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Alcohol and dietary fibre intakes affect circulating sex hormones among premenopausal women

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Abstract

Background: The association of alcohol and fibre intake with breast cancer may be mediated by circulating sex hormone levels, which are predictors of breast cancer risk.

Objective: To evaluate the relationship of alcohol and dietary fibre intake with circulating sex hormone levels among premenopausal women.

Methods: A total of 205 premenopausal women completed a validated food-frequency questionnaire at baseline and after 2 years; blood samples taken at the same time were analysed for circulating sex hormone concentrations, including oestrone (E_1), oestradiol (E_2), free E_2, progesterone, androstenedione and sex hormone-binding globulin, by radioimmunoassay. We used mixed models to estimate least-square means of sex hormone concentrations for alcohol intake categories and quartiles of dietary intake.

Results: After adjustment for covariates, alcohol consumption was moderately associated with higher circulating oestrogen levels; those who consumed more than one drink per day had 20% higher E_2 ($P_{trend} = 0.07$) levels than non-drinkers. In contrast, higher dietary fibre intake was associated with lower serum levels of androstenedione (−8% between the lowest and highest quartiles of intake, $P_{trend} = 0.06$), but not oestrogens. Similarly, consumption of fruits (−12%, $P_{trend} = 0.03$), vegetables (−9%, $P_{trend} = 0.15$) and whole grains (−7%, $P_{trend} = 0.07$) showed inverse associations with androstenedione levels.

Conclusions: The consistency of the observed differences in sex hormone levels associated with alcohol and fibre-rich foods indicates that these nutritional factors may affect sex hormone concentrations and play a role in breast cancer aetiology and prevention.

Keywords
Sex hormones
Breast cancer risk
Alcohol
Dietary fibre
Premenopausal women

Alcohol consumption is considered a possible risk factor for breast cancer and dietary fibre may protect against the disease[1]. There is fairly strong evidence that alcohol consumption is associated with higher breast cancer risk[2]. A pooled analysis of 53 cohort and case–control studies estimated that alcohol consumption might account for 4% of all breast cancers in developed countries and that every 10 g of daily alcohol consumption increases breast cancer risk by 7%. However, the mechanism of action for this association is not fully understood. It is possible that alcohol increases[3–5] and fibre-rich foods[6–8] (such as fruits and vegetables and whole grains) lower sex hormone levels. Circulating oestrogen levels appear to be a biomarker for breast cancer risk[9], although the evidence for an association between endogenous hormones and breast cancer is stronger for postmenopausal[10] than for premenopausal[11–13] women. In the present paper, we perform a cross-sectional data analysis among 205 premenopausal women who had participated in a 2-year soy feeding trial and provided blood samples and dietary information. The objective of the analysis was to investigate the relationship of alcohol and dietary fibre intake with circulating sex hormone concentrations among this population of premenopausal women.

Materials and methods

Study design and population

The study was approved by the Committee on Human Studies at the University of Hawaii and the Institutional Review Boards of the participating clinics. The original objective of the study was to investigate the possible effects of soy consumption on circulating oestrogen levels and mammographic densities. Details of the recruitment strategy and study procedures have been given previously[14,15]. In brief, 220 premenopausal women recruited

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from mammography clinics were randomised to an intervention group consuming 2 daily servings of soy foods and to a control group maintaining their regular diet[14]. Inclusion criteria ensured that all subjects had a normal screening mammogram, were not taking oral contraceptives or other sex hormones, had no history of cancer, had a complete uterus and ovaries, menstruated regularly, and consumed less isoflavones than the equivalent of 6 servings of soy per week during the previous year. All women provided signed informed consent before entry into the trial. The 205 women (100 women in the intervention group and 105 women in the control group) who had complete baseline serum oestrogen data available were included in the present analysis. We considered all women as one group because we did not observe any effect of the soy intervention on circulating hormone levels. The mean difference in change between groups was $9\,\mathrm{pg\,ml^{-1}}$ ($P = 0.44$) for oestrone (E_1), $30\,\mathrm{pg\,ml^{-1}}$ ($P = 0.15$) for oestradiol (E_2) and $34\,\mathrm{pg\,ml^{-1}}$ ($P = 0.48$) for androstenedione (Adione)[15]. There was also no significant difference in hormone levels among the three ethnic categories (Asian, Caucasian and other).

