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The effect of occasional smoking on smoking-related cancers

In the European Prospective Investigation into Cancer and Nutrition (EPIC)

Bine Kjøller Bjerregaard · Ole Raaschou-Nielsen · Mette Sørensen · Kirsten Frederiksen · Anne Tjønneland · Sabine Rohrmann · Jakob Linseisen · Manuela M. Bergman · Heiner Boeing · Sabina Sieri · Domenico Palli · Rosario Tumino · Carlotta Sacerdote · H. Bas Bueno-de-Mesquita · Frederike L. Büchner · Inger Torhild Gram · Tonje Braaten · Eiliv Lund · Göran Hallmans · Åsa Ågren · Elio Riboli

Abstract

Objective Most studies on tobacco smoking have focused on daily-smokers. Occasional smokers, who have never smoked daily, have often been included in the reference group of never-smokers. We have investigated the association between occasional smoking and cancer of the bladder, kidney, pancreas, upper aerodigestive tract and lung.

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Methods The study population consisted of 158,488 persons, who provided information on occasional smoking, within the European Prospective Investigation into Cancer and Nutrition (EPIC), 780 of whom developed a smoking-related cancer. We used Cox proportional hazard model, stratified by gender and country to estimate incidence rate ratios (IRR) for smoking-related cancers.

Results The results suggest that occasional smokers have a higher risk of bladder cancer (IRR: 1.92, 95% confidence interval (CI) 0.93–3.98) and of the major smoking-related cancers combined (IRR: 1.24, 95% CI 0.80–1.94) than true never-smokers. Including occasional smokers in the reference group resulted in a lower risk estimate for former and current smokers.

Conclusions Occasional smoking should be discouraged.

Keywords Cancer · Cohort Study · Epidemiology · Tobacco smoke

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Abbreviations

IRR	Incidence rate ratio
CI	Confidence intervals
EPIC	European Prospective Investigation into Cancer and Nutrition
IARC	International Agency for Research on Cancer

Introduction

Smoking is a well-established cause of cancers of the bladder, kidney, pancreas, upper aero-digestive tract, lung and other cancers [1]. In most studies on tobacco smoking, where smoking status is defined in detail, ever-smokers are defined as persons who have ever smoked daily. Occasional-smokers, who have never smoked daily, have often been included in the reference group of never-smokers. Few studies have investigated the adverse health effects of occasional smoking: occasional smoking has been found to increase total- and cancer-mortality [2–4], to increase total and cardiovascular mortality among men [5] and to cause a reduced birth weight in children of occasionally smoking mothers [6].

We used the large European Prospective Investigation into Cancer and Nutrition (EPIC) cohort to estimate whether participants who reported to smoke occasionally, had a higher risk of one of the major smoking-related cancers than true never-smokers. Further, we investigated differences in relative risk estimates for former and current daily-smokers using two different reference groups: (1) true never-smokers (2) true never-smokers and occasional-smokers.

Materials and methods

Population

EPIC is a multi-center prospective cohort study consisting of 23 centers from Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden,

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and the UK. The methods have been reported in full by Riboli et al. (2002) [7]. In brief, the study populations were mostly aged 33–67 years and were mostly recruited from the general population residing in a specific geographical region. Eligible subjects who accepted to participate gave informed consent and completed lifestyle questionnaires. The lifestyle questionnaires included questions on education and socioeconomic status, occupation, previous illness, alcohol and tobacco consumption, and physical activity. In addition, in nine centres, never daily-smokers were asked about occasional smoking. In most centers diet was measured by country-specific, self-administered questionnaires, though some used interviewers.

In the five countries included in this study, Italy, the Netherlands, Germany, Sweden and Norway, follow-up was based on population cancer registries and medical records for self-reported cancer not found in the cancer registries (Germany) and mortality data were obtained from cancer registries, mortality registries or health departments at the regional or national level. For the current analysis participants were followed from study entry (1992–1998) until a primary cancer diagnosis, death, emigration or end of the follow-up period which occurred between 2000 and 2004, depending on the country. Cases were all participants diagnosed with a first primary cancer of the bladder, kidney (renal parenchyma or renal pelvis), pancreas, upper aero-digestive tract or lung, where strong smoking associations has been documented (denoted as “major smoking-related cancer”).

Current daily-smokers were defined as participants who smoked cigarettes, cigars or pipe daily at the time of inclusion. Former daily-smokers were participants who used to smoke cigarettes, cigars or pipe daily, but did not smoke daily at the time of inclusion. Occasional-smokers were defined as participants who smoked or had ever smoked cigarettes, cigars or pipe occasionally e.g., on social occasions or during a particular period of life, but never daily. Participants with missing or unknown smoking status were excluded (2,663 participants).

The analyses in the present study were based on information from the 158,488 participants from the nine EPIC centers where never smokers were asked about occasional smoking.

Statistical methods

The analyses were based on Cox proportional hazard models, in which age was defined as the follow-up variable. Through this, an optimal adjustment for the possible confounding effect of age is obtained. Time

under study was included as the time-dependent variable and was modeled by a linear spline with a boundary at 2 years after entry into the cohort study [8]. All models were stratified by gender and country. Two-sided 95% confidence intervals (CI) for the incidence rate ratio (IRR) were calculated based on Wald's test of the Cox regression parameter, that is, on the log rate ratio scale. In models adjusted for body mass index, alcohol consumption and intake of fruit and vegetables, baseline values were entered linearly in the Cox model. Educational level was adjusted for in five levels: no school, primary school, secondary school, professional or technical school, university degree.

