Baseline and lifetime alcohol consumption and risk of differentiated thyroid carcinoma in the EPIC study

Citation
Sen, A., K. K. Tsilidis, N. E. Allen, S. Rinaldi, P. N. Appleby, M. Almqquist, J. A. Schmidt, et al. 2015. “Baseline and lifetime alcohol consumption and risk of differentiated thyroid carcinoma in the EPIC study.” British Journal of Cancer 113 (5): 840-847. doi:10.1038/bjc.2015.280. http://dx.doi.org/10.1038/bjc.2015.280.

Published Version
doi:10.1038/bjc.2015.280

Permanent link
http://nrs.harvard.edu/urn-3:HUL.InstRepos:29407814

Terms of Use
This article was downloaded from Harvard University’s DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA

Share Your Story
The Harvard community has made this article openly available. Please share how this access benefits you. Submit a story.

Accessibility
Baseline and lifetime alcohol consumption and risk of differentiated thyroid carcinoma in the EPIC study

Abhijit Sen¹,², Konstantinos K Tsilidis*¹,³,⁴, Naomi E Allen⁵, Sabina Rinaldi⁶, Paul N Appleby³, Martin Almquist⁷,⁸, Julie A Schmidt³, Christina C Dahm⁹, Kim Overvad⁹, Anne Tjønneland¹⁰, Agnetha L Rostgaard-Hansen¹⁰, Françoise Clavel-Chapelon¹¹,¹²,¹³, Laura Baglietto¹⁴,¹⁵, Marie-Christine Boutron-Ruault¹¹,¹²,¹³, Tilman Kühn¹⁶, Verena A Katze¹⁶, Heiner Boeing¹⁷, Antonia Trichopoulou¹⁸,¹⁹,²⁰, Christos Tsironis¹⁸, Pagona Lagiou¹⁹,²⁰,²¹, Domenico Palli²², Valeria Pala²³, Salvatore Panico²⁴, Rosario Turino²⁵, Paolo Vineis²⁴,²⁶, HB(as) Bueno-de-Mesquita²⁴,²⁷,²⁸,²⁹, Petra H Peeters³⁰, Anette Hjartåker³¹, Eiliv Lund³², Elisabete Weiderpass³²,³³,³⁴,³⁵, J Ramón Quirós³⁶, Antonio Agudo³⁷, María-José Sánchez³⁸,³⁹, Larraitz Arriola³⁹,⁴⁰, Diana Gavrila³⁹,⁴¹, Aurelio Barricarte Gurrea³⁹,⁴², Joakim Hennings⁴⁴, Maria Sandström⁴⁵, Isabelle Romieu⁶, Pietro Ferrari⁶, Raul Zamora-Ros⁶, Kay-Tee Khaw⁴⁶, Nicholas J Wareham⁴⁷, Elio Riboli⁴, Marc Gunter⁴ and Silvia Franceschi⁶

Background: Results from several cohort and case–control studies suggest a protective association between current alcohol intake and risk of thyroid carcinoma, but the epidemiological evidence is not completely consistent and several questions remain unanswered.

Methods: The association between alcohol consumption at recruitment and over the lifetime and risk of differentiated thyroid carcinoma was examined in the European Prospective Investigation into Cancer and Nutrition. Among 477,263 eligible participants (70% women), 556 (90% women) were diagnosed with differentiated thyroid carcinoma over a mean follow-up of 11 years. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using multivariable Cox proportional hazards models.

Results: Compared with participants consuming 0.1–4.9 g of alcohol per day at recruitment, participants consuming 15 or more grams (approximately 1–1.5 drinks) had a 23% lower risk of differentiated thyroid carcinoma (HR = 0.77; 95% CI = 0.60–0.98). These findings did not differ greatly when analyses were conducted for lifetime alcohol consumption, although the risk estimates were attenuated and not statistically significant anymore. Similar results were observed by type of alcoholic beverage, by differentiated thyroid carcinoma histology or according to age, sex, smoking status, body mass index and diabetes.

Conclusions: Our study provides some support to the hypothesis that moderate alcohol consumption may be associated with a lower risk of papillary and follicular thyroid carcinomas.

Thyroid carcinoma incidence rates have been rapidly increasing in high-income countries, and the disease is more common among women (Davies and Welch, 2006; Kilfoy et al, 2009). Differentiated thyroid carcinoma, including papillary and follicular carcinoma, represents 98% of thyroid cancer (Kilfoy et al, 2009; Dal Maso et al, 2011). The only well-defined risk factors for thyroid carcinoma are exposure to ionizing radiation especially in childhood (Reynolds et al, 2005), thyroid adenoma and history of goiter (Franceschi et al, 1999; Balasubramaniam et al, 2012). Alcohol consumption is an important correlate to other dietary and lifestyle factors, and...
results from several prospective (Galanti et al, 1997; Navarro Silvera et al, 2005; Allen et al, 2009; Meinhold et al, 2009; Kabat et al, 2012; Kitahara et al, 2012) and case-control studies (Rossing et al, 2000; Mack et al, 2003) have suggested a protective association between current moderate alcohol intake and thyroid carcinoma risk. However, the extent of the lower risk has been varying, and only two prospective studies of women from the United Kingdom and the United States (Allen et al, 2009; Meinhold et al, 2009) and a pooled-analysis of five prospective studies on both sexes from the United States (Kitahara et al, 2012) have shown statistically significant inverse associations. A few smaller studies have observed null results (Iribarren et al, 2001; Mack et al, 2002; Guignard et al, 2007). Data about alcohol intake and thyroid carcinoma in men are limited, and no study has previously reported on the association between lifetime alcohol consumption and thyroid carcinoma risk. In the present large study within the European Prospective Investigation into Cancer and Nutrition (EPIC), we investigated the association between both baseline and lifetime alcohol consumption with risk of differentiated thyroid carcinoma, and also performed analyses by cancer stage, type of alcoholic beverage and according to potential modifying variables.

**Study design and recruitment.** EPIC is a multicentre prospective cohort study designed to investigate the relation between diet, other lifestyle factors, environmental factors and cancer risk. The cohort consists of approximately half a million participants, 70% of which are women, mostly aged 35–70 years and recruited between 1992 and 2000 in 23 centres in 10 European countries, that is, Denmark, France, Greece, Germany, Italy, the Netherlands, Norway, Spain, Sweden and United Kingdom. The rationale, design and data collection methods of EPIC have been previously described in detail elsewhere (Riboli et al, 2002). This study was approved by the Internal Review Boards of the International Agency for Research on Cancer and of the participating centres.

