

**Appendix 1 to CC/98/23. Summary of original data on the relationship of alcohol to incidence of breast cancer (reviews, comments and editorials are not included).**

Description of study	Results	Comments/Reference
<p><u>Cohort studies</u></p>		
<p>1995 A sub-cohort of 1812 women from the Netherlands Cohort Study aged 55-69 years was investigated. After 3.3 years of follow-up (1986-1989), 422 incident breast cancer cases with data on alcohol consumption were available for analysis</p>	<p>RR for breast cancer in drinkers versus nondrinkers was 1.31 (95% CI 1.00-1.71).            &lt; 5 g/day 1.30 (0.66-1.15)            5-14 g/day 1.29 (0.89-1.85)            15-29 g/day 1.28 (0.81-2.03)            ≥30 g/day 1.72 (0.90-3.28)            The trend with increasing consumption was significant (P=0.047).            Consumption of different types of beverage was not associated with increased breast cancer risk (RR (95% CI) for beer, 0.93 (0.82-1.05), P for trend analysis=0.06; wine, 1.01 (0.99-1.02), P for trend=0.039; liquor, 1.02 (0.99-1.04), P for trend = 0.005).            The results supported a borderline association between alcohol and breast cancer among postmenopausal women</p>	<p>The association with alcohol was stronger in women with a history of benign breast disease, women with a family history of breast cancer and women with an early menopause. Consumption based on detailed questionnaire with conversion for different beverage types. RRs adjusted for age, history of benign breast cancer, family history of breast cancer, age at menarche, use of oral contraceptives, parity, age at first birth, Quetelet index, education, smoking, energy intake<sup>5</sup></p>
<p>Geographic variation study in 9778 white women aged 20-79 years selected from the 1987 National Health Interview Cancer Epidemiology Supplement interviews, and 3795 white women aged 50-79 years selected from 1987 National Health Interview Cancer Control Supplement interviews. Comparison of four regions: South (reference region: S),</p>	<p>Mortality ratios relative to the South region for alcohol consumption:            20-49 years of age:            0.98 (W), 1.05 (MW), 1.05 (NE)            50-79 years of age:            1.10 (W), 1.15 (MW), 1.28 (NE). Effect could be accounted for by age alone.            (no significance values or confidence intervals</p>	<p>No details provided for assessment of alcohol consumption. Study was not designed to investigate effects of alcohol. All of the differences observed could be accounted for by age alone<sup>6</sup></p>

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<p>West (W), Midwest (MW) and Northeast (NE) 1997</p> <p>Of women in the USA who reported their alcohol and tobacco use in 1982, 230,552 were suitable for this study, of whom 13,669 died during the following 9 years. Cause-specific death rates and rates of death from all causes across categories of baseline alcohol consumption, adjusted for other risk factors, and related drinking and smoking habits were compared. Ages ranged from 30 – 111 years.</p>	<p>were provided)</p> <p>Breast cancer mortality was associated with drinking in women (&lt;1 drink/day: RR 1.1, 95% CI 0.9-1.3, 1 drink/day: RR 1.2, 95% CI 1.0-1.6: 2-3 drinks/day: RR 1.5 (95% CI 1.2-1.9: ≥4 drinks/day: RR 1.0 (0.7-1.4). The trend with increasing alcohol consumption was significant (P=0.02). The mortality from breast cancer was 30% higher among women reporting at least one drink daily than among non-drinkers</p>	<p>RRs were adjusted for age, race, education, body mass index, smoking, fat consumption, use of oestrogen replacement therapy, family history of breast cancer, number of sisters, age at menarche, age at first birth, age at menopause, use of oral contraceptives, presence of breast cysts. Alcohol consumption assessed from limited questioning<sup>7</sup></p>									
