

## RESEARCH ARTICLE

# Occupational Cooking and Risk of Uveal Melanoma: a Meta-analysis

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### Abstract

**Background:** Many observational studies have assessed the possible association between occupational cooking and uveal melanoma risk, but reported results are controversial. Our goal was to evaluate the association between occupational cooking and uveal melanoma risk by conducting a meta-analysis of observational studies. **Methods:** PubMed, EMBASE, and Web of Science were searched through June 2012 to identify all eligible studies. The pooled odds ratio (OR) with its 95% confidence interval (95% CI) was used to evaluate this association. Either a fixed- or a random-effects model were used to calculate pooled ORs. **Results:** Five case-control studies involving a total of 1,199 cases and 6,927 controls were included in the meta-analysis. Overall, occupational cooking was associated with an increased risk of uveal melanoma (OR: 1.81, 95% CI 1.33-2.46,  $P < 0.001$ ). Subgroup analysis by gender suggested occupational cooking was associated with increased risk of uveal melanoma in both men (OR: 2.16, 95% CI 1.06-4.40,  $P = 0.034$ ) and women (OR: 1.92, 95% CI 1.19-3.10,  $P = 0.008$ ). **Conclusion:** This meta-analysis suggests that occupational cooking is associated with an increased risk of uveal melanoma in both men and women.

**Keywords:** Occupational cooking - uveal melanoma - meta-analysis - gender

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### Introduction

Uveal melanoma is the most common primary intraocular malignancy, and its overall mortality rate remains high because of the frequent development of metastatic disease (Singh et al., 2011; Spagnolo et al., 2012). Although multiple epidemiologic reports have contributed to our understanding of the risk factors for uveal melanoma, the results remain inconsistent and the etiology of uveal melanoma remains poorly understood (Ehlers et al., 2006; Sato et al., 2008). Besides, to help generate the knowledge necessary to develop preventive methods, it is important to elucidate the etiology of this lethal disease (Couturier et al., 2012; Spagnolo et al., 2012). An improved understanding of this issue may have important public health and clinical implications given the possibility that some preventive interventions for occupational cooking might reduce the incidence of uveal melanoma. Cooking fumes may be responsible for the higher risk of cancer, and has been postulated as one risk factor of uveal melanoma (Ekpanyaskul et al., 2010; Santibanez et al., 2012). Several epidemiologic studies have investigated the link between occupational cooking and risk of uveal melanoma, but the magnitudes of the association varied among those studies (Guenel et al., 2001; Stang et al., 2003; Lutz et al., 2005; Schmidt-Pokrzywniak et al., 2010; Behrens et al., 2011). With recently accumulating evidence, our goal, therefore, was

to evaluate the association between occupational cooking and risk of uveal melanoma by conducting a meta-analysis of observational studies.

### Materials and Methods

#### Search strategy

We attempted to follow the proposed MOOSE (Meta-Analysis of Observational Studies in Epidemiology) guidelines to report the present meta-analysis (Stroup et al., 2000). We searched the literature databases from 1966 to June 2012 using PubMed, EMBASE, and Web of Science with the following key words: occupation, occupational, cooking, or cook; uveal melanoma, eye cancer, eye melanoma, or uveal melanoma. No restrictions were imposed. In addition, we reviewed the reference lists of retrieved papers and recent reviews. When necessary, additional information was sought from the authors.

#### Study selection

We first performed an initial screening of titles or abstracts. A second screening was based on full-text review. Studies were considered eligible if they met the following criteria: 1) the study design was case-control study; 2) evaluate the association between occupational cooking and risk of uveal melanoma; and 3) Odds Ratio (OR) and the corresponding 95% confidence interval (95%CI) (or data to calculate them) were reported. We

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excluded studies that did not use standard epidemiologic methodology allowing for comparisons between cases and controls or did not supply enough information from which to calculate OR with the corresponding 95%CI.

**Data extraction**

Data extraction was then performed using a standardized data-collection form. We extracted any reported ORs for the association between occupational cooking and risk of uveal melanoma. If provided by the original studies, adjusted ORs were preferred over crude estimates. We also extracted study characteristics for each trial. Data were recorded as follows: first author’s last name; year of publication; country of origin; characteristics of study population and age at baseline; number of participants; and statistical adjustments for confounding factors. Two authors independently conducted the studies selection and data extraction, and any disagreements were resolved by discussion.

**Statistical analyses**

The pooled OR with its 95%CI was used to assess this association and an OR with a P value <0.05 was considered statistically significant. All meta-analyses were assessed for heterogeneity as a preliminary test. Heterogeneity across studies was tested by using the Q statistic (significance level at P <0.10) (Cochran, 1954) and the I<sup>2</sup> statistic, which is a quantitative measure of inconsistency across studies (significance level at I<sup>2</sup> > 50%) (Higgins et al., 2003). A random-effects model was used if the test of heterogeneity was significant (P<0.10) (DerSimonian et al., 1986), otherwise a fixed-effects model was used (Mantel et al., 1959). Subgroup analysis was performed by the gender. Potential publication bias was assessed by visual inspection of the Begg’s funnel plot (Begg et al., 1994). We also performed the Begg’s rank correlation test (Begg et al., 1994) and Egger’s linear regression test (Egger et al., 1997) at the P < 0.10 level of significance. All analyses were performed using STATA version 11.0 (StataCorp LP, College Station, Texas). A P value < 0.05 was considered statistically significant, except where otherwise specified.

