Alcohol consumption, metabolic cardiovascular risk factors and hypertension in women

Kiran Nanchahal, W David Ashton and David A Wood

**Background** Low to moderate alcohol consumption is associated with reduced mortality, primarily due to a reduction in coronary heart disease (CHD). Conversely, heavy drinking increases mortality, mainly due to haemorrhagic stroke and non-cardiovascular diseases. It is important to identify the threshold of alcohol consumption above which the balance of risk and benefit becomes adverse. We examine the relationship between reported alcohol consumption, cardiovascular disease (CVD) risk factors, a 10-year CHD risk score and hypertension in women.

**Methods** In all, 14 077 female employees aged 30–64 years, underwent screening for CVD risk factors. Information was available on a range of personal and lifestyle factors, including height, weight, blood pressure, lipids, lipoproteins, apolipoproteins and blood glucose. Age-adjusted means were computed for the risk factors in each of five groups of reported alcohol intake: <1 (non-drinkers), 1–7, 8–14, 15–21, ≥22 units/week. The relationships between alcohol and a derived coronary risk score and hypertension were also examined.

**Results** Increasing consumption was associated with an age-adjusted increase in high density lipoprotein cholesterol (HDL-C) and apolipoprotein A1 (both P < 0.001), a decline in body mass index, total cholesterol (TC), TC/HDL-C ratio, low density lipoprotein cholesterol (LDL-C) and apolipoprotein B (all P < 0.001), and no trend in triglycerides (P = 0.06), lipoprotein (a) (P = 0.09) or fasting glucose (P = 0.14). Except for LDL-C (P = 0.06) the relationships remained statistically significant after adjustment for possible confounders. Compared to non-drinkers, there was a decrease in 10-year CHD risk with increasing consumption, with the greatest reduction in risk in women consuming 1–7 units/week, odds ratio (OR) = 0.79, (95% CI: 0.72–0.87), and an increase in the prevalence of hypertension among those consuming 15–21 units/week, OR = 1.68, (95% CI: 1.14–2.46).

**Conclusions** This study provides biological support for an inverse association between alcohol intake and CHD in women, associated with favourable changes in lipid and lipoprotein risk factors. Women consuming 1–14 units/week had a reduction in CHD risk, but there was an increased prevalence of hypertension among those consuming ≥15 units/week. These data suggest that, in terms of the reduced risk of CVD, women should be advised to restrict their alcohol consumption to ≤14 units/week.

**Keywords** Women, alcohol, risk factors, coronary heart disease, hypertension, safe limits

Accepted 17 August 1999

Alcohol consumption has both adverse and beneficial effects on survival and ill health. Several studies show that low-to-moderate alcohol consumption is associated with a 20–25% reduction in all-cause mortality compared to non-drinkers. This reduction in mortality is largely due to a reduction of 30–40% in coronary heart disease (CHD). Conversely, heavy drinking is associated with an increase in all-cause mortality, mainly due to an increase in deaths from stroke and non-cardiovascular causes. Thus the J-shaped association between alcohol intake and all-cause mortality represents the sum of its protective effect on CHD mortality and
detrimental effect on other, primarily non-cardiovascular, causes of death.

The reduction in CHD associated with low-to-moderate alcohol consumption appears to be partially mediated by the dose-related increase in high-density-lipoprotein cholesterol (HDL-C), although this appears to explain only about half of the protective effect. Additional mechanisms, particularly anti-thrombotic effects such as reduced platelet aggregation and fibrinolysis, and increased tissue plasminogen activator, have been reported in association with moderate alcohol intake and may also contribute to its cardioprotective effects.

There is evidence of a causal association between alcohol intake and prevalence of hypertension mediated by neural, humoral and direct vascular mechanisms. However, the precise role of each of these mechanisms is unclear and there is uncertainty about the level of alcohol consumption at which the strong pressor effects of alcohol become apparent.

Attempting to set a threshold of alcohol consumption above which the balance of risk and benefit becomes adverse is of considerable public health importance since the difference between consuming small-to-moderate amounts and drinking larger quantities may mean the difference between preventing disease and causing it. In December 1995, the UK Government changed the safe limit drinking guidelines for women from 14 units/week to 2–3 units/day, despite the fact that the Royal Colleges had earlier that year affirmed the original limits. The revised guidelines were widely reported in the media and resulted in a widespread public perception that women could safely drink 21 units/week. In the following year, 1996, the Health Survey for England reported an increase in average alcohol consumption among women compared to the levels in 1993–1995.