<p><u>Case control studies</u></p> <p>1995</p> <p>Lifetime alcohol consumption was studied as a risk factor for breast cancer in 740 patients and 810 controls (1986-1991) in the USA, aged 40-85 years. Among patients, 301 premenopausal, 439 postmenopausal, among controls, 316 premenopausal, 494 postmenopausal. Alcohol intake calculated at 2, 10, 20 years before interview and at 16 years of age. Analysis based on consumption of wine, beer or hard liquor</p>	<p>There was no apparent increase in OR of breast cancer with total intake of alcohol or of hard liquor or wine 2, 10 or 20 years ago or at 16 years of age (P =0.25-0.93). For beer, there was a weak, non-significant increase in OR for intakes of at least one beer per day [OR (95% CI)] e.g.:</p> <table border="0"> <tr> <td>2 yrs</td> <td>1-2 drinks/mo</td> <td>0.93 (0.71-1.21)</td> </tr> <tr> <td></td> <td>3-27</td> <td>1.02 (0.74-1.41)</td> </tr> <tr> <td></td> <td>≥28</td> <td>1.37 (0.83-2.25)</td> </tr> </table> <p>For drinking at 16 years of age, there was weak evidence of increased risk associated with intake of hard liquor but not wine or beer, but this was not significant</p>	2 yrs	1-2 drinks/mo	0.93 (0.71-1.21)		3-27	1.02 (0.74-1.41)		≥28	1.37 (0.83-2.25)	<p>Analysis controlled for age, education, menopausal status, age at menarche, age at first pregnancy, family history of breast cancer, previous benign breast disease, Quetelet index, and intake of kilocalories, fat, carotenoids, vitamin C, α-tocopherol, folic acid, dietary fibre.</p> <p>Possible measurement bias, as no details provided about portion size of alcohol. Generally, consumption of alcohol was low in the subjects studied<sup>8</sup></p>
2 yrs	1-2 drinks/mo	0.93 (0.71-1.21)									
	3-27	1.02 (0.74-1.41)									
	≥28	1.37 (0.83-2.25)									
<p>Selection of a population of women at high</p>	<p>The combined selection power of the two</p>	<p>Small number of cases studied. ORs adjusted</p>									

Description of study	Results	Comments/Reference
<p>risk of invasive breast cancer using two markers of high risk lifestyle, aged &gt;25 at first birth and daily alcohol intake <math>\geq 7</math> g/day (30 cases, 30 controls). Subjects were 39-86 years of age. Carried out in general practice in Copenhagen, Denmark.</p>	<p>markers was significant (OR 4.3, 95% CI 1.2-15.6). However, the selection power for alcohol alone was not significant</p>	<p>only for age at first birth. Very little information on how alcohol consumption was assessed<sup>9</sup></p>
<p>Lifetime alcohol consumption was compared in 6163 breast cancer patients and 8480 control subjects, aged 58.7 years on average (74% of whom were &gt; 50 years), during 1991 in the USA.</p>	<p>The multivariate RR (95% CI) of breast cancer in those who drank compared with abstainers was 1.39 (1.16-1.67) for 12-18 g/day, 1.69 (1.36-2.10) for 19-32 g/day, 2.3 (1.51-3.51) for 33-45 g/day and 1.75 (1.16-2.64) for <math>\geq 45</math>/day. The RR per 13 g/day (multivariate logistical regression) was 1.31 (95% CI 1.20-1.43). The trend with increasing alcohol consumption was very significant (<math>P &lt; 0.0001</math>). Whereas the effects of beer (RR (95% CI) for 13 g/day, 1.25 (1.13-1.39) and spirits (RR for 13 g/day, 1.18 (1.07-1.31), considered separately, were significant, those of wine were not (RR for 13 g/day, 0.93 (0.79-1.08) (<math>P</math> for difference <math>&lt; 0.01</math>). Menopausal state had no significant effect.</p>	<p>The relationship between risk and alcohol intake in the previous age interval seemed to depended on the level of intake before 30 years of age. Consumption was based on alcohol content of typical portion sizes, e.g. bottle of beer, glass of beer. Controlled for age, menopausal state, age at first birth, parity, body mass index, age at menarche, education, benign breast disease, family history of breast cancer. No adjustment was made for oral contraceptive use or oestrogen replacement therapy as these showed no confounding with alcohol intake. The authors state that "A lifetime average intake of even one drink per day appears to be associated with a modest increase in risk"<sup>10</sup></p>