**Results**

**Study characteristics**

We initially retrieved 15 unique citations from PubMed, Embase and Web of Science databases. Of these, the majority were excluded after the first screening based on abstracts or titles, mainly because they were reviews, case reports, or not relevant to our analysis. 9 full-text publications were preliminarily included into this meta-analysis (Ajani et al., 1992; Holly et al., 1996; Guenel et al., 2001; Monarrez-Espino et al., 2002; Stang et al., 2003; Lutz et al., 2005; Schmidt-Pokrzywniak et al., 2009; Schmidt-Pokrzywniak et al., 2010; Behrens et al., 2011). After full-text review of those 9 papers, 2 studies were excluded because they contained overlapping data (Monarrez-Espino et al., 2002; Schmidt-Pokrzywniak et al., 2009), and another studies excluded because they were lack of necessary data (Ajani et al., 1992; Holly et

al., 1996). Thus, five case-control studies involving a total of 1199 cases and 6927 controls were finally included into our meta-analysis (Guenel et al., 2001; Stang et al., 2003; Lutz et al., 2005; Schmidt-Pokrzywniak et al., 2010; Behrens et al., 2011). These studies were published between 2001 and 2011. All five studies were conducted in the Europe. The sizes of the samples ranged from 529 to 3364 (total 8126).

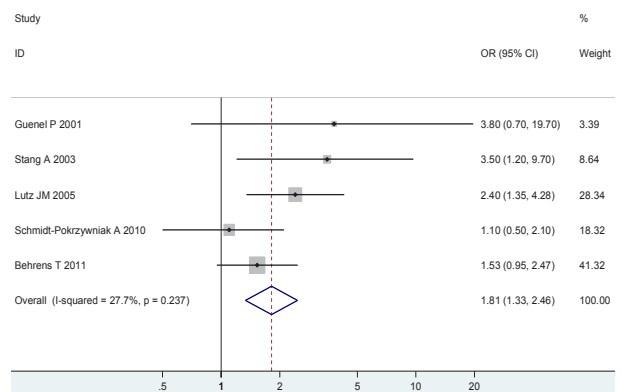
**Meta-analysis**

Among those five studies, only two studies reported significant association between occupational cooking and risk of uveal melanoma (Figure 1). There was no obvious heterogeneity among those five studies, thus the fixed-effects model was used to pool those results (I<sup>2</sup> = 27.7%, P = 0.237). Overall, occupational cooking was associated with increased risk of uveal melanoma (OR = 1.81, 95%CI 1.33-2.46, P < 0.001) (Figure 1).

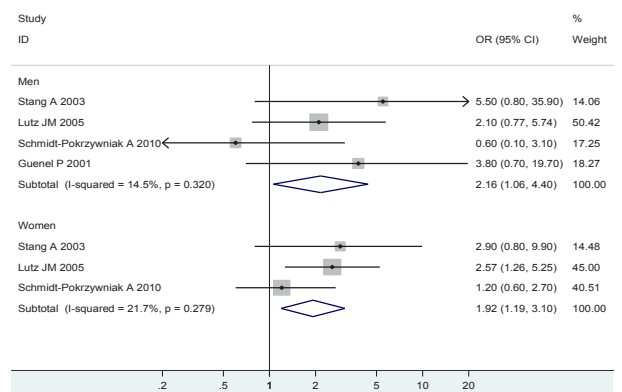
Subgroup analysis was performed by gender, and there was also no obvious heterogeneity among those studies in both the subgroup analysis of men (I<sup>2</sup> = 14.5%, P = 0.320) and the subgroup analysis of women (I<sup>2</sup> = 21.7%, P = 0.279), thus the fixed-effects model was used to pool those results. Subgroup analysis by gender suggested occupational cooking was associated with increased risk of uveal melanoma in both men (OR = 2.16, 95%CI 1.06-4.40, P = 0.034) and women (OR = 1.92, 95%CI 1.19-3.10, P = 0.008) (Figure 2).