Subjects were excluded if they had prevalent cancer (other than non-melanoma skin cancer) at recruitment, if they were in the top or bottom 1% of the distribution of the ratio of energy intake to estimated energy requirement, and if they had missing information on baseline alcohol consumption. Therefore, this study used data from 477,263 participants, 335,020 (70%) of whom were women.

**Assessment of thyroid carcinoma.** Data on incident cases of thyroid carcinoma were collected by linkage to regional or national cancer registries from all EPIC centres except those from Greece, France and Germany. Outcome follow-up data from these countries were based on a combination of methods, including the use of health insurance records, contact with cancer and pathology registries, and active follow-up. Closure dates for the present study were defined as the latest update for both cancer registries, and active follow-up. Closure dates for the study centre to control for differences in questionnaires and follow-up procedures, and for sex and age at recruitment in 5-year categories. All multivariate models were adjusted for known or suspected risk factors of thyroid carcinoma, such as smoking status (never, former quitted ≤10 years ago, former quitted 11–20 years ago, former quitted >20 years ago, current with 1–15 cigarettes per day, current with 16–25 cigarettes per day, current with >25 cigarettes per day, current with pipe/cigar or occasional cigarette use, missing), education (up to high school, university graduate, missing), BMI (in quintiles, missing), physical activity (inactive, moderate inactive, moderate active, active, missing), diabetes status (no, yes, missing), energy from non-alcohol sources (continuously, missing), number of full-term pregnancies (0, 1, 2, 3, 4, 5, 6), medullary (n = 28), lymphoma (n = 1) and other rare morphologies (n = 3), which are usually considered poorly differentiated tumours with lower cure rates, were excluded. Data on the stage of differentiated thyroid carcinomas at diagnosis were collected from each centre, where possible. A total of 372 cases (67%) had stage information, of which 266 were classified as localised (tumour-node-metastasis staging score of T0–T3 and N0/Nx, and M0, or stage coded in the recruitment centre as localised) and 106 were classified as advanced thyroid carcinoma (T3–T4 and/or N1–N3 and/or M1, or stage coded in the recruitment centre as metastatic).

**Assessment of alcohol intake and other variables.** Dietary assessment was performed by self-administered country- or centre-specific dietary questionnaires or food records (Riboli et al, 2002). The intake of alcoholic beverages at baseline was calculated from these questionnaires that have been previously validated for alcohol consumption (Kaaks et al, 1997; Riboli et al, 2002; Hjertaker et al, 2007). Participants reported the number of standard glasses of beer, wine and distilled spirits consumed per day or week during the 12 months before recruitment. Alcohol intake was calculated by multiplying the mean glass volume with the alcohol content for each type of alcoholic beverage (Simian et al, 2007), using information collected in standardised 24-h dietary recalls from a subset of the cohort (Simian et al, 2000). Information of past alcohol consumption was assessed as glasses of different beverages consumed per week at 20, 30, 40 and 50 years of age in all EPIC centres except for Naples, Bilthoven, Umea, Malmo and Norway (Klipstein-Grobusch et al, 2007). Average lifetime alcohol intake was determined as a weighted average of intake at different ages with weights equal to the time of individual exposure to alcohol at different ages.

Information on physical activity, smoking status, level of education, diagnosis of diabetes mellitus, and in women only, age at menarche and menopause, use of oral contraceptives and hormone replacement therapy and number of full-term pregnancies (defined as the sum of live and still births) was self-reported at the baseline questionnaire (Tsilidis et al, 2011a, b). Weight and height were measured at recruitment, except for most of the Oxford cohort, the Norwegian cohort, and approximately two-thirds of the French cohort, among whom weight and height were self-reported. Body mass index (BMI) was calculated as weight in kilograms divided by height in metres squared. Menopausal status was defined according to information on menstruation status, hysterectomy, ovariectomy, use of exogenous hormone and age, details of which are provided elsewhere (Tsilidis et al, 2011b).

**Statistical analysis.** Cox proportional hazard models were used to study the association between alcohol intake and differentiated thyroid carcinoma incidence using age as the underlying time scale. Age at entry was defined as the participants’ age at recruitment, and exit time was age at diagnosis of thyroid cancer, death, loss to follow-up or censoring at the end of the follow-up period, whichever came first. The proportionality of hazards was verified based on the slope of the Schoenfeld residuals over time, and no evidence of violation was detected. The models were stratified by study centre to control for differences in questionnaires and follow-up procedures, and for sex and age at recruitment in 5-year categories. All multivariate models were adjusted for known or suspected risk factors of thyroid carcinoma, such as smoking status (never, former quitted ≤10 years ago, former quitted 11–20 years ago, former quitted >20 years ago, current with 1–15 cigarettes per day, current with 16–25 cigarettes per day, current with >25 cigarettes per day, current with pipe/cigar or occasional cigarette use, missing), education (up to high school, university graduate, missing), BMI (in quintiles, missing), physical activity (inactive, moderate inactive, moderate active, active, missing), diabetes status (no, yes, missing), energy from non-alcohol sources (continuously in kcs) and hormone replacement therapy (never, former, current, missing), use of oral contraceptives (never, former, current, missing), age at menarche (<12, 12, 13, 14, ≥15, missing), number of full-term pregnancies (0, 1, 2, 3, 4, ≥4, missing) and menopausal status in women (premenopausal, perimenopausal, postmenopausal). Missing values were assigned to separate
categories for smoking status (4%), education (3.6%), BMI (0.8%), physical activity (8.8%), diabetes (3.5%), hormone replacement therapy (10.8%), oral contraceptives (3.2%), age at menarche (2.3%) and full-term pregnancies (5.8%) — and missing indicators were used in the statistical models. Analyses that excluded participants with missing values for any of these covariates, and analyses that included further adjustments for currently having a paid employment, waist circumference, hip circumference, waist to hip ratio, self-reported personal history of thyroid diseases and infertility problems gave very similar results and are not presented here. When we further adjusted the lifetime alcohol consumption models for an indicator variable for participants who quitted alcohol drinking and for time since alcohol quitting to deal with the potential existence of former drinkers who quitted drinking because of an illness (Shaper et al, 1988), the results remained very similar and are not presented.