<p>This Swedish case control study examined 177 premenopausal and 216 postmenopausal breast cancer patients and 195 premenopausal and 254 postmenopausal controls (1981-1984). The exact ages of the subjects was not specified</p>	<p>Beer consumption of &lt;4 bottles/week was not associated with increased breast cancer risk. Consumption of <math>\geq 4</math> bottles/week was associated with an increase in risk in premenopausal women (RR<sub>adjusted</sub> 5.7; 95% CI 1.8-17.7). Weekly, or less than weekly, consumption of wine and spirits appeared to</p>	<p>Risk estimates adjusted for differences in age at menarche, age at first full-term pregnancy, age at diagnosis, smoking and use of exogenous hormones, and for postmenopausal women, age at menopause. Little information on assessment of alcohol consumption other than that beer intake was estimated in bottles<sup>11</sup></p>

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<p>Study conducted among non-Hispanic white and Hispanic women in Los Angeles. Cases aged 55-64 years at diagnosis in 1987-1989 were enrolled through the Cancer Surveillance Program. Community controls individually matched to cases by age, ethnicity and neighbourhood. 1431 matched pairs. Alcohol consumption recorded at age 25 years, age 40 years and in recent past</p>	<p>be protective (<math>RR_{adjusted} = 0.4</math>, 95% CI = 0.3-0.7 for weekly wine consumption and <math>RR_{adjusted} = 0.6</math>, 95% CI = 0.4-0.9 for occasional consumption of spirits) among postmenopausal but not premenopausal women (<math>RR_{adjusted} = 0.8</math>, 95% CI = 0.7-2.3 and <math>RR_{adjusted} = 1.0</math>, 95% CI = 0.7-1.8 respectively)</p> <p>ORs (95% CI) associated with estimated average lifetime intake were: for &lt; 6 g/day, 1.01 (0.84-1.22); for 6-11 g/day, 1.21 (0.95-1.55); for 12-18 g/day, 0.94 (0.69-1.29); for 19-32 g/day, 1.63 (1.14-2.33); for 33-45 g/day, 2.45 (1.22-4.93); and for <math>\geq 46</math> g/day, 0.94 (0.46-1.93) compared with abstainers. The trend with increasing consumption was significant (<math>P=0.01</math>). RR (95% CI) for 13 g/day spirits: 1.22 (1.04-1.24); wine: 1.04 (0.79-1.36); beer: 0.91 (0.71-1.17). These differences between types of beverage were not significant. Comparison of consumption per 13 g/day at 40 years of age (OR 1.14, 95% CI 1.04-1.24), with the change per 13g/day from 40 years to present (OR 1.12, 95% CI 1.03-1.23) suggested increased risk when drinking started later in life. There was no increase in risk when drinking started in early adulthood (<math>P=0.25</math>)</p>	<p>ORs were adjusted for age at menarche, education, benign breast disease, family history of breast cancer, body mass index, parity, age at first birth, age at menopause, ethnicity, oestrogen replacement therapy. Authors attribute the “odd” result for <math>\geq 46</math> g/day as due to misreporting, confounding factors or selection bias<sup>12</sup></p>
<p>This Swedish study was conducted in women aged from 40 to 75 years old, participating in a</p>	<p>Alcohol intake did not affect breast cancer risk among women under 50 years of age, but</p>	<p>Analysis controlled for education, number of children, body mass index, family history of</p>

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screening programme during 1987-1990. 276 cases and 452 controls participated	among those over 50 years, ever-drinking conferred an OR of 1.8 (95% CI = 1.2-2.6). Drinking later in life appeared to have a greater effect than drinking earlier in life. Age at first use: 15-27 years, OR 1.7 (1.0-2.7); ≥28 years, OR 1.8 (1.2-2.7). Total years of drinking had no effect. In postmenopausal women, years of use: ≤10 years, OR 1.5 (0.9-2.5); 11-20 years, OR 1.8 (1.1-3.0); >20 years, OR 1.9 (1.2-3.0). No consistent effect of dose above 0.75 g/day. Consumption of ≤0.75 g/day, OR 1.2 (0.8-1.8); 0.76-2.0 g/day, OR 1.9 (1.2-2.9); ≥2.0 g/day, OR 1.6 (1.0-2.4)	breast cancer, education. Data on oestrogen replacement therapy were not obtained <sup>13</sup>
This Japanese case control study compared 1052 women with breast cancer and 23,163 controls (1988-1992). Subjects were <29 to >80 years of age.	<p>Premenopausal women:</p> <p>≤1 unit of sake/day OR=1.18 (95% CI 0.88-1.59)</p> <p>≥1 unit of sake/day OR=2.03 (95% CI 1.36-3.03)</p> <p>Postmenopausal women:</p> <p>≤1 unit of sake/day OR=0.73 (95% CI 0.43-1.24)</p> <p>≥1 unit of sake/day OR=1.26 (95% CI 0.58-2.77)</p>	Significant effect only for premenopausal women, but older women in Japan drink very little anyway. No control for possible confounding factors <sup>14</sup>