Data collection

A validated food-frequency questionnaire (FFQ)[16], which reflected dietary intake during the previous 12 months, was administered at baseline and after 2 years. The FFQ was originally developed for use in the Hawaii–Los Angeles Multiethnic Cohort Study and included foods commonly consumed among the ethnically diverse cohort population. Completed FFQs were analysed for daily intakes of nutrients and food group servings using the Cancer Research Center of Hawaii's Food Composition Database (FCD) and Food Group Servings Database (FGSD), respectively[17,18]. The FCD contains information for more than 2500 food items and is based on nutritional data from the US Department of Agriculture (USDA)[19], as well as on additional laboratory analyses and existing professional and commercial publications. The FGSD was developed according to the USDA Food Guide Pyramid's food categories and serving sizes[20]. Alcohol consumption was estimated as number of drinks per day; the USDA Food Guide Pyramid defines one drink as equivalent to 12 oz of regular beer, 5 oz of wine or 1.5 oz of 80-proof distilled spirits[20].

We measured height for all subjects at baseline and body weight throughout the study. For this analysis, we calculated the body mass index (BMI) at baseline and at the end of the study by dividing the weight in kilograms by the square of height in metres. Blood samples were obtained 5 days after ovulation as determined by an ovulation kit, at baseline and months 3, 6, 12 and 24[15]. Less than 1% of women donated blood on a different day, but 61 blood samples out of the possible 1025 samples were missing because the women had either left the study or were not able to detect an ovulation. The missing samples were distributed equally by group. The serum analysis for E_1, E_2, sex hormone-binding globulin (SHBG), progesterone (Prog) and Adione was performed by radioimmunoassay in the Reproductive Endocrine Research Laboratory at the University of Southern California Keck School of Medicine after the study was completed[15]. The analyses were conducted in batches of 30 or 40 samples. Each batch contained all five samples collected from the same woman and an equal number of intervention and control samples. For quality control, we included two or three blind samples obtained from a pooled blood sample into each batch. Based on the 60 blind samples, we obtained the following inter-assay coefficients of variation: E_1, 17.7%; E_2, 11.2%; Adione, 14.2%; SHBG, 6.2%; Prog, 8.6%.

Statistical analysis

The SAS software package (version 8.2; SAS Institute, Cary, NC, USA) was used for all statistical analyses. The PROC CORR procedure was used to calculate Spearman rank-order correlation coefficients among sex hormone variables and between baseline and final FFQs for each dietary variable. The sex hormone variables were distributed normally within acceptable limits and transformations did not improve them. Food intake, except alcohol, was expressed per 1000 kcal to adjust for differences in energy intake. Alcohol intake was not adjusted for total energy intake because the majority of the published literature reports alcohol consumption as number of drinks per day or week. Women who consumed less than one drink per month were classified as non-drinkers, women drinking one drink per day or less as low consumers, and women reporting more than one drink per day as high consumers. Because of the repeated measurements we used the PROC MIXED procedure to evaluate the relationships between dietary variables and sex hormone levels and to estimate least-square means of sex hormone concentrations by quartile of intake. The model included age, BMI, dietary information, physical activity level and serum measurements collected at baseline and at the end of the study. Ethnicity (Asian, Caucasian and other), age at menarche, age at first live birth and parity (none, 1–2 children, ≥ 3 children) assessed at baseline were added as covariates because they showed an association with at least one of the hormone or dietary variables of interest. A sub-analysis of the same data that included the group assignment (intervention vs. control) as a covariate in the mixed model changed the results only slightly (data not shown) and justified keeping all women as one group.

Results

Of the 205 subjects, 80 were Asian, 76 were Caucasian and 49 were of mixed or other ethnicity including Native Hawaiian. The mean age at baseline was 43.0 ± 2.8 years.

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Mean BMI increased slightly from 26.1 to 26.4 kg m^{-2} at the end of the study (Table 1). According to the baseline FFQ, mean energy intake was 1834 ± 795 kcal day^{-1} and mean dietary fibre intake was 18.6 ± 9.6 g day^{-1}. Alcohol consumption at baseline ranged from 0 to 2.6 drinks per day, with a mean of 0.3 ± 0.5 drinks per day. By category, 96 women were classified as non-drinkers, another 100 women consumed less than one drink per day, and nine women reported more than one daily drink. Most women were considered sedentary ($n = 12$) or lightly active ($n = 159$); only 34 women were moderately to extremely active.

