<td>28.0%</td>
<td>26.2%</td>
<td>25.5%</td>
<td>22.8%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>University (M)6,7</td>
<td>8.4%</td>
<td>17.8%</td>
<td>9.3%</td>
<td>6.6%</td>
<td>5.4%</td>
<td>6.5%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>University (P)6,8</td>
<td>14.6%</td>
<td>5.8%</td>
<td>11.3%</td>
<td>15.4%</td>
<td>19.2%</td>
<td>21.2%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mandatory (M)9,10</td>
<td>8.6%</td>
<td>22.9%</td>
<td>14.8%</td>
<td>11.5%</td>
<td>9.8%</td>
<td>10.6%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mandatory (P)9,10</td>
<td>13.5%</td>
<td>7.1%</td>
<td>12.4%</td>
<td>15.8%</td>
<td>19.6%</td>
<td>21.7%</td>
<td>****</td>
<td>&lt;0.0001</td>
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<tr>
<td><strong>Education</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Lifestyle factors</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Binge drinking11</td>
<td>0.5</td>
<td>0.1</td>
<td>0.3</td>
<td>0.5</td>
<td>0.7</td>
<td>1.4</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Binge drinking (yes)12</td>
<td>30.3%</td>
<td>10.2%</td>
<td>22.4%</td>
<td>31.7%</td>
<td>39.8%</td>
<td>52.7%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cumulated alcohol intake13</td>
<td>32 (0/84)</td>
<td>0 (0/0)</td>
<td>4.6 (1/9)</td>
<td>19 (12/28)</td>
<td>53 (34/79)</td>
<td>143 (95–209)</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pre-pregnancy alcohol intake14</td>
<td>3.0</td>
<td>0</td>
<td>1.4</td>
<td>2.8</td>
<td>4.6</td>
<td>8.3</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Alcohol intake 1st intake (yes)15</td>
<td>44.8%</td>
<td>0%</td>
<td>12.2%</td>
<td>50.8%</td>
<td>80.4%</td>
<td>93.9%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Alcohol intake 2nd intake (yes)16</td>
<td>49.5%</td>
<td>0%</td>
<td>8.5%</td>
<td>60.6%</td>
<td>92.2%</td>
<td>98.0%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Alcohol intake 3rd intake (yes)17</td>
<td>46.9%</td>
<td>0%</td>
<td>8.7%</td>
<td>54.5%</td>
<td>87.7%</td>
<td>97.0%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pre-pregnancy alcohol intake (yes)18</td>
<td>87.2%</td>
<td>0%</td>
<td>97.1%</td>
<td>98.2%</td>
<td>99.6%</td>
<td>99.9%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cumulated smoking (cig.)19</td>
<td>63</td>
<td>100</td>
<td>62</td>
<td>54</td>
<td>50</td>
<td>78</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking (yes)20,21</td>
<td>25.2%</td>
<td>31.5%</td>
<td>24.1%</td>
<td>23.3%</td>
<td>23.5%</td>
<td>30.9%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nicotine substitution22</td>
<td>2.2%</td>
<td>2.6%</td>
<td>1.8%</td>
<td>2.2%</td>
<td>2.3%</td>
<td>3.0%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Partner smoking (yes)19</td>
<td>29.6%</td>
<td>37.0%</td>
<td>29.6%</td>
<td>27.9%</td>
<td>27.1%</td>
<td>31.2%</td>
<td>****</td>
<td>0.05, NS</td>
</tr>
<tr>
<td>Coffee (yes)23</td>
<td>41.9%</td>
<td>33.4%</td>
<td>34.1%</td>
<td>41.0%</td>
<td>49.0%</td>
<td>65.0%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vitamin A (yes)24</td>
<td>84.1%</td>
<td>81.8%</td>
<td>84.8%</td>
<td>84.1%</td>
<td>81.5%</td>
<td>80.0%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Iron (yes)25</td>
<td>71.2%</td>
<td>69.4%</td>
<td>71.8%</td>
<td>72.0%</td>
<td>72.1%</td>
<td>68.2%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fish oil (yes)26</td>
<td>5.1%</td>
<td>5.2%</td>
<td>5.1%</td>
<td>5.2%</td>
<td>5.0%</td>
<td>5.4%</td>
<td>****</td>
<td>0.09, NS</td>
</tr>
<tr>
<td>Fish eating (never)22</td>
<td>3.4%</td>
<td>8.9%</td>
<td>4.3%</td>
<td>2.7%</td>
<td>2.1%</td>
<td>1.8%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI27</td>
<td>67.6%</td>
<td>56.8%</td>
<td>64.0%</td>
<td>68.4%</td>
<td>72.8%</td>
<td>76.0%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cola24</td>
<td>16.5%</td>
<td>24.0%</td>
<td>17.2%</td>
<td>15.0%</td>
<td>14.1%</td>
<td>15.4%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TV25</td>
<td>21.1%</td>
<td>29.6%</td>
<td>23.4%</td>
<td>20.1%</td>
<td>17.4%</td>
<td>15.7%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Exercise (yes)26</td>
<td>24.3%</td>
<td>17.5%</td>
<td>22.3%</td>
<td>25.2%</td>
<td>27.8%</td>
<td>27.2%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Painkillers (yes)27</td>
<td>25.0%</td>
<td>26.5%</td>
<td>23.3%</td>
<td>24.4%</td>
<td>25.8%</td>
<td>27.7%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sleep medication (yes)21</td>
<td>0.7%</td>
<td>0.8%</td>
<td>0.7%</td>
<td>0.6%</td>
<td>0.7%</td>
<td>0.7%</td>
<td>P = 0.51, NS</td>
<td>0.09, NS</td>
</tr>
<tr>
<td>Diabetes (yes)27</td>
<td>2.1%</td>
<td>3.0%</td>
<td>2.4%</td>
<td>2.1%</td>
<td>1.8%</td>
<td>1.6%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Asthma (yes)27</td>
<td>3.3%</td>
<td>4.3%</td>
<td>3.7%</td>
<td>3.0%</td>
<td>2.9%</td>
<td>2.8%</td>
<td>****</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anaemia (yes)27</td>
<td>3.7%</td>
<td>3.7%</td>
<td>3.5%</td>
<td>3.6%</td>
<td>3.7%</td>
<td>4.4%</td>
<td>****</td>
<td>0.00**</td>
</tr>
</tbody>
</table>