<p>1996</p> <p>The relationship between alcohol consumption and breast cancer risk was considered using data from 230 hospital-based cases aged 27-75 years in Switzerland (1990-1995) and 507 age matched controls. Overall, 70.4% of cases</p>	The multivariate odds ratio (OR) with alcohol consumption was 1.5 (95% CI 1.1-2.2), and varied significantly (P for trend <0.01) with consumption level, being 1.3 (0.8-1.9) for <1 drink per day, 1.8 (1.1-2.9) for 1-2 drinks/day,	The authors estimate that alcohol consumption could account for 8-42% of breast cancer cases. Consumption was assessed from type and number of drinks. ORs adjusted for age, education, marital status, age at menarche,

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consumed alcohol, compared with 57.4% of controls	1.5 (0.8-2.7) for 2-4 drinks/day and 2.7 (1.3-5.8) for >4 drinks per day. The association was consistent for wine, beer or spirits and was apparently stronger in premenopausal women (OR in premenopausal women for $\geq 1$ drink per day, 5.4 (95% CI 2.5-11.9 <i>cf</i> OR in postmenopausal women, 1.3 (95% CI 0.8-2.2), P for difference <0.01). Risk was increased when drinking commenced under 30 years of age. OR (95% CI) was 1.8 (1.2-2.8) for women who started to drink below the age of 30 years and 1.4 (0.9-2.0) for those starting at age $\geq 30$ years. Duration of drinking had no significant effect on risk. Duration: <20 years, OR 1.6 (1.0-2.6); 20-29 years, OR 1.4 (0.9-2.3); $\geq 30$ years, OR 1.5 (1.0-2.4)	parity, age at first birth, menopausal status, age at menopause, family history of breast cancer, smoking, use of oral contraceptives, oestrogen replacement therapy <sup>15</sup>
This Swedish case control study evaluated the site-specific cancer risk in 15,508 alcoholic women, matched to non-drinking controls. The alcoholic women were ascertained through a review of records of Temperance Boards in Sweden, and from the Swedish Cancer Registry (dating from 1958). The ages of the subjects were not provided	There was an increased risk for any cancer (RR = 1.6, 95% CI = 1.5-1.8), with a RR for breast cancer specifically of 1.4 (95% CI = 1.2-1.7)	The authors state that their results could have been confounded by nutritional factors, tobacco consumption and reproductive factors, none of which was assessed in this study. No specific information on type or amount of alcohol consumed <sup>16</sup>
Case-control study of premenopausal bilateral breast cancer patients under 50 years of age, with their unaffected sisters (144 cases with 232 sister controls) in North America. A number of lifestyle factors were analysed,	There was "some evidence" that high alcohol consumption (3 drinks per week or more) increased the risk of premenopausal breast cancer [OR = 1.2 for 1-3 drinks/week (95% CI = 0.6-2.3) and 1.8 for $\geq 3$ drinks/week (95% CI	This study adjusted for cigarette smoking, oral contraceptive use and education, but not for dietary factors. Family history did not affect the association between alcohol and breast cancer. No adjustment for other possible

Description of study	Results	Comments/Reference
including oestrogen use, progestin use, smoking and alcohol consumption	=1.0-3.4)], but this failed to reach significance	confounding factors. Alcohol consumption was based on drinks per week; the type of beverage was not specified <sup>17</sup>
This study involved women aged between 20 and 44 years who were newly diagnosed with breast cancer between 1990 and 1992 in the USA. Controls were age-matched. In total, 1614 cases were available for analysis	Frequent alcohol consumption was associated with an increased risk of local and regional/distant tumours. For regional/distant tumours, there was a significant increase in risk associated with an average consumption of 14 or more drinks per week (RR = 2.52, 95% CI = 1.6-4.1). For local tumours, the RR among women drinking 14 or more drinks per week was 1.62 (95% CI = 1.0-2.6). No increase in RR with high alcohol consumption was found with <i>in situ</i> tumours, although the number of subjects was much smaller. In women with regional/distant tumours, the risk increased with amount of alcohol