Baseline and average lifetime consumption of total alcohol were modelled primarily as categorical variables based on the distribution of intake in EPIC (0, 0.1–4.9, 5–14.9, ≥ 15 g per day) after evaluating non-parametric lowess plots of alcohol on thyroid cancer risk for non-linearity. Alcohol consumption of 0.1–4.9 g per day was used as the reference category in all statistical models to allow for comparisons with the non-consumer category. In addition, non-consumers might be a biased group as some participants may have stopped drinking due to ill health. However, when different cutpoints of alcohol consumption were used (0, 0.1–4.9, 5–14.9, 15–29.9, ≥ 30 or 0, 0.1–2.9, 3–9.9, 10–19.9, ≥ 20 g per day or quartiles based on the distribution in the whole cohort or in each EPIC centre) or when the non-consumers were the reference category, the results were very similar and are not presented. Alcohol consumption was also evaluated using a continuous variable per 10 g per day or 3 g per day, depending upon the range of intake of each alcoholic beverage, after adjusting for consumer vs non-consumer status using an indicator variable or after performing analyses only among consumers. Alcohol consumption of 10 g per day equals approximately to a small glass of wine (100 ml), a can of beer (330 ml) or a shot of spirit (30 ml). Separate analyses were performed by type of alcohol consumption (beer, wine, spirits) after mutually adjusting each time for energy obtained from the other two types of beverages. Non-consumers were defined here as participants who did not consume the alcoholic beverage under evaluation, but could consume other alcoholic beverages.

To evaluate whether the association of alcohol intake with thyroid cancer risk differed by age at recruitment (< 50 vs ≥ 50 years), sex, smoking status (never, former, current smokers), BMI (< 25 vs ≥ 25 kg m⁻²) and diabetes (no vs yes), interaction terms were incorporated in the multivariable models and its significance assessed with Wald tests. Country-specific analyses were also performed, and heterogeneity of associations across countries (and by type of alcoholic beverage) were assessed using Cochran’s Q-test and the I² metric of inconsistency (Higgins et al, 2003). A sensitivity analysis was conducted excluding the first two years of follow-up to limit the likelihood that the observed associations were due to change of alcohol consumption produced by extant cancers, but the results were very similar to the main analysis and are not shown. All P-values (P) were two-sided and all analyses were performed using STATA version 12 (College Station, TX, USA).

Table 1 describes the distribution of participant characteristics at recruitment by country in the EPIC study. The mean age at enrolment in the cohort was 51 years and 70% of the participants were women. The majority of the 556 differentiated thyroid carcinoma cases, 90% (n = 499) of which occurred in women, were identified in France (n = 202) followed by Italy (n = 82) and Germany (n = 79). Of the 477 263 total participants, 14% were non-consumers of alcohol at baseline (17% in women and 7% in men), and 25% consumed 15 or more grams of alcohol per day (16% in women and 45% in men), a percentage that ranged from 1% in Norway (100% of Norwegian participants were women) to 46% in Denmark (52% of Danish participants were women). The mean baseline alcohol consumption among consumers was 13.5 g per day (9.5 g per day in women and 21.8 g per day in men), whereas it was almost 14 g per day when alcohol consumption during lifetime was considered. Overall, the female participants in EPIC had a low-to-moderate alcohol consumption with very few heavy drinkers in the data set (only 5% of the female population had alcohol intake of >33.5 g per day and 1% of the population had intake of >56.9 g per day at recruitment). Men consumed on average more alcohol than women with ~25% consuming more than 31 g per day at recruitment.

Table 2 presents sex-specific frequencies of selected baseline characteristics by categories of baseline alcohol intake adjusted for country and age at recruitment. Compared with women consuming no alcohol, alcohol consumers had on average a higher level of education, were more likely to be current or ever smokers, were more physically active, were more likely to be ever users of hormone replacement therapy and oral contraceptives, were less likely to be postmenopausal and have diabetes and were on average leaner. These associations generally increased linearly with increasing alcohol consumption. Similar but smaller in magnitude differences were observed among men with the exception of mean BMI, which was similar across alcohol consumption categories.

Table 3 reports hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations of baseline and lifetime alcohol intake with differentiated thyroid carcinoma risk. Compared with men and women consuming 0.1–4.9 g of alcohol per day at recruitment, individuals consuming 15 or more grams per day had a 24% lower risk of differentiated thyroid carcinoma (HR = 0.76; 95% CI = 0.60–0.97) in age, sex and centre stratified models. Further adjustment for smoking, education, BMI, physical activity, diabetes, energy from non-alcohol sources, hormone replacement therapy, oral contraceptives, age at menarche, number of full-term pregnancies and menopausal status yielded an identical association (HR = 0.77; 95% CI = 0.60–0.98). Non-consumers of alcohol at recruitment were at a similar risk for thyroid carcinoma (HR = 0.97; 95% CI = 0.76–1.25) compared with consumers of 0.1–4.9 g per day. For every 10 g of alcohol consumed per day among consumers, the risk of thyroid carcinoma was lowered by 9% (HR = 0.91; 95% CI = 0.84–0.98). Very similar and statistically significant associations were observed for intake of alcohol from wine (HR per 10 g per day among consumers = 0.91 (0.82–0.99)). The risk estimates were smaller and not statistically significant for beer (HR per 3 g per day among consumers = 0.96; 95% CI = 0.90–1.03) and spirits intake (HR per 3 g per day among consumers = 0.99; 95% CI = 0.89–1.10), but overall the associations by type of alcoholic beverage did not differ from each other (P-heterogeneity = 0.38; I² = 0%)

When analyses were performed for lifetime alcohol intake, similar associations with the alcohol at baseline analyses were observed, but the risk estimates for total alcohol and alcohol from wine intake and thyroid carcinoma risk were attenuated and were not statistically significant anymore (Table 3). The HR per 10 g per day of total lifetime alcohol intake among consumers was 0.93 (95% CI = 0.84–1.02). Moreover, similar results were observed for baseline and lifetime alcohol intake and risk of papillary thyroid carcinoma (Supplementary Table 1) as well as by thyroid carcinoma stage (Supplementary Tables 2 and 3).

