

LETTER to the EDITOR

Comparison of Apples with their Parts: Rethinking a Meta-analysis on the Association between Cooking and Uveal Melanoma Risk

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Dear Editor

We read with interest Ge et al. (2012) article entitled "Occupational Cooking and Risk of Uveal Melanoma: a Metaanalysis". We believe that this meta-analysis is helpful because a synthesis of the growing evidence of the association between cooking and uveal melanoma risk is overdue. Uveal melanoma is a rare disease and only a few consistent risk factors have been identified (Behrens et al., 2011; Epidemiologisches Krebsregister NRW, 2013). However, we are concerned about three aspects.

First, the authors included published study results that were not derived from independent study samples. Guenel et al. (2001), Stang et al. (2003), Lutz et al. (2005) and Behrens et al. (2011) used data of the multicentric case-control study entitled "Study of Occupational Risk Factors for Rare Cancers of Unknown Aetiology" (in short "Rare Cancer Study") from nine European countries (Ge et al., 2012).

Guenel et al. (2001). similar to Stang et al. only included their national data, that is, French and German data, respectively. Lutz et al. used data from Italy, Denmark, Latvia, Sweden, Spain, Portugal. That means, these three papers used disjunct data sets from the international Rare Cancer Study. Finally, Behrens et al. (2011) used the largest data set of the Rare Cancer Study including France, Germany, Italy, Denmark, Latvia, Sweden, Spain, Portugal, UK. Therefore, the effect estimate from Behrens et al. is not independent of the effect estimates presented in the previous papers of the Rare Cancer Study (Table 1).

We therefore excluded the data from Behrens et al. and re-ran the metaanalysis of Ge et al. (2012) to avoid statistical dependence between the study-specific effect estimates. We provide both results from the fixed-effect and from the random-effect model. The newly estimated

pooled OR for the association between cooking and uveal melanoma risk were higher than the original once reported by Ge et al. (2012) (fixed-effects model: our OR 1: 1.99, 95%CI 1.34-2.95, random-effect model: 2.09, 95%CI 1.18-3.71, Ge et al. (2012) (fixed-effects model OR: 1.81, 95%CI 1.33-2.46) (Figure 1 and 2). Comparing Ge et al. (2012) estimates with ours, we observed a relative change in estimate of 10%.

Second, Ge et al. (2012) wrote that they excluded the studies from Monarrez-Espino et al. (2002) and Schmidt-Pokrzywniak et al. (2009) containing overlapping data.

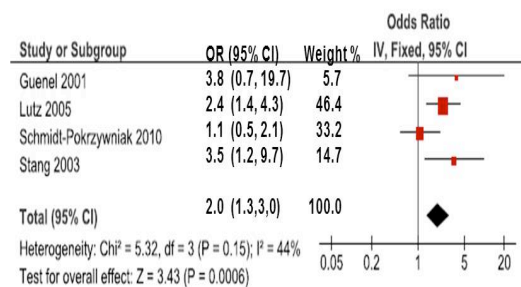


Figure 1. Meta-analysis of the Association between Occupational Cooking and the Risk Of Uveal Melanoma (fixed-effect model)

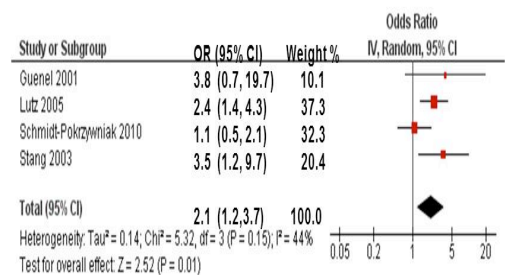


Figure 2. Metaanalysis of the Association between Occupational Cooking and the Risk Of Uveal Melanoma (random-effect model)

Table 1. Overview of the Five Publications on the Etiology of Uveal Melanoma that Contributed to the Pooling by Ge et al.

	RIFA	Study of Occupational Causes of Rare Cancers of Unknown Aetiology (Rare Cancer Study)			
Publication year	Schmidt-P et al., 2010	Stang et al., 2003*	Guenel et al., 2001	Lutz et al., 2005	Behrens et al., 2011
Population	Catchment population, single hospital	Germany	France	Italy, Denmark, Latvia, Sweden, Spain, Portugal	France, Germany, Italy, Denmark, Latvia, Sweden, Spain, Portugal, UK
No. of cases	455	118	50	176	280
No. of controls	827	475	479	1936	3084

*Study population enriched with an additional hospital-based case-control population

This is not correct. However, data from Monarrez-Espino et al. (2002) and Stang et al. (2003) used in part the same population. Therefore it was correct to exclude the study from Monarrez-Espino et al. (2002).

Third, Ge et al. (2012) concluded that “more well-designed observational studies with large sample size or prospective cohort studies are needed”. To the best of our knowledge, the case-control studies included in the meta-analysis by Ge et al. (2012) were well-designed. Furthermore, a prospective cohort study appears to be statistically inefficient. For example, a prospective population-based cohort study of people aged 40-79 years in Germany that included 200.000 people would provide an expected number of 28 newly diagnosed uveal melanoma events during a 10 year follow-up. For this calculation, we used current incidence estimates (2006-2010) of the cancer registry in Northrhine-Westphalia (Epidemiologisches Krebsregister NRW, 2013), Germany and assumed that no cohort members died due to competing outcomes.

Our concerns emphasize that obviously all three stages of peer-review are important for quality control: pre-peer review (authors), peer-review (journal), and post publication peer-review (readers) (Stang et al., 2008).

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