consumed. Consumption: <1-6.9 drinks/week, RR 1.15 (0.9-1.4); 7-13.9 drinks per week, RR 1.21 (0.8-1.8); ≥14 drinks per week, RR 2.52 (1.6-4.1)	The authors suggested that the relatively small number of subjects in their study may have been responsible for the lack of association between alcohol and primary breast cancer. Alcohol consumption was expressed in standard units (“drinks”). RRs adjusted for age at diagnosis, study site, race, family history of breast cancer, previous breast biopsy, number of births, age at first birth, age at menarche, use of oral contraceptives, number of mammograms, smoking, body mass index, education <sup>18</sup>
1997 The role of alcohol consumption on breast cancer risk was investigated in this French study of 154 premenopausal patients, 30-50 years of age, with primary breast cancer and age and socio-economically matched controls (1986-1989)	A significant relative risk (2.69, 95% CI 1.40-5.17) was shown for consumption of 9 g or more of alcohol per day, but only in association with red wine, although the authors point out that red wine was the preferred alcoholic beverage among this population. A RR of 3.96 (95% CI 1.59-9.84)	The authors commented that young women appear to be particularly sensitive to breast cancer in relation to alcohol consumption. Assessment of alcohol consumption was well controlled, with measurements of portion sizes and type of beverage. RRs adjusted only for total energy intake and parity <sup>19</sup>

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<p>This Italian study included 2569 cases of breast cancer, aged 23-74 years, and 2588 age-matched controls (1991-1994), and studied the effects of several macronutrients, including alcohol, on breast cancer risk</p>	<p>was found for a monthly consumption of <math>\geq 4</math> litres. RR (95% CI) for <math>&gt;1</math> l of beer per month: 1.93 (0.78-4.80); <math>&gt;2</math> l fortified wine per month: 1.03 (0.39-2.72); <math>&gt;1</math> litre of white wine per month: 1.62 (0.46-5.62)</p> <p>The odds ratio for alcohol was 1.07 (9% CI 1.02-1.13).</p>	<p>Consumption appears to have been assessed carefully, but few details are provided. ORs adjusted for age, study centre, education, parity, energy intake<sup>20</sup></p>
<p>This Greek case control study involved 692 women with breast cancer and 1261 controls. Various demographic and social factors were studied, including alcohol consumption, use of oestrogens, obesity. Ages of the subjects were not provided, but the study population had been described previously</p>	<p>Alcohol consumption was related to an increased incidence of breast cancer (positive family history: OR in those drinking <math>\geq 3</math> glasses/day compared with those drinking <math>&lt;3</math> glasses/day 5.35, 95% CI 0.60-47.79; negative family history: OR 3.10, 95% CI 1.30-6.98; all women: OR 2.99, 95% CI 1.37-6.48)</p>	<p>The authors suggested that patients with a family history of breast cancer might “benefit disproportionately” by reduced exposure to adult life risk factors. Minimal information is provided on assessment of alcohol consumption. ORs adjusted for family history of breast cancer, age, birth place<sup>21</sup></p>
<p>This European international case control study looked at the relationship between alcohol consumption and breast cancer in 315 breast cancer patients and 364 age and centre matched controls aged between 50 and 74 years (1991-1992)</p>	<p>Compared to never drinkers, the overall RR for current drinkers was 1.00 (95% CI 0.70-1.43). The overall RR estimates for current drinkers in the first, second and third tertile of alcohol intake compared to never drinkers was 1.00 (0.63-1.59), 0.98 (0.63-1.58) and 1.06 (0.65-1.73), respectively. The overall RR for ex-drinkers compared with never drinkers was 1.66 (95% CI 1.06-2.62, <math>P = 0.028</math>). There was no evidence for a dose-effect relationship (<math>P</math> for trend 0.8).</p>	<p>The authors say that their results do not support a dose-response effect of alcohol on breast cancer risk, but admit that consumption levels were probably too low to exclude such a relationship with high regular intake. Alcohol consumption was converted to standard units based on beverage type. RRs were not altered when adjusted for age, study centre, body mass index, smoking, parity, age at menopause, age at menarche, oestrogen replacement therapy, family history of breast cancer, benign breast disease, age at first birth.</p>