**Publication bias**

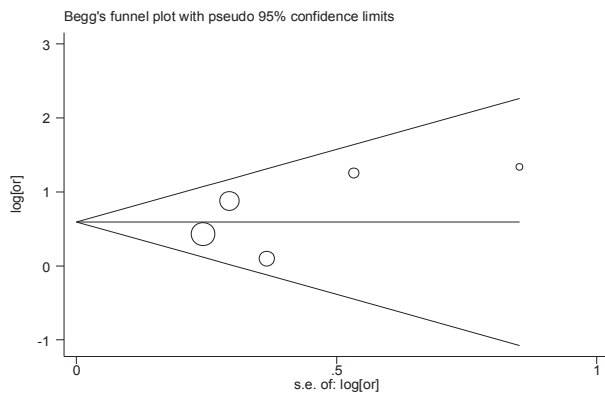
The potential publication bias was assessed by visual



**Figure 1. Meta-analysis of the Association Between Occupational Cooking and Risk of Uveal Melanoma**



**Figure 2. Meta-analysis of the Association Between Occupational Cooking and Risk of Uveal Melanoma in Men and Women**



**Figure 3. Begg's Funnel Plot Showed No Obvious Asymmetry**

inspection of the Begg's funnel plot. Though there was no obvious asymmetry of Begg's funnel plot (Figure 3), there were only five studies included into this meta-analysis, and it was hard to assess the risk of publication bias. The P value of Egger's test was 0.370, providing statistical evidence for the symmetry of Begg's funnel plot. Thus, there was low risk of publication bias in this meta-analysis.

## Discussion

To evaluate the association between occupational cooking and risk of uveal melanoma, we performed a meta-analysis of observational studies by searching PubMed, EMBASE, and the Web of Science. Five case-control studies involving a total of 1199 cases and 6927 controls were included into the meta-analysis (Guenel et al., 2001; Stang et al., 2003; Lutz et al., 2005; Schmidt-Pokrzywniak et al., 2010; Behrens et al., 2011). Overall, occupational cooking was associated with increased risk of uveal melanoma (OR = 1.81, 95%CI 1.33-2.46,  $P < 0.001$ ). Subgroup analysis by gender suggested occupational cooking was associated with increased risk of uveal melanoma in both men (OR = 2.16, 95%CI 1.06-4.40,  $P = 0.034$ ) and women (OR = 1.92, 95%CI 1.19-3.10,  $P = 0.008$ ). Besides, there was low risk of publication bias in this meta-analysis. Thus, this meta-analysis suggests that occupational cooking is associated with an increased risk of uveal melanoma in both men and women.

Uveal melanoma is the most common noncutaneous melanoma in the United States (Singh et al., 2011; Spagnolo et al., 2012). Despite the increase in treatment options, the mortality rate has not changed significantly, and has caused serious damage to human health (Singh et al., 2011; Spagnolo et al., 2012). As such, it is important to elucidate potentially modifiable causal factors for uveal melanoma, and make effective preventions. Epidemiologic studies have suggested ultraviolet exposure, cutaneous nevi, iris nevi, and several other host factors as risk factors of uveal melanoma (Shah et al., 2005; Weis et al., 2006; Weis et al., 2009). Besides, our meta-analysis further provides a new evidence suggesting occupational cooking as a risk factor of uveal melanoma.

In this meta-analysis, we found an increased risk of uveal melanoma in relation to the occupational cooking in both men and women. Several exposures of occupational cooking including carcinogenic cooking fumes, strong

light from incandescent ovens, infrared radiation and microwave might be relevant to the higher risk of uveal melanoma (Schmidt-Pokrzywniak et al., 2010; Ganesh et al., 2011). During the cooking, workers may expose to many cooking fumes, high radiation from microwaves, strong light from incandescent ovens, and infrared radiation (Yenugadhathi et al., 2009; Santibanez et al., 2012). Cooking fumes are produced and released into the environment when food is fried or grilled using cooking oil at high temperatures (Pan et al., 2008; Santibanez et al., 2012). The degradation of sugar, the pyrolysis of proteins and amino acids, and the degradation of fat during the high-temperature treatment of food can generate harmful degradation products, such as particulate matter (PM), polycyclic aromatic hydrocarbons (PAH), aromatic amines, and aldehydes (Pan et al., 2008; Santibanez et al., 2012). Those subjects may cause the reactive oxygen species in human body, and may further cause oxidative damage to nucleic acids, proteins, and lipids. Such damage has been suggested to be associated with aging, cancer, and other degenerative diseases (Pan et al., 2008; Schmidt-Pokrzywniak et al., 2010). Thus, Oxidative stress caused by cooking fumes may be implicated in the development of uveal melanoma (Pan et al., 2008; Schmidt-Pokrzywniak et al., 2010).

There were some potential limitations to this meta-analysis. This meta-analysis had only 5 studies which might result in a small meta-analysis. The relative total sample size of this meta-analysis may inevitably increase the risk of random error. Thus, further well-designed observational studies with large sample size are needed to identify this association between occupational cooking and increased risk of uveal melanoma. Besides, this meta-analysis combined data from different observational studies. The quality of the results from this meta-analysis depended on the quality of each individual study that was included in the analysis. Since observational studies are prone to biases and confounding factors when controls do not represent the base populations, prospective cohort studies are needed to assess this association between occupational cooking and increased risk of uveal melanoma more precisely.

Thus, this meta-analysis suggests that occupational cooking is associated with increased risk of uveal melanoma in both men and women. Besides, more well-designed observational studies with large sample size or prospective cohort studies are needed to identify this association between occupational cooking and uveal melanoma risk.

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The author(s) declare that they have no competing interests.

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