Whilst most previous studies have included only men, in this study we investigate the metabolic basis for the alcohol CHD mortality relationship in women and determine the prevalence of hypertension in relation to reported alcohol intake. We further explore whether a threshold of alcohol consumption associated with an adverse risk of cardiovascular disease can be identified.

**Methods**

The Marks and Spencer Cardiovascular Risk Factor Study is a cross-sectional study of cardiovascular disease risk factors in women throughout the UK. This report is based on 14,077 women screened between June 1988 and July 1991.

**Screening and measurements**

Details of the methods are given elsewhere. Briefly, all female Marks and Spencer employees (excluding managers) aged ≥ 30 years, with a minimum of 6 months employment, were invited to participate in the ‘Healthplus’ programme, an on-site nurse-administered cardiovascular risk assessment. A total of 107 stores throughout the UK were included in the programme and the overall response rate was 75%. The screening assessment consisted of a brief questionnaire on personal and lifestyle factors, including personal and family history of CHD; hypertension; diabetes; smoking habits; alcohol intake; leisure-time physical activity and current drug therapy including oral contraceptive (OC), hormone replacement therapy (HRT) and anti-hypertensive medication. Responses were entered by the nurse onto a laptop computer. Height and weight (with outdoor clothing and shoes removed) were measured using a digital scale (Seca: model 707) with stadiometer. Systolic and diastolic blood pressures were measured twice using a standard mercury sphygmomanometer, with the mean value being recorded. A venous blood sample (15–20 ml) was taken from the nondominant arm. Each individual screening session took 30–40 min and it took 2–3 weeks to complete the screening programme at each store. Standard lipid, lipoprotein and blood glucose analyses were carried out using an automated system, lipoprotein(a) (Lp(a)) was determined using an enzyme immunoassay and low density lipoprotein cholesterol (LDL-C) was calculated in fasting samples using the Friedewald formula. Apolipoprotein A1 (Apo A1), apolipoprotein B (Apo B), Lp(a) and triglycerides were only measured in subjects screened at a later stage in the study.

The level of alcohol consumption for each subject was ascertained based on the following two questions: ‘Do you drink alcohol at least once a week? Yes/No’. ‘If Yes, how many units do you average per week?’ One unit of alcohol is equivalent to half a pint of beer, one glass of wine or one standard measure of spirits. Alcohol consumption was categorized into five levels: none (<1), 1–7, 8–14, 15–21 and >22 units per week.

Hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mm Hg and/or a diastolic blood pressure (DBP) ≥ 90 mm Hg and/or receiving antihypertensive medication.

As CHD risk factors tend to cluster within individuals, and coronary disease is a multi-factorial disease, a measure of overall disease risk is required for each participant. The 10-year predicted probability of developing coronary disease (10-year CHD risk) was estimated using the Framingham Study CHD risk equations. Variables included in the estimate of risk were age, SBP, total cholesterol/high density lipoprotein cholesterol (TC/HDLC) ratio, cigarette smoking and diabetes. Electrocardiographic data for left ventricular hypertrophy (ECG-LVH), which is included in the Framingham risk equations, were not available and were therefore excluded from the calculation. This would have had little impact on the results since the prevalence of ECG-LVH in asymptomatic employed women is negligible.

**Possible confounders**

We examined the effect of a number of potential confounders of the relationship between alcohol and cardiovascular risk factors, prevalence of hypertension or having a relatively high 10-year CHD risk score. Body mass index (BMI) was calculated as weight (kg)/height (m²) and divided into quintiles. Participants were categorized as inactive/active according to whether or not they undertook regular vigorous physical activity at least once/week; as current (>1 cigarette/day) or non/ex-smokers; and according to whether or not they had a family history of CHD before the age of 65 years, or used HRT or OC. To allow for any effect of socioeconomic status, the postcode of each subject’s home address was used to categorize her level of affluence using quintiles of the Carstairs deprivation index.