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<p>This analysis focused on interviews obtained from 1645 newly diagnosed cases and 1497 controls in USA (1991-1992). Controls were matched for age and region. All subjects were 20-44 years of age. Detailed lifetime history of alcohol use was obtained to evaluate the effects of drinking during different periods of life in relation to breast cancer risk</p>	<p>The adverse affects of recent drinking were restricted to women consuming <math>\geq 14</math> drinks/week (RR 1.7, 95% CI 1.2-2.5). Compared with nondrinkers, the risk estimate associated with recent consumption of <math>\geq 14</math> drinks per week was 2.4 (95% CI 1.6-3.8) for women with regional/distant disease. At levels of consumption below this, there was no evidence for a dose-effect relationship. Drinking pattern in teens and twenties did not increase risk of breast cancer, only pattern of recent drinking had a significant effect. Consumption of <math>\geq 7</math> drinks/week in teens, RR 1.34 (0.9-2.0); <math>\geq 14</math> drinks/week in 20s, RR 1.29 (0.9-2.0); <math>\geq 14</math> drinks/week in 30s, RR 1.8 (1.2-2.6). Age at which drinking commenced did not alter the risk. Drinking started at <math>&lt; 17</math> years, RR 0.81 (0.6-1.1); 17-19 years, RR 1.19 (1.0-1.4); <math>\geq 20</math> years, RR 1.15 (1.0-1.4). The number of years since drinking started had no effect on the risk of breast cancer.</p>	<p>No adjustment for diet or total energy intake was included<sup>22</sup></p> <p>Authors commented that alcohol appears to act at a late stage in breast carcinogenesis. They also suggested that it may be more useful to elucidate the relation between alcohol consumption and endogenous hormones. Alcohol consumption was assessed in detail. RRs were adjusted for age, study centre, race, parity, use of oral contraceptives. No meaningful analysis by type of beverage was possible, because consumption was generally mixed<sup>23</sup></p>
<p>A total of 1214 women aged 20-79 years with breast cancer and a similar number of matched controls were studied during 1984 to 1986 in the USA, and alcohol consumption assessed</p>	<p>After adjustment for breast cancer risk factors, the OR for ever versus never drinking was 1.40 (95% CI 1.09-1.79). ORs for <math>&gt; 0-5</math> and <math>\geq 5</math> g alcohol per day, as compared to nondrinkers, were 1.29 (95% CI 1.00-1.65) and 1.46 (95% CI 1.13-1.89), respectively. After covariate</p>	<p>The authors have calculated that assuming an OR of 1.4 for women ever drinking alcohol compared to never drinkers and a prevalence of ever drinking of around 83%, 25% of breast cancer among women between 20 and 79 years is attributable to ever drinking alcohol:</p>

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	<p>adjustment, risk from alcohol intake did not differ between pre- and postmenopausal women. The greater the total years of drinking up to 40 years, the greater the risk: &gt;0 - &lt;20 years, OR 1.33 (0.89-1.98); 20-40 years, OR 1.48 (1.13-1.77); ≥40 years, OR 1.32 (0.98-1.77) (P for trend 0.54), but when adjusted for grams per day, duration was not important. Intensity of drinking may therefore be more important. The type of alcohol (beer, wine or liquor) was not important. (RR<sub>adjusted</sub> (95% CI) for beer: 1.28 (0.72-2.29); wine: 1.32 (1.00-1.72); spirits: 1.30 (0.96-1.75). Age at which drinking started had no effect on risk. Age at start of drinking: ≤17 years, OR (<i>cf</i> starting to drink at 25 years) 0.79 (0.58-1.08); 18-24 years, OR 1.01 (0.79-1.29</p>	<p>“If the alcohol-breast cancer hypothesis is correct, many breast cancers would be preventable by reducing alcohol consumption”. Alcohol consumption was standardised on an average portion. ORs were adjusted for religion, income, marital status, family history of breast cancer, benign breast disease, age at menarche, parity, age at first birth, weeks breast feeding, smoking<sup>24</sup></p>