No statistically significant interactions were observed for total baseline or lifetime alcohol consumption and thyroid cancer risk for non-linearity. Alcohol consumption of 0.1–4.9 g per day was used as the reference category in all statistical models to allow for comparisons with the non-consumer category. In addition, non-consumers might be a biased group as some participants may have stopped drinking due to ill health. However, when different cutpoints of alcohol consumption were used (0, 0.1–4.9, 5–14.9, 15–29.9, ≥ 30 or 0, 0.1–2.9, 3–9.9, 10–19.9, ≥ 20 g per day or quartiles based on the distribution in the whole cohort or in each EPIC centre) or when the non-consumers were the reference category, the results were very similar and are not presented. Alcohol consumption was also evaluated using a continuous variable per 10 g per day or 3 g per day, depending upon the range of intake of each alcoholic beverage, after adjusting for consumer vs non-consumer status using an indicator variable or after performing analyses only among consumers. Alcohol consumption of 10 g per day equals approximately to a small glass of wine (100 ml), a can of beer (330 ml) or a shot of spirit (30 ml). Separate analyses were performed by type of alcohol consumption (beer, wine, spirits) after mutually adjusting each time for energy obtained from the other two types of beverages. Non-consumers were defined here as participants who did not consume the alcoholic beverage under evaluation, but could consume other alcoholic beverages.

To evaluate whether the association of alcohol intake with thyroid cancer risk differed by age at recruitment (< 50 vs ≥ 50 years), sex, smoking status (never, former, current smokers), BMI (< 25 vs ≥ 25 kg m⁻²) and diabetes (no vs yes), interaction terms were incorporated in the multivariable models and its significance assessed with Wald tests. Country-specific analyses were also performed, and heterogeneity of associations across countries (and by type of alcoholic beverage) were assessed using Cochran’s Q-test and the I² metric of inconsistency (Higgins et al, 2003). A sensitivity analysis was conducted excluding the first two years of follow-up to limit the likelihood that the observed associations were due to change of alcohol consumption produced by extant cancers, but the results were very similar to the main analysis and are not shown. All P-values (P) were two-sided and all analyses were performed using STATA version 12 (College Station, TX, USA).
Alcohol consumption and differentiated thyroid carcinoma

The evidence for an association between alcohol consumption and risk of differentiated thyroid carcinoma in men is sparse, because this disease is much more common among women. In EPIC, we observed that moderate alcohol consumption at baseline or during the lifetime was associated with a lower but not statistically significant risk of differentiated thyroid carcinoma in men. Studies that have reported results in men and women have generally not observed significantly different findings by sex (Galanti et al., 1997; Guignard et al., 2009; Meinhold et al., 2009; Kabat et al., 2012; Kitahara et al., 2012), in agreement with our findings. Moreover, other studies have also not observed great differences in the associations of alcohol and thyroid carcinoma by type of alcoholic beverage, by thyroid carcinoma histology, by age, BMI or smoking status at recruitment (Galanti et al., 1997; Allen et al., 2009; Meinhold et al., 2009; Kabat et al., 2012; Kitahara et al., 2012), in agreement with findings in EPIC.

The mechanisms explaining the potential link between alcohol consumption and differentiated thyroid carcinoma risk are not well known and are potentially complex. Some studies have described thyroid dysfunction in alcoholic individuals, and have suggested either a direct toxic effect of alcohol on the thyroid or a disturbance on the hypothalamic–pituitary–thyroid axis (Hegedus et al., 1988; Zoeller et al., 1996). However, the potential effects of low-to-moderate alcohol consumption on the thyroid are much less studied and should be considered speculative. Alcohol metabolism results in generation of free radicals, which has been hypothesised to induce oxidative stress in tissues poorly metabolising alcohol, such as the thyroid, and subsequently lead to hypothalamic–pituitary–thyroid axis dysfunction and reduction of peripheral thyroid hormone concentrations (Valeix et al., 2008). However, a recent nested case–control study in EPIC did not find an association between pre-diagnostic concentrations of total or free T3 and T4 with differentiated thyroid carcinoma risk, although Tg and TSH concentrations were significantly associated with the disease in a positive and negative manner, respectively (Rinaldi et al., 2014).

The present study has a number of strengths, including its prospective nature that precludes reverse causation to a large extent, and the large size of the EPIC cohort that gave rise to the largest number of differentiated thyroid carcinoma cases to date by any single cohort study. In addition, information on the histological subtype and stage of thyroid cancer and on drinking habits at recruitment and over lifetime as well as data on a wide

DISCUSSION

In this large prospective study involving 477 263 participants and 556 incident differentiated thyroid carcinoma cases, we observed that moderate alcohol intake at recruitment was associated with a statistically significant lower risk of thyroid carcinoma. These findings did not materially differ by whether baseline or lifetime alcohol consumption was considered, although the risk estimates for lifetime alcohol and thyroid carcinoma were not nominally statistically significant, by type of alcoholic beverage, by thyroid carcinoma histology and stage, or according to age, sex, BMI, smoking status and diabetes.

In parallel to our findings, several large cohort (Galanti et al., 1997; Navarro Silvera et al., 2005; Allen et al., 2009; Meinhold et al., 2009; Kabat et al., 2012; Kitahara et al., 2012) and case–control (Rossing et al., 2000; Mack et al., 2003) studies have also reported suggestive inverse associations for moderate alcohol intake at recruitment and risk of thyroid carcinoma. The Million Women Study enrolled 1 280 296 women in the United Kingdom, 491 of recruitment and risk of thyroid carcinoma. The Million Women Study enrolled 1 280 296 women in the United Kingdom, 491 of

Table 1. Distribution of participant characteristics at recruitment in the EPIC cohort by country

| Characteristic                     | All          | Denmark | France | Germany | Greece | Italy | Netherlands | Norway | Spain | Sweden | UK          |
|-----------------------------------|--------------|---------|--------|---------|--------|-------|-------------|--------|-------|--------|-------------|
| Mean age, years                   | 50.1         | 50.5    | 50.7   | 50.1    | 50.2   | 50.4  | 50.1        | 50.1   | 49.8  | 50.4   | 50.0        |
| Female, n (%)                     | 535 018 (70.2)| 527 138 (68.6)| 532 381 (66.6)| 527 098 (63.4)| 532 416 (63.5)| 528 169 (64.6)| 520 956 (62.7)| 524 206 (62.7)| 526 656 (62.7)| 528 010 (62.7)| 532 014 (64.3) |
| Person years                      | 54 704       | 52 661 | 54 704 | 54 704  | 54 704 | 54 704 | 54 704      | 54 704 | 54 704 | 54 704 | 54 704      |
| No. of cases, n                   | 556          | 526     | 54 704 | 52 661  | 54 704 | 54 704 | 54 704      | 54 704 | 54 704 | 54 704 | 54 704      |
| Mean, g per d*                    | 13.5         | 12.7    | 12.7   | 12.7    | 12.7   | 12.7  | 12.7        | 12.7   | 12.7  | 12.7   | 12.7        |