**Statistical analyses**

Age-adjusted means for the risk factors in each alcohol consumption category were computed using linear regression, with age as a categorical variable in 10-year groups as a covariate in
the models. Alcohol was represented in the regression models by an ordinal variable with each alcohol category assigned its median value. A quadratic term for alcohol was included to assess non-linearity. The 10-year CHD risk score was divided into quintiles and logistic regression was used to estimate the odds ratio (OR) of being in the top quintile of risk for each category of alcohol consumption relative to non-drinkers and to adjust for potential confounders.

Sub-group analyses were conducted to determine whether the relationship between alcohol consumption and CHD risk was modified by age-group (<50/≥50 years) or by smoking habit (current/non or ex-smoker). These variables could not be included in the logistic regression analyses as they are included in the calculation of the 10-year CHD risk.

Logistic regression was used to estimate the OR of being hypertensive for each category of alcohol consumption relative to non-drinkers. Interaction tests were carried out to examine whether or not this relationship varied according to age group or smoking status.

The logistic regression models are based on subjects with no missing data for any of the explanatory variables used in the analyses (12 891 for hypertension; 12 817 for 10-year CHD risk).

The 91 women who reported a previous diagnosis of CHD were excluded from all analyses, as were non-fasting values for triglycerides and blood glucose (only 35% of samples were from women who had fasted overnight).

**Results**

**Alcohol consumption**

Overall, 50% (7018/13 986) of the women reported drinking alcohol less than once a week (classified as non-drinkers). Women who reported drinking alcohol at least once a week had an average (geometric mean, GM) intake of 4.1 units/week with 0.5% (N = 69) drinking >21 units/week. Consumption of alcohol declined with increasing age with 61% of women aged 60–64 years reporting not drinking compared with 49% of those aged 30–34 years (Figure 1) and, among drinkers, the average (GM) alcohol intake decreased as follows: 4.4 (30–34 years), 4.3, 4.3, 4.1, 3.8, 3.5, 3.1 (60–64 years) units/week.

**Alcohol and coronary heart disease risk factors**

Table 1 shows the age-adjusted relationships between a number of CHD risk factors and the level of alcohol consumption. It is important to note that, because of the very small number of women reporting a weekly consumption of ≥22 units/week, the results for this group are relatively imprecise compared to the other drinking categories. Body mass index decreased with increasing alcohol consumption except for the highest alcohol category, as did TC, TC/HDL-C ratio and Apo B (quadratic term for alcohol: all (P < 0.001) and DBP (quadratic P = 0.03). There was a decrease in LDL-C with increasing alcohol intake (linear: P < 0.001). There was an increase in HDL-C and Apo A1 with increasing alcohol consumption up to 15–21 units/week with no further increase in the highest alcohol category (quadratic: both P < 0.001). There was no evidence of a linear relationship between alcohol consumption and SBP (P = 0.63), triglyceride (P = 0.09), Lp(a) (P = 0.09) or fasting glucose levels (P = 0.14), although there was some evidence of a J-shaped relationship for SBP (quadratic: P = 0.03). The relationships between alcohol consumption and lipids (except for LDL-C) and lipoproteins remained statistically significant after adjustment for smoking, BMI, physical activity, use of OC or HRT, family history of premature CHD and socioeconomic status. The relationships between alcohol and DBP and SBP were no longer statistically significant after adjustment for the possible confounders.

![Figure 1](https://academic.oup.com/ije/article-abstract/29/1/57/666807)
Alcohol and 10-year coronary heart disease risk

There was a steady decrease in the predicted 10-year CHD risk with increasing alcohol consumption, except for women consuming ≥22 units/week, although the latter category included very few women (Figure 2). The median risks (%) in each of the alcohol categories were 2.4 (non-drinkers), 1.8, 1.5, 1.4, 1.8 (distributions across the categories.

There was a steady decrease in the predicted 10-year CHD risk among women consuming 1–7 units/week and an increase in prevalence of hypertension with increasing alcohol consumption up to 14 units/week in the lowest quintile to 3.7 units/week in the highest quintile.

Compared with non-drinkers, the OR (95% CI) for being in the top quintile of 10-year CHD risk decreased with increasing alcohol consumption (Table 2). After adjusting for possible confounders, the reduction in risk between non-drinkers and women consuming 1–7 units/week was 21% with a further 13% reduction in those drinking 8–14 units/week and little further change among those drinking ≥15 units/week (linear: P < 0.001, quadratic: P = 0.03).