The within-person intraclass correlations for E_1, E_2, Adione, SHBG and Prog were 0.26, 0.12, 0.57, 0.80 and 0.32, respectively. Sex hormone levels were highly correlated with each other, in particular E_1 and E_2 ($r = 0.67$, $P < 0.001$). Adione and SHBG also showed significant correlations with oestrogens ($r = 0.38$, $P < 0.001$ for Adione and E_1; $r = 0.30$, $P < 0.001$ for SHBG and E_2). Dietary intakes as reported in the baseline and final FFQ were highly correlated: $r = 0.85$ for alcohol; $r = 0.60$ for dietary fibre; $r = 0.68$ for fruits; $r = 0.66$ for vegetables; $r = 0.42$ for whole grains ($P < 0.001$ for all).

After adjustment for confounding factors, non-significantly higher serum levels of oestrogens and androgens were observed in women who consumed more than one drink per day than in non-drinkers (Table 2). The difference was 14% for E_1, 20% for E_2, 7% for free E_2 and 3% for Adione. We observed a clear dose–response for the oestrogens; the combined E_1 and E_2 levels were 223, 241 and 260 pg ml^{-1} for non-drinkers, low alcohol consumers and high alcohol consumers, respectively, but the trend was not statistically significant. Only SHBG levels were significantly associated with alcohol intake.

Dietary fibre intake was associated with lower circulating Adione levels (Table 3). Women in the highest quartile of dietary fibre had 8% lower concentrations than those in the lowest quartile; however, no difference was observed for oestrogens, Prog or SHBG (Table 3). Similarly, consumption of fruits (Table 4), vegetables (Table 5) and whole grains (Table 6) showed inverse associations with Adione; the concentrations were lower in the highest quartile of intake than in the lowest quartile by 12% for fruits, 9% for vegetables and 7% for whole grains, but the trend was significant only for fruits. In addition, Prog was lower by 9% ($P_{trend} = 0.05$) and SHBG by 7% ($P_{trend} = 0.05$) in the highest quartile than in the lowest quartile of fruit consumption (Table 4).

Table 1 Characteristics of study subjects ($n = 205$)

Variable	Baseline	Final
Age (years)	43.0 ± 2.8	–
Age at menarche		–
Younger than 13 years (n)	120	
13 years and older (n)	85	
Age at first live birth		–
Younger than 30 years (n)	109	
30 years and older (n)	96	
Parity		–
0 children (n)	55	
1–2 children (n)	103	
≥ 3 children (n)	47	
Body mass index (kg m^{-2})	26.1 ± 5.8	26.4 ± 6.0
Energy intake (kcal day^{-1})	1834 ± 795	1628 ± 627
Alcohol consumption (drinks daily)	0.3 ± 0.5	0.3 ± 0.6
Fibre intake (g day^{-1})	18.6 ± 9.6	17.6 ± 9.0
Sex hormone levels		
E_1 (pg ml^{-1})	93 ± 53	90 ± 54
E_2 (pg ml^{-1})	143 ± 79	136 ± 84
Free E_2 (pg ml^{-1})	3.2 ± 1.6	3.1 ± 2.0
$E_1 + E_2$ (pg ml^{-1})	237 ± 122	226 ± 124
SHBG (nmol l^{-1})	58 ± 30	58 ± 31
Adione (pg ml^{-1})	987 ± 398	911 ± 338
Prog (ng ml^{-1})	11 ± 5	10 ± 6

E_1 – oestrone; E_2 – oestradiol; SHBG – sex hormone-binding globulin; Adione – androstenedione; Prog – progesterone.

Discussion

Despite the low alcohol intake in our population of premenopausal women who had participated in a nutritional trial, alcohol intake showed a positive association with circulating serum oestrogen levels during the luteal phase. In particular, drinking more than one drink per day was associated with 20% higher E_2 levels than not drinking alcohol. In contrast, intake of dietary fibre and fibre-containing foods (fruits, vegetables and whole grains) was inversely related with Adione levels; the concentrations were 8% lower in the highest than in the lowest quartile of fibre intake. The association with fruits was stronger than with vegetables and whole grains. Although most of our findings did not reach statistical significance, the consistent trends between the dietary variables and sex hormone levels provide support for the hypothesis that dietary components may influence breast cancer risk through an effect on sex hormone levels.