Results

The average follow up time was 5.3 years. Overall, 65% of the included participants were female, who contributed 36% of the cancer cases. Adjustment for possible confounders resulted only in minor changes in the results (unadjusted results not shown).

Occasional-smokers had a non-significant 24% (95% CI -20–94%) higher risk of developing one of the major smoking-related cancer than true never-smokers (Table 1). Stratification by cancer site showed non-significantly increased risks for occasional-smokers of 92% (95% CI -7–298%) for bladder cancer, based on ten occasionally smoking cases (Table 1) and 30% (95% CI -41–186%) for kidney cancer, based on

eight occasionally smoking cases (data not shown). For cancer of the pancreas, upper aero-digestive tract and lung there were few occasionally smoking cases ($n \leq 3$). For both bladder cancer and the major smoking-related cancers, all risk estimates for current and former smokers were higher when compared to a reference group of true never-smokers than when compared to a reference group of true never-smokers and occasional-smokers combined (Table 1). Results showed a dose-response relationship between smoking intensity and risk of developing one of the major smoking-related cancers and there was no evidence of a no-effect level of smoking (Table 1).

Discussion

The present study suggests that occasional-smokers have a higher risk of developing one of the major smoking-related cancers than never-smokers. Further, the results indicate a higher risk for former and current daily-smokers when compared to true never-smokers than when compared to occasional-smokers and true never-smokers combined.

One of the strengths of the present study was the prospective design with low potential for recall and selection bias. A limitation of the study was that no information on smoking intensity and duration of occasional-smoking was available. In teenagers occasional smoking likely leads to daily smoking [9], but

Table 1 Effects of smoking status on the risk for cancer of the bladder, kidney, pancreas, upper aero-digestive tract and lung

Cigarette smoking status	Cancer of the bladder, kidney, pancreas, upper aero-digestive tract and lung						Bladder cancer			
	Number of cases	True never-smokers and occasional smokers as reference		True-never-smokers as reference		Number of cases	True never-smokers and occasional smokers as reference		True-never-smokers as reference	
		IRR ^a	CI ^b	IRR ^a	CI ^b		IRR ^a	CI ^b	IRR ^a	CI ^b
Never daily-smokers	139	1				39	1			
True never-smokers	115			1		29			1	
Occasional smokers	24			1.24	0.80–1.94	10			1.92	0.93–3.98
Former daily-smokers	237	1.62	1.30–2.02	1.68	1.33–2.12	62	1.34	0.88–2.05	1.53	0.96–2.42
Current daily-smokers	404									
≤2 cig/day	33	2.45	1.66–3.60	2.53	1.71–3.75	10	2.36	1.16–4.81	2.70	1.29–5.64
2–10 cig/day	99	3.14	2.41–4.08	3.24	2.47–4.26	19	2.13	1.22–3.73	2.42	1.35–4.34
10–16 cig/day	71	4.24	3.15–5.71	4.39	3.23–5.97	15	3.02	1.62–5.61	3.45	1.81–6.60
16–20 cig/day	93	5.41	4.11–7.13	5.59	4.20–7.43	13	2.74	1.43–5.25	3.10	1.58–6.08
>20 cig/day	108	7.01	5.36–9.19	7.26	5.49–9.62	23	4.82	2.77–8.40	5.52	3.07–9.93

^a IRR = Incidence rate ratio

^b CI = Confidence interval

Adjusted for intake of fruit and vegetables, body mass index, educational level and alcohol intake at recruitment

since most participants were never-daily smokers in their 50s at the time of the interview and since few persons start smoking daily at that age it is not likely that the occasional smokers in the present study started to smoke daily after the interview. Obtaining statistically significant risk estimates of weak effects requires high statistical power. Although the present study is large—with almost 800 cases—an even larger cohort, or a future meta-analysis of several studies, may be required to obtain statistically significant results.

In a majority of studies on smoking and cancer the focus is on daily smoking and though some studies include information on occasional-smokers and exclude these from the analysis, many studies use all participants who have never smoked daily as reference group. In the present study, removing the occasional-smokers from the reference group resulted in a higher risk estimate for former and current daily-smokers. The effect might be marginal in our study with only 6% occasional smokers, but in other studies it might be of considerable importance to consider occasional smokers as a separate group. In several recent studies the proportion of occasional smokers are as high as 15–25% [10–12]. The effect of smoking on the development of cancer and other diseases may therefore be underestimated in many studies.

Previous studies have shown relative risks of smoking-related cancers up to 2.5 for daily smoking intensities of 1–4 cigarettes/day [13–16], as well as effects of exposure to environmental tobacco smoke [17, 18]. It is, therefore, not surprising that we find suggestions of an effect of occasional smoking on the major smoking-related cancers. The few studies that have investigated the effects of occasional smoking indicate adverse health effects and occasional smoking should be discouraged [2–5, 19]. It is common for occasional-smokers not to perceive themselves as smokers and therefore they do not respond to traditional anti-smoking campaigns [10]. Anti-smoking campaigns aimed at occasional-smokers should be given high priority for two reasons: First, occasional smoking is a growing phenomenon thought to be a less lethal alternative to daily smoking [20]. Second, in adolescents, occasional smoking is the strongest predictor for later daily smoking. Preventing this transition would have a large personal and public health potential [9].

The indication in the present study that occasional smoking increases the risk of the major smoking-related cancers encourages more research into cancer risk in non-daily smokers, underlines the importance of a careful choice of reference group, and emphasizes the

need for anti-smoking campaigns aimed at occasional smokers.

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