**P-value:** one way ANOVA (for means) and chi square (for percentages) tests, two-tailed probability. NS, non-significant.

1 Age at birth.
2 M, maternal.
3 P, paternal.
4 Married or cohabiting with the child’s biological father 6 months post-partum.
5 Tenant, homeless or living with parents.
6 Register-based information on educational level in 2010.
7 Self-reported psychological problems prior to pregnancy.
8 Register-based information on contact with the psychiatric system prior to pregnancy.
9 Self-reported psychological problems in pregnancy.
10 Contact with the psychiatric system in the first 7 years of the child’s life.
11 Average number of binge episodes in pregnancy.
12 Binge episodes in pregnancy (yes/no).
13 Use of nicotine substitution in the early part of pregnancy.
14 Partner smoking in early part of pregnancy (yes/no).
15 Maternal intake of coffee in early part of pregnancy (yes/no).
16 Information from last part of pregnancy.
17 Maternal exercise in last part of pregnancy.
18 Television watching ≥ 2 h/day in last part of pregnancy.
19 Use of nicotine substitution in pregnancy (yes/no).
20 Reported average alcohol intake prior to pregnancy.
21 Reporting an average alcohol intake in pregnancy (yes/no) in the interviews conducted approximately in Weeks 16 and 30 in pregnancy and 6 months post-partum.
22 Cumulated smoking in pregnancy calculated in the same manner as the cumulated alcohol exposure variable.
23 Reported smoking in pregnancy (yes/no).
24 Use of nicotine substitution in the early part of pregnancy.
25 Partner smoking in early part of pregnancy (yes/no).
26 Maternal intake of coffee in early part of pregnancy (yes/no).
27 Information from early part of pregnancy.
28 Pre-pregnant body mass index (BMI) outside normal range. BMI normal range: 18.5–24.99.
29 Intake of ≥ 1 l of Cola per week in early part of pregnancy.
30 >10 Cumulated alcohol intake
31 ≥ 10 >30 Cumulated alcohol intake
32 >30 >90 Cumulated alcohol intake
33 >90 Linear trend
lying on opposite sides of the total sample mean. **Socio-demographic factors:** significant differences were observed for all the education variables. The percentages for the pregnancy abstainers were generally very close to the total sample. The all-time abstainers, on the other hand, included more than twice as many women with mandatory education only, and correspondingly less than half as many women with a university degree. Furthermore, significantly more women had psychological problems/psychiatric diagnoses in the all-time abstaining group compared with the pregnancy-abstaining group. **Lifestyle factors:** The means and percentages for the pregnancy abstainers on the lifestyle factors resembled those for the total sample, whereas the estimates for the all-time abstaining group were significantly different from the pregnancy-abstaining group. This was, for example, true for the smoking variables: significant differences were observed between the two intake groups, the all-time abstainers showing high smoking estimates and the pregnancy-abstainers estimates similar to those observed for the total sample. For the remaining lifestyle factor variables two overall patterns emerged: one where the estimates for the pregnancy-abstaining group resembled those for the total sample and one where the estimates for the all-time abstainers were more adverse. This was so for the fish-eating variable, BMI, Cola, TV, exercise, diabetes and asthma variables. The other pattern that appeared was one where the estimates for the all-time abstainers were similar to the total sample, but with the pregnancy abstainers having more beneficial estimates. This was true for the vitamin, analgesics and anaemia variables.