The relationship was essentially similar in women aged 30–49 years (linear trend: P = 0.07), although the OR were more for the younger age group due to the smaller number of women in the top quintile of risk in this age group. There was little difference in the OR for each alcohol category in non/ex-smokers and smokers except for the highest alcohol consumption group.

Alcohol and hypertension

There was no difference in the proportion of non-drinkers (54%) among hypertensives whether or not they were taking anti-hypertensive medication. A slightly smaller proportion (50%) reported themselves to be non-drinkers among women who were normotensive. Amongst drinkers, women taking anti-hypertensive drugs consumed an average (GM) of 3.6 units per week compared to 4.0 units/week for untreated hypertensives and 4.1 units/week for normotensives. There was a decrease in prevalence of hypertension with increasing alcohol consumption up to 14 units/week and an increase in prevalence among women consuming ≥15 units/week (Figure 3).

The OR for the prevalence of hypertension decreased with increasing alcohol consumption up to 14 units/week in the unadjusted analysis but this apparent protective effect of low-to-moderate alcohol consumption was largely explained by women not in the top quintile of risk (48%). Among women who consumed alcohol, the average (GM) number of drinks decreased steadily with increasing risk from 4.5 units/week in the lowest quintile to 3.7 units/week in the highest quintile.
confounding by age, BMI, physical activity and family history of premature CHD (Table 3). Further adjustment for other possible confounders had no effect on this relationship. Compared to non-drinkers, women reporting a consumption of 15–21 units/week had a 68% (95% CI: 14–146%) increased prevalence of hypertension while there was no effect in women consuming <14 units/week.

The pattern of this relationship was essentially similar in women aged 30–49 years and those aged 50–64 years as was the case in non/ex-smokers and smokers.

Discussion

This study describes the relationship between reported alcohol consumption and a range of metabolic CHD risk factors in a large sample of women in the UK. There was an inverse relationship between alcohol consumption and a 10-year CHD risk score, the protective effect being largely realised at a consumption of <14 units/week.

The prevalence of hypertension was higher among women consuming 15–21 units/week than in those drinking <14 units/week. As with other studies in women, the number of

Table 2 Odds ratios (95% CI) for prevalence of being in the top quintile of 10-year probability of developing coronary heart disease\(^a\) by level of alcohol consumption

<table>
<thead>
<tr>
<th>Alcohol (units/week)</th>
<th>Unadjusted odds ratio (95% CI)</th>
<th>Fully adjusted(^b) odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1–7</td>
<td>0.72 (0.66–0.80)</td>
<td>0.79 (0.72–0.87)</td>
</tr>
<tr>
<td>8–14</td>
<td>0.60 (0.50–0.71)</td>
<td>0.66 (0.55–0.78)</td>
</tr>
<tr>
<td>15–21</td>
<td>0.59 (0.40–0.88)</td>
<td>0.67 (0.45–1.01)</td>
</tr>
<tr>
<td>&gt;22</td>
<td>0.57 (0.28–1.16)</td>
<td>0.54 (0.26–1.11)</td>
</tr>
</tbody>
</table>

\(^a\) Determined using the Framingham risk equations.\(^{24}\)
\(^b\) Adjusted for body mass index, vigorous physical activity, hormone replacement therapy, oral contraceptive use and socioeconomic status; additional term for family history of premature coronary heart disease was not statistically significant.

\(^c\) Based on model including linear term for alcohol.

\(^d\) Likelihood ratio test.