<p>Age-adjusted breast cancer incidence rates from 1980 to 1982 were studied to assess the extent to which differences in the regional distribution of established and probable risk factors could explain the increased incidence of breast cancer in the San Francisco Bay area. Controls were matched by age and centre. All subjects were 20-55 years of age</p>	<p>Alcohol consumption did not appear to have any effect on breast cancer incidence, and the results could be entirely explained by regional differences in known risk factors. Depending on the statistical analysis used, the adjusted RR of breast cancer relative to other regions for white women changed from 0.97-1.02 to 0.96-0.99 after adjusting for alcohol consumption. In black women the RR decreased from 0.77-0.88 to 0.75-0.83</p>	<p>Alcohol consumption was assessed as drinks per week; the type of beverage was not specified. RRs were adjusted for age, parity, age at first birth, months breast feeding, age at menarche, age at menopause<sup>25</sup></p>
<p>In a study of 1647 breast cancer cases and 1501 population controls under 45 years of</p>	<p>In women aged under 35 years, there was a non-significant positive relationship between</p>	<p>The authors commented that the relationship between oral contraceptive use and alcohol</p>

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age in the USA, potential modifying effects of other risk factors, including alcohol, on the relationship of oral contraceptives to breast cancer were examined (1990-1992)	heavier consumption of alcoholic beverages and incidence of breast cancer ( $\geq 7$ drinks per week, RR = 1.20, 95% CI 0.9-1.5). A possible interaction between heavy alcohol consumption ( $\geq 7$ drinks per week) and oral contraceptive use in women < 35 years was suggested, but this was not significant (P=0.20)	with breast cancer deserves further investigation. Alcohol consumption was assessed at interview, full details being provided in an earlier paper. RRs were adjusted for age, study centre, use of oral contraceptives, race, parity, age at first birth, age at menarche, previous breast biopsy, body mass index, family history of breast cancer <sup>26</sup>
<p>1998</p> <p>Using data from a case-control study conducted in Italy on 2569 breast cancer patients and 2588 controls, multivariate odds ratios and population-attributable risks for breast cancer were calculated in relation to alcohol consumption and a variety of other dietary factors. Subjects were 23-74 years of age</p>	<p><math>\leq 20</math> g alcohol/day: premenopausal women OR 1.37 (95% CI 1.09-1.72), postmenopausal women OR 1.10 (0.93-1.29); <math>&gt; 20</math> g alcohol/day: premenopausal women OR 1.60 (1.23-2.08), postmenopausal women OR 1.11 (0.92-1.33). The risk is therefore apparently greater in premenopausal women</p>	<p>The authors estimate that approximately one-third of breast cancer cases in their population could be avoided by reducing alcohol intake and having a diet richer in fruit and vegetables. A detailed history of alcohol consumption was obtained by questionnaire. ORs were adjusted for vitamin E and <math>\beta</math>-carotene intake, physical activity, body mass index, total energy intake, education, age, study centre, menopausal status<sup>27</sup></p>
<p>470 breast cancer patients and 472 controls, all under 45 years, were compared between 1991 and 1994. A comparison was made between this study, carried out in Italy, and that of Swanson <i>et al.</i><sup>23</sup>, carried out in an American population</p>	<p>In this Italian study, consumption of 21 or more drinks per week showed an especially marked elevation of risk, but no clear difference was found by type of beverage</p>	<p>The pattern of drinking differed between the US and Italy, but the authors suggest that more than two drinks per day may be a suitable threshold value for increased risk of breast cancer<sup>28</sup></p>
<p>A multi-centre case control study from Italy on 2569 incident cases of breast cancer and</p>	<p>A significant effect of alcohol consumption, compared with abstinence, on risk of breast</p>	<p>The majority of women in this study were described as relatively high consumers of</p>