**Baseline alcohol intake, n (%)**

| No-consumer | Non-consumer | 0.1–4.9 | 5.0–14.9 | ≥15 | Mean, g per d* |
|-------------|-------------|---------|----------|-----|---------------|
| Mean age, years | 50.1 | 50.1 | 50.1 | 50.1 | 50.1 |
| Female, n (%) | 535 018 (70.2) | 527 138 (70.0) | 532 381 (66.6) | 527 098 (63.4) | 532 416 (63.5) |
| Person years | 54 704 | 54 704 | 54 704 | 54 704 | 54 704 |
| No. of cases, n | 556 | 526 | 54 704 | 52 661 | 54 704 |
| Mean, g per d* | 13.5 | 12.7 | 12.7 | 12.7 | 12.7 |

**Lifet ime alcohol intake, n (%)**

| No-consumer | Non-consumer | 0.1–4.9 | 5.0–14.9 | ≥15 | Mean, g per d* |
|-------------|-------------|---------|----------|-----|---------------|
| Mean age, years | 50.1 | 50.1 | 50.1 | 50.1 | 50.1 |
| Female, n (%) | 535 018 (70.2) | 527 138 (70.0) | 532 381 (66.6) | 527 098 (63.4) | 532 416 (63.5) |
| Person years | 54 704 | 54 704 | 54 704 | 54 704 | 54 704 |
| No. of cases, n | 556 | 526 | 54 704 | 52 661 | 54 704 |
| Mean, g per d* | 13.5 | 12.7 | 12.7 | 12.7 | 12.7 |

**Table 1. Distribution of particip ant characteristics at recruitment in the EPIC cohort by country**

Abbreviations: EPIC – European Prospective Investigation into Cancer and Nutrition; UK – United Kingdom; NA – not available.

*Mean values of alcohol consumption only among alcohol consumers.

www.bjcancer.com | DOI:10.1038/bjc.2015.280

843
Table 3. Association of alcohol intake and differentiated thyroid carcinoma in the EPIC cohort

| Intake at baseline | Average lifetime intakea |
|--------------------|---------------------------|
|                     | Cases/cohort HRb (95% CI) | Cases/cohort HRc (95% CI) |
| **Total alcohol (g per day)** | | |
| 0                  | 98/66.566 0.98 (0.76–1.26) | 81/37.868 1.16 (0.89–1.52) |
| 0.1–4.9           | 224/164.336 1.00 (reference) | 201/120.525 1.00 (reference) |
| 5–14.9           | 217/127.393 0.76 (0.61–0.94) | 125/109.377 0.86 (0.68–1.08) |
| ≥15              | 107/118.412 0.76 (0.60–0.97) | 76/94.946 0.90 (0.68–1.21) |
| Per 10 g per dayd | 458/410.141 0.91 (0.84–0.98) | 402/324.848 0.93 (0.84–1.02) |
| **Alcohol from wine (g per day)** | | |
| 0                  | 124/98.185 0.95 (0.75–1.21) | 102/63.771 1.07 (0.83–1.38) |
| 0.1–4.9           | 224/194.805 1.00 (reference) | 232/161.738 1.00 (reference) |
| 5–14.9           | 116/116.785 0.80 (0.63–0.99) | 110/91.736 0.94 (0.74–1.19) |
| ≥15              | 72/66.932 0.74 (0.56–0.97) | 112/159.462 0.81 (0.56–1.17) |
| Per 10 g per dayd | 458/410.141 0.90 (0.82–0.99) | 402/324.848 0.96 (0.84–1.09) |
| **Alcohol from beer (g per day)** | | |
| 0                  | 321/213.960 1.10 (0.88–1.38) | 255/150.311 1.01 (0.79–1.28) |
| 0.1–0.9           | 118/89.139 1.00 (Reference) | 109/70.825 1.00 (Reference) |
| 1.0–2.9           | 54/71.766 0.77 (0.55–1.07) | 60/55.400 0.97 (0.70–1.34) |
| ≥3               | 63/101.840 0.90 (0.65–1.26) | 59/86.180 1.06 (0.74–1.53) |
| Per 3 g per d     | 458/410.141 0.96 (0.90–1.03) | 402/324.848 0.99 (0.92–1.07) |
| **Alcohol from spirits (g per day)** | | |
| 0                  | 384/273.418 1.10 (0.86–1.41) | 312/179.769 1.27 (0.97–1.66) |
| 0.1–0.9           | 106/102.921 1.00 (Reference) | 79/63.692 1.00 (Reference) |
| 1.0–2.9           | 38/44.975 0.89 (0.61–1.29) | 52/55.831 1.17 (0.82–1.68) |
| ≥3               | 28/55.393 0.82 (0.53–1.27) | 40/64.424 1.25 (0.82–1.91) |
| Per 3 g per d     | 458/410.141 1.00 (0.90–1.10) | 402/324.848 0.92 (0.81–1.03) |

P-heterogeneity by type of beveragee, f: 0.38, 0%; 0.42, 0%

Abbreviations: EPIC = European Prospective Investigation into Cancer and Nutrition; HR = hazard ratio; CI = confidence interval.

This information was missing for participants from the EPIC centres of Naples, Bihoven, Umea, Malmo and Norway.

*From Cox proportional hazard models stratified by centre and age at recruitment; alcohol intake of one alcoholic beverage is mutually adjusted for the intake of the other two beverages.

†From Cox proportional hazard models stratified by centre and age at recruitment and adjusted for cigarette smoking intensity, education, body mass index, physical activity, diabetes, energy from non-alcoholic sources, hormone replacement therapy, oral contraceptives, age at menarche, number of full-term pregnancies and menopausal status; alcohol intake of one alcoholic beverage is mutually adjusted for the intake of the other two beverages.

‡Among consumers of alcoholic beverages only. When we performed analyses including both consumers and non-consumers of alcoholic beverages but after adjusting for being a consumer or not, the results were identical.

§This group includes participants who did not consume wine, but consumed other alcoholic beverages.

‖This group includes participants who did not consume beer, but consumed other alcoholic beverages.