Table 3 Odds ratios (95% CI) for prevalence of hypertension\(^a\) according to level of alcohol consumption

<table>
<thead>
<tr>
<th>Alcohol (units/week)</th>
<th>Unadjusted odds ratio (95% CI)</th>
<th>Age-adjusted odds ratio (95% CI)</th>
<th>Fully-adjusted(^b) odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1–7</td>
<td>0.83 (0.75–0.92)</td>
<td>0.87 (0.78–0.96)</td>
<td>0.94 (0.84–1.04)</td>
</tr>
<tr>
<td>8–14</td>
<td>0.74 (0.61–0.89)</td>
<td>0.87 (0.72–1.05)</td>
<td>0.96 (0.79–1.17)</td>
</tr>
<tr>
<td>15–21</td>
<td>1.17 (0.82–1.68)</td>
<td>1.47 (1.01–2.13)</td>
<td>1.68 (1.14–2.46)</td>
</tr>
<tr>
<td>&gt;22</td>
<td>1.03 (0.54–1.98)</td>
<td>1.12 (0.57–2.22)</td>
<td>1.06 (0.52–2.14)</td>
</tr>
</tbody>
</table>

\(^a\) Defined as systolic blood pressure \(\geq 140\) mmHg &/or diastolic blood pressure \(\geq 90\) mmHg &/or taking anti-hypertensive medication.

\(^b\) Adjusted for age, body mass index, vigorous physical activity, family history of premature coronary heart disease; additional terms for smoking, hormone replacement therapy, oral contraceptive use and socioeconomic status were not statistically significant.

\(^c\) Likelihood ratio test.
women reporting higher levels of alcohol consumption (≥22 units/week) was very small, hence our ability to examine the metabolic effects of alcohol in this group was limited.

**Alcohol consumption**

In this study women classified as non-drinkers included lifelong abstainers, ex-drinkers and occasional drinkers (<1 unit/week). A higher proportion of women reported themselves to be non-drinkers and a lower proportion as drinking ≥15 units/week compared to the general population. For example, in 1996 33% of women in Britain consumed none or <1 unit/week and 14% consumed ≥15 units/week. In a representative sample of Scottish women there were 38% abstainers, and 6.8% exceeded 14 units/week.

**Lipid and lipoprotein coronary heart disease risk factors**

This study corroborates previous evidence in women of the relationships between alcohol consumption and increases in HDL-C and Apo A, decreases in cholesterol and triglycerides and no change in Lp(a). There was a significant quadratic relationship between Apo B and alcohol consumption, although no significant relationship was found among women in the Whitehall II study. There was a decrease in TC/HDL-C ratio with increasing alcohol consumption except in the highest intake group, and a steady decline in LDL-C with increasing alcohol intake, although the latter relationship was not statistically significant after adjustment for possible confounders. Alcohol consumption has been reported to be negatively associated with both TC/HDL-C ratio and LDL-C in Japanese American women.

**Coronary risk**

There was a greater proportion of non-drinkers amongst women with the highest 10-year CHD risk compared to those with a lower risk. Furthermore, women at high risk who did drink, drank less than those with a lower risk. The largest reduction in CHD risk was associated with consuming 1–14 units/week compared to non-drinkers, with little further reduction in women consuming ≥15 units/week. Other studies have also reported that the protective effect of alcohol on CHD is fully realised within low-to-moderate levels of consumption with no additional benefit at higher levels of intake. We found little difference in the association between alcohol and CHD risk in younger compared to older women as reported by Fuchs et al., although there were few younger women at relatively high 10-year CHD risk. It has been reported that the beneficial effects of alcohol are greater for smokers than non-smokers but we found little difference between current and non/ex-smokers.

**Hypertension**

Amongst women not taking anti-hypertensive medication, there was a slight decrease in age-adjusted mean SBP and DBP with increasing alcohol up to 14 units/week followed by an increase with higher levels of consumption but these relationships were not statistically significant after adjustment for possible confounders. Women consuming 15–21 units/week had a higher prevalence of hypertension compared to those consuming ≤14 units/week. The pattern of the relationship was similar in smokers and non/ex-smokers. The Nurses Health Study reported that 32% of the incidence of self-reported diagnosis of hypertension was attributable to alcohol consumption of >2 drinks/day. English et al. found a J-shaped relationship between alcohol and hypertension and similar results have recently been reported by Moreira et al. who found a non-linear association between alcohol and blood pressure and prevalence of hypertension. Our observation that women with medically treated hypertension consumed the same amount of alcohol as untreated hypertensives is of concern as reducing alcohol intake can help to lower blood pressure.

**Strengths and limitations**

This is the largest study of cardiovascular risk factors in women in the UK, and we were able to examine the relationship between alcohol and both high CHD risk and hypertension within the same sample.