**Differences in background characteristics between high (>90–180) and very high (>180) intakers**

Subdividing the high-intake (>90 units) group into a high (>90–180 units) (n = 4605) and a very high (>180 units) (n = 871) intake group revealed two groups that were statistically significant on some variables (Supplementary material, Table S2) but fewer than appeared between the two abstaining groups. **Socio-demographic factors:** The very high intake-group (>180 units) included significantly older fathers and twice as many unmarried women. No significant differences were observed for maternal age and housing. Significantly more women had mandatory education only in the very high-intake (>180 units) group (9.1 versus 6.0%), whereas significantly more women had a university degree in the high-intake (>90–180 units) group (21.7 versus 18.2%). Similar patterns were observed for fathers. The percentages for the psychological problems/psychiatric diagnoses variables for the high-intake group (>90–180 units) resembled those of the total sample. The percentages for the very high-intake group (>180 units) on the other hand were almost twice as large compared with the high-intake group (>90–180 units) for both self-reported and register-based variables. The differences were mostly statistically significant. Regarding alcohol intake the groups differed on prior-to-pregnancy and in-pregnancy alcohol intake. The very high-intake group (>180 units) reported on average (twice as many episodes of binge drinking (2.3 versus 1.2 binge episodes in pregnancy), more than twice as high cumulated smoking frequencies (138 versus 66 cigarettes in pregnancy), more smoking partner (42.5 versus 29.8%) versus more women reported drinking coffee (70.6 versus 64.0%) and ≥1 of cola/week (17.7 versus 14.9%), women reporting watching ≥2½ h of TV/ day (19.1 versus 15.1%), but fewer women reported doing exercise in the last part of pregnancy (28.1 versus 22.7%). Significantly more women in the very high-intake group (>180 units) reported eating vitamins (84.1 versus 77.1%). All differences were statistically significant.

**Factor analysis**

It was hypothesized that the large number of potential confounding factors presented above could possibly intercorrelate to a lesser or greater degree. For this reason, it was decided that exploratory factor analyses (EFA) be carried out to investigate the magnitude of inter-correlations between the observed variables and potentially to identify subtle latent variables underlying these. Specifically, principal component analysis (PCA) with Varimax rotation was employed. The results revealed that a total of 11 components showed an initial Eigenvalue of >1. Because of this large number, a six-factor solution was decided on following examination of the scree plot. Table 2 shows that the first ‘Average alcohol consumption’ factor explained 11.5% of the total variance, and included all of the non-binge alcohol variables. Likewise, the second ‘Stimulants’ factor explained 7.4% of the total variance and included all the smoking as well as the coffee variable. The third ‘Parental age’ factor explained 4.9% of the total variance, and included the age and housing variables. The fourth factor ‘Maternal mental health’ factor explained 4.4% of the total variance and included the four maternal psychiatric variables, but none of the paternal psychiatric variables. The fifth ‘binge drinking’ factor explained 3.7% of the total variance and included the binge drinking variables, whereas the sixth ‘educational-related lifestyle’ factor explained 3.4% of the total variance and included both the maternal and paternal educational variables as well as the BMI, exercise and TV variables. The variables not presented in Table 2 correlated <0.30 with the six extracted factors. However, the variables were included in the factor analyses. Hereafter, another series of PCAs was carried out (shown in brackets) specifying the number of factors to one. Each of these PCAs only included the variables identified as having large >0.30 factor loading in the initial PCA. These figures thus represent factor loadings not ‘contaminated’ by the variables from the other factors.