¶This group includes participants who did not consume spirits, but consumed other alcoholic beverages.

Table 2. Country and age-adjusted participant characteristics by categories of baseline alcohol intake and sex in the EPIC cohorta

| Characteristics | Non-consumers | 0.1–4.9 | 5.0–14.9 | ≥15 |
|----------------|--------------|--------|---------|-----|
| **Women (n = 335 018)** | | | | |
| Mean age (s.d.), years | 51.8 (9.9) | 49.6 (9.9) | 50.1 (9.9) | 51.2 (9.9) |
| University graduate, % | 12.1 | 19.0 | 26.0 | 29.4 |
| Current smoker, % | 18.8 | 17.5 | 18.3 | 27.6 |
| Ever smoker, % | 34.2 | 40.6 | 45.8 | 56.8 |
| Physically active, % | 23.5 | 32.9 | 39.7 | 43.0 |
| Ever hormone replacement therapy users, % | 17.4 | 23.2 | 25.5 | 27.6 |
| Ever oral contraceptive users, % | 42.0 | 57.6 | 65.9 | 69.2 |
| Parous, % | 90.3 | 87.9 | 85.4 | 84.1 |
| Postmenopausal (naturally or surgically), % | 45.4 | 42.3 | 39.3 | 38.1 |
| Diabetes, % | 3.6 | 2.0 | 1.3 | 1.3 |
| Mean body mass index (s.d.), kg m² | 26.6 (4.14) | 25.2 (4.13) | 24.6 (4.12) | 24.4 (4.15) |
| Mean energy from non-alcohol (s.d.), kcal per day | 1811 (554) | 1847 (553) | 1895 (552) | 1913 (555) |
| **Men (n = 142 245)** | | | | |
| Mean age (s.d.), years | 53.3 (9.9) | 50.7 (9.9) | 51.3 (9.9) | 51.9 (9.9) |
| University graduate, % | 15.3 | 22.4 | 29.7 | 29.9 |
| Current smoker, % | 30.2 | 22.0 | 23.4 | 33.8 |
| Ever smoker, % | 63.7 | 55.2 | 60.3 | 73.4 |
| Physically active, % | 41.7 | 46.0 | 48.9 | 52.2 |
| Diabetes, % | 4.9 | 3.4 | 2.5 | 2.6 |
| Mean body mass index (s.d.), kg m² | 26.8 (4.12) | 26.3 (4.12) | 26.3 (4.12) | 26.7 (4.14) |
| Mean energy from non-alcohol (s.d.), kcal per day | 1811 (552) | 1847 (552) | 1895 (554) | 2322 (554) |

Abbreviations: EPIC = European Prospective Investigation into Cancer and Nutrition; s.d. = standard deviation.

aCountry and age at recruitment-adjusted means with standard deviations are presented for continuous variables and percentage for categorical variables using linear and logistic regression models, respectively.
Alcohol consumption and differentiated thyroid carcinoma

The table below shows the association of alcohol intake (per 10 g per day among consumers) and differentiated thyroid carcinoma by subgroups in the EPIC cohort.

| Subgroups | Cases/cohort | HR \(^b\) (95% CI) | Cases/cohort | HR \(^b\) (95% CI) |
|-----------|--------------|---------------------|--------------|---------------------|
| **Country** | | | | |
| Denmark  | 22/53 749 | 1.02 (0.81-1.27) | 22/52 988 | 0.97 (0.66-1.43) |
| France  | 174/57 717 | 0.91 (0.81-1.03) | 166/56 327 | 0.92 (0.77-1.10) |
| Germany | 75/46 283 | 0.79 (0.62-0.99) | 79/47 774 | 0.84 (0.65-1.09) |
| Greece | 17/19 526 | 1.04 (0.76-1.41) | 17/20 331 | 0.71 (0.41-1.22) |
| Italy | 63/37 035 | 0.96 (0.81-1.13) | 57/34 405 | 0.99 (0.81-1.22) |
| Norway | 27/27 886 | 0.54 (0.15-1.99) | NA | NA |
| Spain | 23/24 628 | 1.06 (0.75-1.50) | 28/29 332 | 1.08 (0.92-1.27) |
| Sweden | 18/41 850 | 0.77 (0.35-1.67) | NA | NA |
| The Netherlands | 11/30 728 | 0.11 (0.02-0.81) | 7/13 570 | 0.96 (0.35-2.64) |
| United Kingdom | 27/70 739 | 0.84 (0.54-1.29) | 26/70 121 | 0.79 (0.50-1.25) |

**Age at recruitment (years)**

| <50 | 222/175 102 | 0.90 (0.80-1.02) | 191/125 040 | 0.86 (0.73-1.00) |
| ≥50 | 236/235 039 | 0.91 (0.82-1.01) | 211/191 352 | 0.97 (0.87-1.09) |

**Sex**

| Male | 52/132 480 | 0.94 (0.82-1.09) | 46/102 326 | 0.94 (0.82-1.07) |
| Female | 406/277 661 | 0.89 (0.81-0.98) | 356/214 066 | 0.91 (0.80-1.04) |

**Body mass index**

| <25 kg m \(^{-2}\) | 259/210 776 | 0.88 (0.79-0.99) | 223/160 200 | 0.88 (0.75-1.03) |
| ≥25 kg m \(^{-2}\) | 199/199 365 | 0.93 (0.84-1.04) | 179/156 192 | 0.96 (0.85-1.08) |

**Smoking status**

| Never smoker | 244/192 158 | 0.83 (0.72-0.95) | 223/155 952 | 0.80 (0.66-0.98) |
| Former smoker | 118/115 574 | 0.90 (0.77-1.03) | 104/88 406 | 0.99 (0.87-1.14) |
| Current smoker | 84/94 199 | 0.99 (0.87-1.12) | 66/67 058 | 0.92 (0.77-1.10) |

**Diabetes**

| No | 440/386 254 | 0.90 (0.83-0.98) | 392/301 062 | 0.93 (0.84-1.02) |
| Yes | 8/9353 | 1.17 (0.82-1.66) | 8/8026 | 0.97 (0.64-1.46) |

Abbreviations: EPIC = European Prospective Investigation into Cancer and Nutrition; HR = hazard ratio; CI = confidence interval; NA = not applicable.

This information was missing for participants from the EPIC centres of Naples, Bilthoven, Umea, Malmo, and Norway.