Our findings agree with several cross-sectional studies among premenopausal women that reported significant associations between alcohol intake and oestrogen levels[21–23]. Among a large prospective cohort of postmenopausal Dutch women, significantly higher levels of E_1 and E_2, but not Adione and SHBG, were observed in subjects who consumed 25 g of alcohol per day compared with non-drinkers[5]. Experimental evidence among pre- and postmenopausal women provides additional support for the hypothesis. An intervention study among younger women found higher levels of oestrogens during consumption of two daily alcohol servings[4]. Alcohol exposure in postmenopausal women on oestrogen replacement therapy, a hormonal setting comparable to premenopausal status, led to a three-fold increase in serum E_2[24]. Despite some negative findings[25–27], there appears to be consistent support for the hypothesis that alcohol intake influences circulating sex hormone levels before and after menopause[5]. The impact of regular alcohol consumption on oestrogen levels may be more

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Table 2 Association of alcohol intake with sex hormone levels*

Alcohol intake† (drinks daily)	*n* (baseline/final)	E_1 (pg ml^{-1})	E_2 (pg ml^{-1})	Free E_2 (pg ml^{-1})	$E_1 + E_2$ (pg ml^{-1})	SHBG (nmol l^{-1})	Adione (pg ml^{-1})	Prog (ng ml^{-1})
None	96/80	90	132	3.0	223	56	945	11
>0 and ≤ 1.0	100/97	93	148	3.3	241	60	958	10
>1.0	9/8	103	158	3.2	260	72	969	12
P_{trend}	–	0.42	0.07	0.16	0.12	0.03	0.74	0.87

E_1 – oestrone; E_2 – oestradiol; SHBG – sex hormone-binding globulin; Adione – androstenedione; Prog – progesterone.
* Hormone values are expressed as least-square means calculated from mixed models adjusted for age, body mass index, ethnicity, age at menarche, age at first live birth, parity and physical activity level.
† Based on the Food Guide Pyramid: one drink is equivalent to 12 oz of regular beer, 5 oz of wine or 1.5 oz of 80-proof distilled spirits. Less than one drink per month is considered no alcohol intake.

pronounced among post- than premenopausal women because of the lower oestrogen levels after menopause. In addition, the evidence that oestrogen levels increase breast cancer risk is considerably stronger for postmenopausal women than for women before menopause, for whom androgens may play a more important role than oestrogens[13,28,29]. It has been hypothesised that alcohol consumption increases circulating oestrogen levels by impairing the hepatic oestrogen metabolism and by enhancing the conversion of androgens to oestrogens[30]. Alcohol may also influence Adione formation at one or more of the biosynthetic steps along the Δ^4 and Δ^5 pathways in the adrenals or ovary or have an effect on the pituitary gland, which could suppress gonadotropin and/or adrenocorticotropic hormone production.

Our observation of lower Adione levels with higher fibre intake agrees with reports that circulating androgen levels are associated with breast cancer risk among premenopausal women[13,31,32]. The non-significant finding of lower free E_2 levels with higher intakes of dietary fibre and whole grains is compatible with the previous finding of an inverse relationship of fibre intake with E_2 levels[33,34] because Adione is a precursor of oestrogens. Our data also showed that serum oestrogen levels were highly correlated with Adione levels. Thus, lower circulating androgen levels may provide less substrate for oestrogen synthesis. Dietary fibre intake may also lower serum oestrogen levels through the promotion of faecal oestrogen excretion[8]. Moreover, it is possible that dietary fibre is a marker for another nutrient that affects Adione levels. Specific effects of dietary fibre from specific foods might have contributed to the inconsistency that lower E_2 levels were associated with high intakes of fibre and whole grains only, but not with intakes of fruits and vegetables. It is also possible that dietary fibre intake needs to be above a certain threshold in order to have a beneficial effect. This explanation has been offered for the protective effect of fibre against colorectal cancer found in a European cohort, but not in the USA[35]. The non-significant findings related to fruits and vegetables are consistent with the accumulating evidence that fruits and vegetables show little association with breast cancer risk in prospective cohort studies[36,37]. The relationship between SHBG and alcohol consumption is not easily interpretable. Higher SHBG levels likely contribute to lower free oestrogen levels. The association of SHBG levels with higher alcohol intake is consistent with the higher SHBG levels found in patients with cirrhosis of the liver, but the mechanism by which this occurs is not known[38]. A relationship of SHBG with nutritional factors is supported by an ecological study in China that found a positive association with green vegetables, rice and fish[39]. Conflicting results have been reported for the relationship between serum SHBG levels and breast cancer risk[13,40,41], but it appears that a weak inverse association may exist[42].