Description of study	Results	Comments/Reference
<p>2588 controls, studied between 1991-1994. All cases were 23-74 years of age. Controls were balanced for age and study region.</p>	<p>cancer was found (OR 1.39, 95% CI 1.21-1.60). The OR (95% CI) increased with the amount of alcohol consumed: <math>\leq 5.87</math> g/day, 1.21 (1.00-1.47); 5.88-13.40 g/day, 1.23 (1.02-1.50); 13.41-24.55 g/day, 1.19 (0.98-1.45); 24.56-27.69 g/day, 1.21 (0.99-1.47); <math>&gt;27.60</math> g/day, 1.41 (1.17-1.71) (P for trend <math>&lt;0.001</math>). The risk was greater in premenopausal drinkers (OR 1.25 (1.12-1.41)) than in postmenopausal drinkers (1.07 (0.92-1.25)). The difference in the effects of alcohol in the two groups was significant (P=0.03). The increase in risk was independent of beverage type. The ORs for consumption of different beverages were: wine <math>&gt;27.6</math> g/day, 1.27 (95% CI 1.06-1.53; P for trend <math>&lt;0.001</math>); beer, 1.44 (1.16-1.79); spirits, 1.51 (1.02-2.2); grappa, 1.57 (1.12-1.82). There was no increase in risk with the duration of drinking (OR 0.95, 95% CI 0.80-1.13 for <math>\geq 40</math> years, P for trend NS). In premenopausal women only, the risk increased as the age at first consumption decreased (P for trend <math>&lt;0.001</math>)</p>	<p>alcohol. The authors concluded that, if real, the association with alcohol could explain 12% (95% CI 5-19%) of breast cancer in Italy. ORs adjusted for age, study centre, measurement error, body mass index, smoking, education, age of first birth, age at menarche, family history of breast cancer, energy intake other than alcohol. There was no confounding by use of oral contraceptives or by oestrogen replacement therapy. Alcohol consumption was assessed from a detailed, validated dietary questionnaire, and standard conversion factors were used for units of different beverages consumed<sup>29</sup></p>
<p><u>Cross-national</u> 1996</p>	<p>A positive correlation was found between breast cancer mortality rates and alcohol, but this was not significant when other variables</p>	<p>This study identified a positive correlation with animal product consumption and protective effects of fish and cereal</p>

Description of study	Results	Comments/Reference
female breast cancer mortality rates	were included in the stepwise regression model (P > 0.20)	consumption. Alcohol consumption was based on Food Balance Sheets, pro-rated on a per capita basis. Hence, only broad national trends could be identified <sup>30</sup>
<p><u>Review</u></p> <p>A pooled analysis of six cohort studies carried out between 1989 and 1994 in the Netherlands, Sweden, Canada and the United States, involving a total of 322,647 women evaluated for up to 11 years, including 4335 subjects with incident invasive breast cancer. Subjects were 34-76 years of age</p>	<p>For alcohol intakes less than 60 g/day (reported by &gt;99% of participants), risk increased linearly with increasing intake; the pooled multivariate relative risk for an increment of 10 g/day of alcohol was 1.09 (95% CI 1.04-1.13). The multivariate-adjusted relative risk for total alcohol intakes of 30 to less than 60 g/day versus non-drinkers was 1.41 (95% CI 1.18-1.69). There was no significant difference between pre- and post-menopausal women in the effect of alcohol (P=0.49)</p>	<p>The authors conclude that alcohol consumption is associated with a linear increase in breast cancer incidence in women over the range of consumption reported by most women, and among women consuming alcohol regularly; reducing alcohol consumption is a potential means to reduce breast cancer risk. Alcohol consumption was based on specific beverage type and amount, determined by questionnaire. RRs were adjusted for age at menarche, parity, age at first birth, menopausal status, oestrogen replacement therapy, use of oral contraceptives, benign breast disease, family history of breast cancer, smoking, education, body mass index, height, fat intake, fibre intake, total energy intake. Study based only on current alcohol consumption, which could lead to some bias<sup>31</sup></p>