From Cox proportional hazard models stratified by centre and age at recruitment and adjusted for cigarette smoking intensity, education, body mass index, physical activity, diabetes, energy from non-alcohol sources, hormone replacement therapy, oral contraceptives, age at menarche, number of full-term pregnancies and menopausal status.

**Table 4. Association of alcohol intake (per 10 g per day among consumers) and differentiated thyroid carcinoma by subgroups in the EPIC cohort.**

range of potential confounders is important and unique aspects of this study.

However, the study also has limitations. First, most women in the EPIC cohort, and in most other published epidemiological studies, were consuming low to moderate amounts of alcohol at enrolment or over their lifetimes, which did not allow investigating the association of heavy sustained drinking on subsequent risk of thyroid carcinoma. Second, information on alcohol consumption at baseline and over the lifetime was self-reported, but due to the prospective nature of the study this is likely to lead to non-differential misclassification (by thyroid carcinoma cases and non-cases) and bias, if any, our results towards the null. However, the information on alcohol consumption at recruitment in EPIC has been shown to be adequately reliable and valid compared with repeat food frequency questionnaires and multiple 24-h diet recalls (Kaaks et al, 1997). Third, data on ionizing radiation exposure and medical history of benign thyroid diseases, the most well-established risk factors for thyroid cancer were not available in EPIC and confounding due to these variables could not be assessed. However, adjustment for radiation and benign thyroid conditions in a prior publication had little influence on the associations (Kitahara et al, 2012). In addition, all of our risk estimates were adjusted for several confounding factors with relatively small difference to the risk estimates compared with unadjusted models. Besides that we cannot rule out the possibility of residual confounding by other unmeasured factors. Finally, individuals with a healthy lifestyle who may consume little or no alcohol might be prone to have their thyroid examined or removed surgically, and thus maybe have an incidental finding of a small localised thyroid cancer without clinical relevance, which could explain the weak inverse association observed in this study. However, this potential detection bias is unlikely to have driven our findings, because risk estimates did not differ between analyses for localised and advanced thyroid carcinomas.

In conclusion, our prospective study provides some support to the hypothesis that moderate alcohol consumption may be associated with a lower risk of differentiated thyroid carcinoma. However, more studies are needed to fully characterise the nature and mechanisms underlying this association. Given that many studies have reported an increased risk of various forms of cancer with alcohol intake, the findings of this study do not change the current public health recommendation that if alcoholic beverages are consumed, consumption should be limited to no more than two drinks a day for men and one drink a day for women (World Cancer Research Fund/American Institute for Cancer Research, 2007).
The coordination of EPIC is financially supported by the European Commission (DG-SANCO) and the International Agency for Research on Cancer. The national cohorts are supported by the Danish Cancer Society (Denmark); the Ligue Contre le Cancer, Société 3M, Mutuelle Générale de l’Education Nationale, Institut National de la Santé et de la Recherche Medicale (France); the Deutsche Krebshilfe, Deutsches Krebsforschungszentrum and Federal Ministry of Education and Research (Germany); the Hellenic Health Foundation (Greece); the Italian Association for Research on Cancer (AIRC) and National Research Council (Italy); the Dutch Ministry of Public Health, Welfare and Sports (VWS), Netherlands Cancer Registry (NKR), LRK Research Funds, Dutch Prevention Funds, Dutch ZON (Zorg Onderzoek Nederland), World Cancer Research Fund (WCRF); the Statistics Netherlands (The Netherlands); the Norwegian Cancer Society (Norway); the Health Research Fund (FIS), Regional Governments of Andalucia, Asturias, Basque Country, Murcia and Navarra, ISCIII RETIC (RD06/0020) (Spain); the Swedish Cancer Society, Swedish Scientific Council and Regional Government of Skåne and Västerbotten, Fundacion Federico SA (Sweden); the Cancer Research UK, Medical Research Council (United Kingdom).

The authors declare no conflict of interest.

REFERENCES

Allen NE, Beral V, Casabonne D, Kan SW, Reeves GK, Brown A, Green J, Davies L, Welch HG (2006) Increasing incidence of thyroid cancer in the United States from 1950 to 1995 observed in eight European countries participating in the European Investigation into Cancer and Nutrition (EPIC). European Prospective Investigation into Cancer and Nutrition. Int J Epidemiol 26(1 Suppl): S26–S36.

Kabat GC, Kim MY, Wactawski-Wende J, Rohan TE (2012) Smoking and alcohol consumption in relation to risk of thyroid cancer in postmenopausal women. Cancer Epidemiol Biomarkers Prev 21(4): 335–340.

Iribarren C, Haselkorn T, Tekawa IS, Friedman GD (2001) Cohort study of thyroid cancer in a San Francisco Bay area population. Int J Cancer 93(5): 745–750.

Kaufman S, Silimani N, Riboli E (1997) Pilot phase studies on the accuracy of dietary intake measurements in the EPIC project: overall evaluation of results. European Prospective Investigation into Cancer and Nutrition. Int J Epidemiol 26(1 Suppl): S26–S36.

Kabat GC, Kim MY, Wactawski-Wende J, Rohan TE (2012) Smoking and alcohol consumption in relation to risk of thyroid cancer in postmenopausal women. Cancer Epidemiol Biomarkers Prev 21(4): 335–340.

Baker D, Zien, W., Hofldred TF, Han X, Ward MH, Sjodin A, Zhang Y, Bai Y, Zhu C, Guo G, Rothman N, Zhang Y (2009) International patterns and trends in thyroid cancer incidence, 1973–2002. Cancer Causes Control 20(5): 525–531.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

The authors declare no conflict of interest.

Iribarren C, Haselkorn T, Tekawa IS, Friedman GD (2001) Cohort study of thyroid cancer in a San Francisco Bay area population. Int J Cancer 93(5): 745–750.

Kaufman S, Silimani N, Riboli E (1997) Pilot phase studies on the accuracy of dietary intake measurements in the EPIC project: overall evaluation of results. European Prospective Investigation into Cancer and Nutrition. Int J Epidemiol 26(1 Suppl): S26–S36.

Kabat GC, Kim MY, Wactawski-Wende J, Rohan TE (2012) Smoking and alcohol consumption in relation to risk of thyroid cancer in postmenopausal women. Cancer Epidemiol Biomarkers Prev 21(4): 335–340.

Acknowledgements

The authors declare no conflict of interest.