**DISCUSSION**

The main results revealed significant differences between intake groups on most of the background characteristics. Compared with the abstainers, the alcohol intakers were older, more likely to have a university degree, eat fish and to have a pre-pregnancy BMI within the normal range. Further, they watch TV and drank cola less. The abstainers on the other hand were younger, more likely to have mandatory education only, drink cola, watch TV, smoke cigarettes, live alone and have psychiatric problems. They were less likely to do exercise and eat fish. Linear trends were observed between all of the intake groups despite the fact that the low alcohol exposure group in the present study included women who reported
drinking as little as less than 10 units of alcohol throughout the entire pregnancy, i.e. less than a quarter of a drink per week. These results are important as they shed light on the fundamental differences that exist between women who drink and women who do not drink alcohol in pregnancy.

The results should be of interest to researchers doing observational studies on prenatal exposure to low-moderate doses of alcohol and child mental health outcomes. Currently, findings from such observational studies are ambiguous. Sometimes they report a negative association between prenatal exposure to low doses of alcohol and mental health development in childhood (Olson et al., 1997; Sood et al., 2001; Sayal et al., 2007), but sometimes they do not (O’Leary et al., 2009; Rodriguez et al., 2009; Skogerbo et al., 2012; Underbjerg et al., 2012; Sayal et al., 2013). Very often they even report a J-shaped association (Kelly et al., 2009, 2012; Robinson et al., 2010), where exposure to lower doses of alcohol apparently acts as a protective factor for the development of mental health problems in childhood. Part of this ambiguity in results may be explained if similar variations in background characteristics exist in the samples applied in the existing observational literature. Unfortunately, it is not standard for observational studies to report on such background variables. Most studies only control for what are considered the most important confounding factors such as maternal age, smoking and education—factors that influence the causal pathway between prenatal alcohol exposure and child development. However, these differences may explain (at least some) of the inconsistency in the observational epidemiological literature. If the effect of low doses of alcohol on mental health in childhood is expected to be low, the total sum of the residual and/or unmeasured confounding of the socio-demographic and lifestyle factors that are not controlled will add up to a larger apparent ‘protective’ factor compared with the small ‘negative’ effect of being exposed to low doses of alcohol prenatally.

Socio-demographic and lifestyle factors, similar to the ones presented above, are part of many birth cohort studies. Information on other strong confounders, such as personality, IQ and social support, is on the other hand rarely included, and therefore not possible to control for. When such strong confounders are not controlled for residual and/or unmeasured confounding remains that potentially bias the results from the statistical analyses. For example, parental psychological problems constitute a very strong risk factor for the development of child mental health problems (Downey and Coyne, 1990; Todorow et al., 2010). Todorow et al. (2010) argue that the differences in mental health between abstainer and light drinkers can directly contribute to the improved mental health outcomes in the latter group, because they have the ability to provide more effective parenting and model more adaptive behavioural and emotional regulation. Significantly higher rates of psychological problems were observed for the abstaining group compared with the low intake group and a similar tendency was observed for all-time abstaining versus pregnancy-abstaining intake groups.