The modest sample size of our population and the low alcohol consumption were serious limitations of the present analysis. The small size of the exposed group – only nine women reported more than one drink per week at baseline – questions the validity of the current findings. There is also a possibility of selection bias; although our subjects were recruited from the general population, only

Table 3 Association of energy-adjusted intake of dietary fibre with sex hormone levels*

Quartile of intake	Intake (g/1000 kcal)	E_1 (pg ml^{-1})	E_2 (pg ml^{-1})	Free E_2 (pg ml^{-1})	$E_1 + E_2$ (pg ml^{-1})	SHBG (nmol l^{-1})	Adione (pg ml^{-1})	Prog (ng ml^{-1})
1	<7.9	93	148	3.3	242	60	1058	10
2	>7.9–10.0	90	137	3.2	228	58	921	11
3	>10.0–12.5	85	136	3.1	219	56	869	10
4	>12.5–25.6	102	147	3.1	250	61	975	10
P_{trend}	–	0.48	0.88	0.37	0.82	0.92	0.06	0.48

E_1 – oestrone; E_2 – oestradiol; SHBG – sex hormone-binding globulin; Adione – androstenedione; Prog – progesterone.
* Hormone values are expressed as least-square means calculated from mixed models adjusted for age, body mass index, ethnicity, age at menarche, age at first live birth, parity and physical activity level.

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Table 4 Association of energy-adjusted intake of fruits with sex hormone levels*

Quartile of intake	Intake (servings/1000 kcal)	E_1 (pg ml^{-1})	E_2 (pg ml^{-1})	Free E_2 (pg ml^{-1})	$E_1 + E_2$ (pg ml^{-1})	SHBG (nmol l^{-1})	Adione (pg ml^{-1})	Prog (ng ml^{-1})
1	<0.6	90	138	3.1	228	60	1029	11
2	>0.6–1.1	97	149	3.2	245	63	948	11
3	>1.1–1.7	88	151	3.4	240	56	929	10
4	>1.7–7.0	95	129	2.9	224	56	908	10
P_{trend}	–	0.87	0.56	0.61	0.77	0.05	0.03	0.05

E_1 – oestrone; E_2 – oestradiol; SHBG – sex hormone-binding globulin; Adione – androstenedione; Prog – progesterone.
*Hormone values are expressed as least-square means calculated from mixed models adjusted for age, body mass index, ethnicity, age at menarche, age at first live birth, parity and physical activity level.

Table 5 Association of energy-adjusted intake of vegetables with sex hormone levels*

Quartile of intake	Intake (servings/1000 kcal)	E_1 (pg ml^{-1})	E_2 (pg ml^{-1})	Free E_2 (pg ml^{-1})	$E_1 + E_2$ (pg ml^{-1})	SHBG (nmol l^{-1})	Adione (pg ml^{-1})	Prog (ng ml^{-1})
1	<0.4	99	154	3.4	253	59	1008	10
2	>0.4–1.8	85	133	3.1	218	54	934	11
3	>1.8–2.5	90	128	2.9	218	58	950	10
4	>2.5–6.7	97	152	3.3	249	63	920	11
P_{trend}	–	0.96	0.71	0.34	0.75	0.21	0.15	0.43

E_1 – oestrone; E_2 – oestradiol; SHBG – sex hormone-binding globulin; Adione – androstenedione; Prog – progesterone.
*Hormone values are expressed as least-square means calculated from mixed models adjusted for age, body mass index, ethnicity, age at menarche, age at first live birth, parity and physical activity level.

Table 6 Association of energy-adjusted intake of whole grains with sex hormone levels*

Quartile of intake	Intake (servings/1000 kcal)	E_1 (pg ml^{-1})	E_2 (pg ml^{-1})	Free E_2 (pg ml^{-1})	$E_1 + E_2$ (pg ml^{-1})	SHBG (nmol l^{-1})	Adione (pg ml^{-1})	Prog (ng ml^{-1})
1	<0.5	92	147	3.3	240	59	986	10
2	>0.5–0.8	88	138	3.3	226	58	996	11
3	>0.8–1.2	97	147	3.2	244	59	914	10
4	>1.2–6.0	93	136	3.0	229	58	918	10
P_{trend}	–	0.65	0.54	0.28	0.83	0.73	0.07	0.45

E_1 – oestrone; E_2 – oestradiol; SHBG – sex hormone-binding globulin; Adione – androstenedione; Prog – progesterone.
*Hormone values are expressed as least-square means calculated from mixed models adjusted for age, body mass index, ethnicity, age at menarche, age at first live birth, parity and physical activity level.