References

Allen NE, Beral V, Casabonne D, Kan SW, Reeves GK, Brown A, Green J. Million Women Study C (2009) Moderate alcohol intake and cancer incidence in women. J Natl Cancer Inst 101(5): 296–305.

Balaubramaniam S, Ron E, Gridley G, Schneider AB, Brenner AV (2012) Association between benign thyroid and endocrine disorders and subsequent risk of thyroid cancer among 4.5 million U.S. male veterans. J Clin Endocrinol Metab 97(8): 2661–2669.

Dal Maso L, Lise M, Zambon P, Falcini F, Crocetti E, Serraino D, Girilli C, Zanetti R, Verrecchi M, Ferretti S, Stracci F, De Lisi V, Busco S, Tagliabue G, Budroni M, Tumino R, Giacomini A, Franceschi S, Group AW (2011) Incidence of thyroid cancer in Italy, 1991-2005: time trends and age-period-cohort effects. Ann Oncol 22(4): 957–963.

Davies L, Welch HG (2006) Increasing incidence of thyroid cancer in the United States, 1973–2002. JAMA 295(18): 2164–2167.

Franceschi S, Preston-Martin S, Dal Maso L, Negri E, La Vecchia C, Mack WJ, McTiernan A, Kolonel L, Mark SD, Mabuchi K, Jin F, Linos D, Lund E, McTiernan A, Mabuchi K, Negri E, Wingren G, Ron E (2003) A pooled analysis of case-control studies of thyroid cancer. IV. Benign thyroid diseases. Cancer Causes Control 10(6): 583–595.

Galanti R, Hallquist A, Jin F, Kolonel L, La Vecchia C, Levi F, Linos D, Lund E, McTiernan A, Mabuchi K, Negri E, Wingren G, Ron E (2003) A pooled analysis of case-control studies of thyroid cancer. IV. Benign thyroid diseases. Cancer Causes Control 10(6): 583–595.

Galanti MR, Hansson L, Bergstrom R, Wolk A, Hjartaker A, Lund E, Engeset D, Gonzalez CA, Barricarte A, Berglund G, Weinhall L, Mulligan A, Allen N, Ferrari P, Riboli E (2007) Trends in self-reported past alcoholic beverage consumption and ethanol intake from 1950 to 1995 observed in eight European countries participating in the European Investigation into Cancer and Nutrition (EPIC). Public Health Nutr 10(6b): 1297.

Mack WJ, Preston-Martin S, Bernstein L, Qian D (2002) Lifestyle and other risk factors for thyroid cancer in Los Angeles County females. Ann Epidemiol 12(6): 395–401.

Mack WJ, Preston-Martin S, Dal Maso L, Galanti R, Xiang M, Franceschi S, Hallquist A, Jin F, Kolonel L, La Vecchia C, Levi F, Linos D, Lund E, McTiernan A, Mabuchi K, Negri E, Wingren G, Ron E (2003) A pooled analysis of case-control studies of thyroid cancer: cigarette smoking and consumption of alcohol, coffee, and tea. Cancer Causes Control 14(8): 773–785.

Meinhold CL, Park Y, Stolzenberg-Solomon RZ, Hollenbeck AR, Schatzkin A (2009) Berrington de Gonzalez A (2009) Alcohol intake and risk of thyroid cancer in the NIH-AARP Diet and Health Study. Br J Cancer 101(9): 1630–1634.

Navarro Silvera SA, Miller AB, Rohan TE (2005) Risk factors for thyroid cancer: a prospective cohort study. Int J Cancer 116(3): 433–438.

Reynolds RM, Weir J, Stockton DL, Brewster DW, Sandeep TC, Strachan MW (2005) Changing trends in incidence and mortality of thyroid cancer in Scotland. Clin Endocrinol (Oxf) 62(2): 156–162.

Riboli E, Hunt KJ, Silimani N, Ferrari P, Norat T, Fahey M, Cherrone Di, Hemon B, Casagrande C, Vignat J, Overvad K, Tjonneland A, Clavel-Chapelon F, Thiebaut A, Wahrendorf J, Boeing H, Trichopoulos D, Trichopoulos A, Vines P, Palli D, Bueno-de-Mesquita HB, Peeters PH, Lund E, Engeset D, Gonzalez CA, Barricarte A, Berglund G, Hallmans G, Day NE, Key TJ, Kaaks R, Saracini R (2002) European Prospective Investigation into Cancer and Nutrition (EPIC): study populations and data collection. Public Health Nutr 5(6b): 1113–1124.

Rinaldi S, Plummer M, Biessy C, Tsilidis KK, Ostergaard JN, Overvad K, Tjonneland A, Klaarj J, Broun-Fromu-RC, Mc Lavel-Cheplon F, Dossus L, Kaaks R, Lukanova A, Boenig H, Trichopoulos A, Lagiou P, Dallou P, Dallou G, Tumino R, Vines P, Parino S, Bueno-de-Mesquita HB, Peeters PH, Wierdappas E, Lund E, Quiros JR, Agudo A, Molina E, Larranaga N, Navarro C, Ardanaz E, Hanjie J, Alquist M, Sandstrom M, Hennings J, Khaw KT, Schmidt J, Travis RC, Byrnes G, Scalbert A, Romieu I, Gunter M, Rivoli E, Franceschi S (2014) Thyroid-stimulating hormone, thyroglobulin, and thyroid hormones and risk of differentiated thyroid carcinoma: the EPIC study. J Natl Cancer Inst 106(6): dju097.

Rossing MA, Cushing KL, Voigt LF, Wicklund KG, Daling JR (2000) Risk of papillary thyroid cancer in women in relation to smoking and alcohol consumption. Epidemiology 11(1): 49–54.

Shaper AG, Wannamethee G, Walker M (1988) Alcohol and mortality in British men: explaining the U-shaped curve. Lancet 2(8623): 1267–1273.

Slusani N, Dehaverg G, Unwin I, Southgate DA, Vignat J, Skie G, Salvini S, Parpinel M, Moller A, Ireland J, Becker W, Farran A, Westenbrink S, et al. (2012) Alcohol consumption and differentiated thyroid carcinoma.
This work is published under the standard license to publish agreement. After 12 months the work will become freely available and the license terms will switch to a Creative Commons Attribution-NonCommercial-Share Alike 4.0 Unported License.

Supplementary Information accompanies this paper on British Journal of Cancer website (http://www.nature.com/bjc)