Although it is possible that residual confounding by unmeasured factors, such as diet, could have affected the results, it is unlikely to have been extensive, since accounting for known risk factors for which information was available did not materially affect the results.

A shortcoming of the use of a risk score as applied in this study is the reliance on risk factors rather than actual cardiovascular outcome. This use of a proxy outcome measure (inevitable in a cross-sectional study) may lead to misclassification in either direction, although the application of the Framingham risk equations has been shown to distinguish low- from high-risk individuals in diverse populations. A further drawback is that women being treated for hypertension may reduce their alcohol consumption which would lead to underestimation of the association between alcohol and hypertension in a cross-sectional study. However, we found little difference in the level of alcohol consumption between the treated and untreated hypertensives. Confirmation of these findings is needed from longitudinal studies where the level of alcohol consumption is known and cardiovascular event data are obtained during follow-up.

A further limitation of this study is the use of self-reported alcohol intake, although other approaches to alcohol assessment are impractical in large epidemiological studies. In the Nurses Health Study, there was a high correlation between alcohol intake based on a simple questionnaire and a more detailed diet assessment, and under-reporting was less likely among low-to-moderate than heavy drinkers. Moreover, the strong positive association between alcohol intake and HDL-C concentration supports the rank order validity of the alcohol data in this study. Whilst we were unable to separate ex-drinkers from lifelong abstainers in this study, the proportion of women who would have become non-drinkers as a consequence of experiencing alcohol-related health problems is likely to be very small in an occupational cohort of this sort, and is unlikely to have altered the results. No account has been taken of the pattern of drinking as this information was unavailable, although binge drinking is likely to be relatively uncommon among women in regular employment.

Finally, there is the issue of selection bias; women who are employed tend to be healthier than those who are not. Furthermore, women who volunteered for the study may differ from those who did not in terms of their alcohol consumption and health status. Nonetheless, there is little biological basis for...
suspecting that the shape of the observed relationships between alcohol consumption and the variables examined here would be materially different in other groups of women.

**Sensible limit drinking guidelines**

The average level of alcohol consumption is rising in women and, as a consequence, the percentage of heavy and problem drinkers is likely to increase. This may lead to an increase in the prevalence of hypertension, haemorrhagic stroke, breast cancer and other non-cardiovascular diseases in the population and an increase in mortality from all causes for women drinking >2 drinks/day.

This study suggests that the beneficial metabolic effects of alcohol are largely realised at a level of consumption of ≤14 units/week, whereas higher levels of consumption confer little further benefit and are associated with an increased prevalence of hypertension. Moreover, preventive strategies such as smoking cessation, avoidance of obesity and moderate physical activity will also reduce the risk of CHD, but without increasing the risk of other diseases.

**Conclusion**

Light-to-moderate alcohol consumption (1–14 units/week) among asymptomatic women is associated with a significantly lower predicted 10-year CHD risk associated with beneficial changes in lipids and lipoproteins, particularly a dose-related increase in HDL-C. However, at higher levels of intake (>14 units/week), there is no additional reduction in CHD risk as the further increase in HDL-C appears to be offset by an increase in the prevalence of hypertension. Although recommendations on safe drinking levels should take into account all relevant evidence of the risks and benefits of alcohol consumption, in terms of the reduced risk of cardiovascular disease, optimal consumption in women is ≤14 units/week.

**Acknowledgements**

We thank the women who participated in this study; the nurses who carried out the Healthplus screening program; Marks and Spencer Health Services & Occupational Health Department for their support; Wei Dong and Stephen Browne for initial organisation of the study data; Neil McLennan for obtaining postcodes; Simon Stevenson for providing the Carstairs index data; Mani Gollapalli for producing the graphs and Ian White for comments on an earlier draft of the paper. Biochemical analyses were carried out at Medical Diagnostic Laboratories, London, except for Lp(a) which was analysed at Innogenetics N.V. Canadastraat 21- Haven 1009, 2070 Zwijndrecht, Belgium. Funding: SG Warburg Resettlement Trust, PPP Healthcare Medical Trust limited.

**References**

3. Rimm EB. Invited commentary—Alcohol consumption and coronary heart disease: Good habits may be more important than just good wine. *Am J Epidemiol* 1996;143:1094–98.