a small fraction of the 10 022 women invited to the study were actually enrolled[15]. Thus, our sample population included more health-conscious women with favourable lifestyles than the general population. Moreover, the subjects' premenopausal status likely resulted in considerable intra-individual variability in sex hormone concentrations, as shown by the low within-person intraclass correlation for E_1 and E_2. Such variability in sex hormone concentrations, as well as the use of self-reported dietary data, would lead to an attenuation of the true correlation. Another weakness of our present analysis relates to the inclusion of multiple types of fibre under the broad definition of dietary fibre[43]. We included both water-soluble and insoluble fibres, and thereby did not distinguish the different physiological functions of these fibres in the human body[8]. Nevertheless, this study had several strengths. We used a validated FFQ[16] supported by a comprehensive food composition database[17]. The blood collection was timed with an ovulation detection kit and ovulations were confirmed by measurements of Prog[15].

The repeated measurement design in our analysis increased the validity of the hormone assessments; the accuracy of a one-time oestrogen measurement has been found to be low in other studies[44,45].

The consistency of the observed differences in sex hormone levels associated with alcohol and fibre-rich foods indicates that these nutritional factors may have important effects on sex hormone concentrations and play a role in breast cancer aetiology. In fact, alcohol may be one of the few known modifiable factors for breast cancer[2,46]. A difference of 26 pg ml^{-1} in E_2 is likely to translate into some protection against breast cancer given mean differences between cases and controls of less than 20 pg ml^{-1} in studies with postmenopausal women[10]. For premenopausal women, it is difficult to estimate a possible effect size with the available data[13,28,29]. The difficulties in assessing oestrogen exposure accurately among premenopausal women due to strong cyclic variations may be partly responsible for the lack of evidence[44,47]. To understand the potential influence of dietary factors on

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sex steroids levels and breast cancer risk among younger women, well-controlled investigations in this population need to be undertaken.

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References

1 World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR). *Food, Nutrition and the Prevention of Cancer: A Global Perspective*. Washington, DC: WCRF/AICR, 1997.

2 Hamajima N, Hirose K, Tajima K, Rohan T, Calle EE, Heath CW Jr, *et al.* Alcohol, tobacco and breast cancer – collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. *British Journal of Cancer* 2002; **87**: 1234–45.

3 Singletary KW, Gapstur SM. Alcohol and breast cancer: review of epidemiologic and experimental evidence and potential mechanisms. *Journal of the American Medical Association* 2001; **286**: 2143–51.

4 Reichman ME, Judd JT, Longcope C, Schatzkin A, Clevidence BA, Nair PP, *et al.* Effects of alcohol consumption on plasma and urinary hormone concentrations in premenopausal women. *Journal of the National Cancer Institute* 1993; **85**: 722–7.

5 Onland-Moret NC, Peeters PH, van der Schouw YT, Grobbee DE, van Gils CH. Alcohol and endogenous sex steroid levels in postmenopausal women: a cross-sectional study. *Journal of Clinical Endocrinology and Metabolism* 2005; **90**: 1414–9.

6 Rose DP, Goldman M, Connolly JM, Strong LE. High-fiber diet reduces serum estrogen concentrations in premenopausal women. *American Journal of Clinical Nutrition* 1991; **54**: 520–5.

7 Bagga D, Ashley JM, Geffrey SP, Wang HJ, Barnard RJ, Korenman S, *et al.* Effects of a very low fat, high fiber diet on serum hormones and menstrual function. *Cancer* 1995; **76**: 2491–6.

8 Rose DP. Dietary fiber and breast cancer. *Nutrition and Cancer* 1990; **13**: 1–8.

9 Henderson BE, Ponder B, Ross RK. *Hormones, Genes, and Cancer*. New York: Oxford University Press, 2003.

10 The Endogenous Hormones and Breast Cancer Collaborative Group. Endogenous sex hormones and breast cancer in postmenopausal women: reanalysis of nine prospective studies. *Journal of the National Cancer Institute* 2002; **94**: 606–16.

11 Key TJ, Pike MC. The role of oestrogens and progestagens in the epidemiology and prevention of breast cancer. *European Journal of Cancer & Clinical Oncology* 1988; **24**: 29–43.

12 Kabuto M, Akiba S, Stevens RG, Neriishi K, Land CE. A prospective study of estradiol and breast cancer in Japanese women. *Cancer Epidemiology, Biomarkers & Prevention* 2000; **9**: 575–9.

13 Kaaks R, Berrino F, Key T, Rinaldi S, Dossus L, Biessy C, *et al.* Serum sex steroids in premenopausal women and breast cancer risk within the European Prospective Investigation into Cancer and Nutrition (EPIC). *Journal of the National Cancer Institute* 2005; **97**: 755–65.