Similarly, few studies control for mediating factors; i.e. factors that causes variation in the outcome variable (child mental health) and are themselves caused to vary by the exposure variable (prenatal alcohol exposure) (Porta, 2008). Strong mediators include attachment, family functioning, parent–infant interaction and child IQ. If such factors are not controlled for, these will also induce bias to the reported

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Data from the 1-factor principal component analyses are shown in brackets. Factor loading between ±0.30 has been omitted.
results. For example, the close association between attachment style and mental health development in children is well known. Secure attachment is a strong predictor of academic performance (Mikulincer and Shaver 2007). Also in the 1950s Bowlby was the first to demonstrate the lasting consequences that the quality of the mother–child relationship has for a wide range of developmental cognitive and mental health outcomes (Bowlby, 1950). He concluded that infants who develop a secure attachment style are those with a history of sensitive and responsive maternal care (Bowlby, 1950). Furthermore, this attachment style is associated with better emotional regulation, higher self-esteem and more developed coping skills in the child. In turn, these factors make the children better able to handle stressful or challenging situations and it lowers the risk for poorer mental health outcomes later in life. On the other hand, children with an insecure attachment are at greater risk for poor mental health outcomes (Ainsworth and Bell, 1970; Sroufe, 2005).

Where one problem with the observational literature is that only a limited number of variables are controlled for, another reason for the ambiguity in the literature could be attributed to the division of the intake groups. The abstaining group is most often not subdivided on the basis of pre-pregnancy abstinence (Sayal, 2007; Kelly et al., 2009; Rodriguez et al., 2009; Sayal et al., 2013). However, one thorough study did report that the socio-economic profile of mothers in the pregnancy-abstaining group was more advantaged than the all-time abstaining group (Kelly et al., 2012). The two abstaining groups also differed significantly in the present study, with observed means and percentages on each side of the total sample mean. It is on this basis recommended that future studies also divide pregnancy abstainers according to pre-pregnancy abstinence.

Differences for the high-intake groups were observed on some, but not on as many variables. However, this could in part be explained by the relatively small size of the very high-exposure group. The high and the very high-intake groups did differ significantly on most other variables, indicating that careful consideration should also be given to the subdivision of the high-intake groups in observational studies. Another point needs to be made regarding the very high intakers. This group reported twice as many binge episodes as the high intakers and ‘binge drinking’ was identified as the fifth factor in the EFA explaining 3.7% of the total variance. It is on this basis suggested that future observational epidemiological studies should control for number of binge episodes.

Taken together, the large differences within the extreme groups (both the abstainers and high intakers) may explain the J-shaped function of alcohol intake. Together with the large variabilities in background characteristics described above, and the potential large differences between groups on other important confounding and mediating factors, it is suggested that the inconsistency in the existing literature, at least in part, can be explained by these factors. In other words, the lack of consistency may reflect spurious associations between unmeasured and residual confounding (and mediating) factors in the existing literature.

The factor analyses identified a number of underlying, latent factors—factors that can be directly applied in epidemiological studies looking at associations between prenatal exposure to alcohol and mental health outcomes in childhood. It is recommended that future observational studies set out by conducting an EFA after which the extracted factors are controlled for, instead of controlling for the observed background variables individually. The factor scores for each factor, for each person in the sample, will, all other things being equal, be more precise because they are calculated on the basis of information from all the variables constituting that particular factor. This way the method will allow for more factors to be controlled for, without the loss of statistical power.

**Limitations**

Firstly, it was decided to describe the background characteristics on the basis of full pregnancy intake and investigate differences between the groups with a very low intake. This was decided on despite the fact that most studies investigate the effects of alcohol intake in the early part of pregnancy. The tendencies between intake groups described above might have been different had they been defined on the basis of first trimester intake only. However, since the aim of the present study was not to specifically show differences between these particular groups, but instead to report potential tendencies between intake groups, this point is of less relevance. Future work, however, could replicate the present study with the groups defined differently, and from other cohorts to investigate to what degree the tendencies reported in present study are replicable. Secondly, a similar study could be carried out describing differences between intake groups on childhood mediating factors. Thirdly, the present study did not report on uses of psychotropic medication, e.g. anti-depressive and benzodiazepines or the use of illicit drugs. It could be relevant to include these variables in future descriptive and observational studies.

**SUPPLEMENTARY MATERIAL**

Supplementary material is available at Alcohol and Alcoholism online.

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Drinking or not drinking in pregnancy: the role of confounding