14 Maskarinec G, Robbins C, Riola B, Kane-Sample L, Franke A, Murphy S. Three measures show high compliance in soy intervention among premenopausal women. *Journal of the American Dietetic Association* 2003; **103**: 861–6.

15 Maskarinec G, Franke AA, Williams AE, Hebshi S, Oshiro C, Murphy SP, *et al.* Effects of a 2-year randomized soy intervention on sex hormone levels in premenopausal women. *Cancer Epidemiology, Biomarkers & Prevention* 2004; **13**: 1736–44.

16 Stram DO, Hankin JH, Wilkens LR, Henderson B, Kolonel LN. Calibration of the dietary questionnaire for a multiethnic cohort in Hawaii and Los Angeles. *American Journal of Epidemiology* 2000; **151**: 358–70.

17 Murphy SP. Unique nutrition support for research at the Cancer Research Center of Hawaii. *Hawaii Medical Journal* 2002; **61** 15, 17.

18 Sharma S, Murphy SP, Wilkens LR, Au D, Shen L, Kolonel LN. Extending a multiethnic food composition table to include standardized food group servings. *Journal of Food Composition and Analysis* 2003; **16**: 485–95.

19 US Department of Agriculture, Agricultural Research Service. *USDA National Nutrient Database for Standard Reference, Release 14* [online], 2003. Available at http://www.nal.usda.gov/fnic/foodcomp/index.html. Accessed 30 April 2003.

20 Center for Nutrition Policy and Promotion. *The Food Guide Pyramid*. Washington, DC: US Department of Agriculture, 1996.

21 Muti P, Trevisan M, Micheli A, Krogh V, Bolelli G, Sciajno R, *et al.* Alcohol consumption and total estradiol in premenopausal women. *Cancer Epidemiology, Biomarkers & Prevention* 1998; **7**: 189–93.

22 Garcia-Closas M, Herbstman J, Schiffman M, Glass A, Dorgan JF. Relationship between serum hormone concentrations, reproductive history, alcohol consumption and genetic polymorphisms in pre-menopausal women. *International Journal of Cancer* 2002; **102**: 172–8.

23 Randolph JF Jr, Sowers M, Gold EB, Mohr BA, Luborsky J, Santoro N, *et al.* Reproductive hormones in the early menopausal transition: relationship to ethnicity, body size, and menopausal status. *Journal of Clinical Endocrinology and Metabolism* 2003; **88**: 1516–22.

24 Ginsburg ES, Mello NK, Mendelson JH, Barbieri RL, Teoh SK, Rothman M, *et al.* Effects of alcohol ingestion on estrogens in postmenopausal women. *Journal of the American Medical Association* 1996; **276**: 1747–51.

25 Verkasalo PK, Thomas HV, Appleby PN, Davey GK, Key TJ. Circulating levels of sex hormones and their relation to risk factors for breast cancer: a cross-sectional study in 1092 pre- and postmenopausal women (United Kingdom). *Cancer Causes & Control* 2001; **12**: 47–59.

26 Sierksma A, Sarkola T, Eriksson CJ, van der Gaag MS, Grobbee DE, Hendriks HF. Effect of moderate alcohol consumption on plasma dehydroepiandrosterone sulfate, testosterone, and estradiol levels in middle-aged men and postmenopausal women: a diet-controlled intervention study. *Alcoholism, Clinical and Experimental Research* 2004; **28**: 780–5.

27 Dorgan JF, Reichman ME, Judd JT, Brown C, Longcope C, Schatzkin A, *et al.* The relation of reported alcohol ingestion to plasma levels of estrogens and androgens in premenopausal women (Maryland, United States). *Cancer Causes & Control* 1994; **5**: 53–60.

28 Key TJ, Appleby PN, Reeves GK, Roddam A, Dorgan JF, Longcope C, *et al.* Body mass index, serum sex hormones, and breast cancer risk in postmenopausal women. *Journal of the National Cancer Institute* 2003; **95**: 1218–26.

29 Micheli A, Muti P, Secreto G, Krogh V, Meneghini E, Venturelli E, *et al.* Endogenous sex hormones and

https://doi.org/10.1017/PHN2005923 Published online by Cambridge University Press

subsequent breast cancer in premenopausal women. *International Journal of Cancer* 2004; **112**: 312–8.

30 Purohit V. Can alcohol promote aromatization of androgens to estrogens? A review. *Alcohol* 2000; **22**: 123–7.

31 Dorgan JF, Longcope C, Stephenson HE, Falk RT, Miller R, Franz C, *et al*. Relation of prediagnostic serum estrogen and androgen levels to breast cancer risk. *Cancer Epidemiology, Biomarkers & Prevention* 1996; **5**: 533–9.

32 Berrino F, Muti P, Micheli A, Bolelli G, Krogh V, Sciajno R, *et al*. Serum sex hormone levels after menopause and subsequent breast cancer. *Journal of the National Cancer Institute* 1996; **88**: 291–6.

33 Nagata C, Kabuto M, Takatsuka N, Shimizu H. Associations of alcohol, height, and reproductive factors with serum hormone concentrations in postmenopausal Japanese women. Steroid hormones in Japanese postmenopausal women. *Breast Cancer Research and Treatment* 1997; **44**: 235–41.

34 Rock CL, Flatt SW, Thomson CA, Stefanick ML, Newman VA, Jones LA, *et al*. Effects of a high-fiber, low-fat diet intervention on serum concentrations of reproductive steroid hormones in women with a history of breast cancer. *Journal of Clinical Oncology* 2004; **22**: 2379–87.

35 Bingham SA, Day NE, Luben R, Ferrari P, Slimani N, Norat T, *et al*. Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study. *Lancet* 2003; **361**: 1496–501.

36 van Gils CH, Peeters PH, Bueno-de-Mesquita HB, Boshuizen HC, Lahmann PH, Clavel-Chapelon F, *et al*. Consumption of vegetables and fruits and risk of breast cancer. *Journal of the American Medical Association* 2005; **293**: 183–93.

37 Smith-Warner SA, Spiegelman D, Yaun SS, Adami HO, Beeson WL, van den Brandt PA, *et al*. Intake of fruits and vegetables and risk of breast cancer: a pooled analysis of cohort studies. *Journal of the American Medical Association* 2001; **285**: 769–76.

38 Rosner W. Plasma steroid-binding proteins. *Endocrinology and Metabolism Clinics of North America* 1991; **20**: 697–720.

39 Gates JR, Parpia B, Campbell TC, Junshi C. Association of dietary factors and selected plasma variables with sex hormone-binding globulin in rural Chinese women. *American Journal of Clinical Nutrition* 1996; **63**: 22–31.

40 Sturgeon SR, Potischman N, Malone KE, Dorgan JF, Daling J, Schairer C, *et al*. Serum levels of sex hormones and breast cancer risk in premenopausal women: a case–control study (USA). *Cancer Causes & Control* 2004; **15**: 45–53.

41 Zeleniuch-Jacquotte A, Shore RE, Koenig KL, Akhmedkhanov A, Afanasyeva Y, Kato I, *et al*. Postmenopausal levels of oestrogen, androgen, and SHBG and breast cancer: long-term results of a prospective study. *British Journal of Cancer* 2004; **90**: 153–9.

42 Key TJ, Allen NE. Hormones and breast cancer. *IARC Scientific Publications* 2002; **156**: 273–6.

43 Li BW, Andrews MC, Pehrsson PR. Individual sugars, soluble, and insoluble dietary fiber contents of 70 high consumption foods. *Journal of Food Composition and Analysis* 2005; **15**: 715–23.

44 Williams AE, Maskarinec G, Franke AA, Stanczyk FZ. The temporal reliability of serum estrogens, progesterone, gonadotropins, SHBG and urinary estrogen and progesterone metabolites in premenopausal women. *BMC Women's Health* 2002; **2**: 13.

45 Rinaldi S, Moret CN, Kaaks R, Biessy C, Kurzer MS, Dechaud H, *et al*. Reproducibility over time of measurements of androgens, estrogens and hydroxy estrogens in urine samples from post-menopausal women. *European Journal of Epidemiology* 2003; **18**: 417–24.

46 Henderson BE, Pike MC, Bernstein L, Ross RK. Breast cancer. In: Schottenfeld D, ed. *Cancer Epidemiology and Prevention*. . New York: Oxford University Press, 1996; 1022–39.

47 Ahmad N, Pollard TM, Unwin N. The optimal timing of blood collection during the menstrual cycle for the assessment of endogenous sex hormones: can interindividual differences in levels over the whole cycle be assessed on a single day? *Cancer Epidemiology, Biomarkers & Prevention* 2002; **11**: 147–51.

https://doi.org/10.1017/PHN2005923 Published online by Cambridge University Press