



THE INDUSTRIAL INJURIES ADVISORY COUNCIL

POSITION PAPER 33

Ocular melanoma and occupation

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Summary

1. As part of its watching brief, the Industrial Injuries Advisory Council has examined the relationship between melanoma of the eye ('ocular melanoma') and occupation, an issue raised in respect of welding by a monograph from the International Agency for Research in Cancer (IARC) published in 2012.
2. The tumour is relatively rare in the UK, affecting about 500 people a year, about half of whom are men.
3. There is consistent evidence that the risk of ocular melanoma is increased by welding but there is uncertainty over the definitions of 'welding' in the published studies and an absence of robust evidence for a relationship between risk and exposure.
4. There may be an increase in the risk of ocular melanoma in cooks but the evidence base is limited and again there is a lack of clarity over the definitions of exposure, and very little information on the duration of exposure that would confer an increase in risk.
5. Studies of other occupational populations suggest risks may be increased in some, but the evidence is neither strong nor consistent.
6. The Council does not feel it possible at this time to prescribe ocular melanoma for any occupational exposures, but will continue to monitor emerging research evidence.

This report contains some technical terms, the meanings of which are explained in a concluding glossary.

Background

7. Malignant melanomas are tumours that arise in pigment-producing cells ('melanocytes'). Most melanocytes are found in the skin and it is there that most melanomas occur. More rarely, the disease can develop in the eye (an 'ocular' melanoma).
8. Ocular melanomas originate in the 'uveal tract' of the eye, comprising the iris, the ciliary body and the choroid; the last of these is the site of most ocular melanomas (Figure 1).

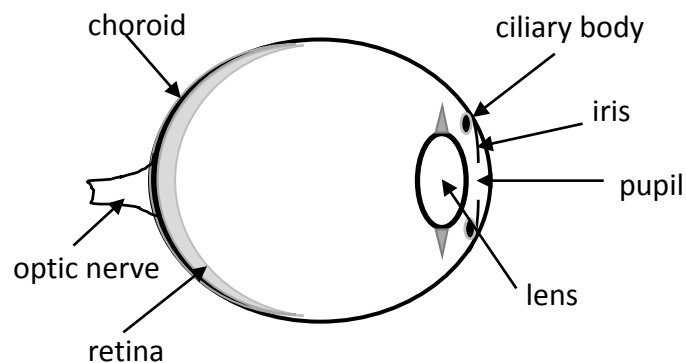


Figure 1: Diagrammatic representation of the eye.

9. Every year about 500 new cases of ocular melanoma are detected in the UK, making it one of the more unusual cancers, although the commonest of the eye. There is no evidence that the frequency of the disease has changed in the last 30 years. The median age at diagnosis is about 55 years; the rate of disease is a little higher in men than women.
10. Treatment of ocular melanomas usually includes radiotherapy with or without local surgery to the affected eye. Although this may successfully treat the local tumour, about half of patients will later be found to have metastatic disease (cancer that has spread to other parts of the body); this is generally fatal in a short period. Between 45 per cent and 85 per cent of patients will survive for five years or more after diagnosis, the variation being dependent on the size and extent of the initial tumour.
11. There is reasonably consistent evidence that the risk of ocular melanoma is increased by intense or prolonged exposures to ultraviolet light, whether arising naturally through sunlight or artificially through tanning devices. The risks are higher for those with fair skin, light-coloured eyes and a tendency to sunburn.

Occupational risk factors

12. Because of the rarity of the disease, most studies of ocular melanoma are based on series of registered cases with comparison to one or more 'control' groups. Case-control studies such as these are liable to generate chance

associations with one or more of the many occupations examined. Increased risks have been reported in several occupational groups with high exposures to ultraviolet radiation. These include construction workers, sailors and fishermen, agricultural workers, airline pilots and those exposed to electromagnetic radiation. Other occupations for which an increased risk has been suggested include chemists, health care workers, laundry workers and service workers. For none of these occupations, however, is the evidence both strong and consistent.

13. In contrast, there is a more coherent body of evidence in relation to two other occupational activities: welding and cooking.

Welding

14. Welding, particularly arc-welding, is an intense source of ultraviolet radiation to which welders work in close proximity. They are also exposed to welding fumes which may contain known carcinogens, such as hexavalent chromium, and to radioactive materials such as thorium oxide.
15. In 2012 the International Agency for Research in Cancer (IARC), in a review of the risks of radiation (100D), concluded that there was sufficient evidence that (occupational) welding was carcinogenic in relation to ocular melanoma, but that it was unclear whether this was a reflection of high exposures to ultraviolet radiation or to other incurred exposure(s). The authors stated that this opinion would not be expected to change after a full review of welding in a subsequent Monograph.
16. The evidence base examined by IARC comprises seven case-control studies, the findings of which are summarised in Table 1. In addition two further studies (Monárrez-Espino *et al.*, 2002, Lutz *et al.*, 2005) identified through a literature search by IARC's Research Working Group, are included.

Table 1. Summary of evidence from case control studies about ocular melanoma and welding.

Study	Country	Number (<i>number exposed</i>)		Source of controls	Exposure	Odds ratio (95% confidence interval)
		Cases	Controls			
Tucker <i>et al.</i> 1985	US	439(4)	419(0)	Hospital	Unclear but occupational: possibly longest held job	10.9 (2.1-56.5)
Seddon <i>et al.</i> 1990	US	197(18)	385(35)	Community	Self-reported exposure to welding arc; probably occupational but not clear	1.3 (0.5-3.1)
Lischko <i>et al.</i> 1990	US	337(38)	800(96)	Siblings	Self-reported exposure to welding arc; probably occupational but not clear	0.9 (0.6-1.5)
Siemiatycki 1991	Canada	33(4)	533	Community	Occupational exposure to arc welding fumes	8.3 (2.5-27.1)
Ajani <i>et al.</i> 1992	US	197(18)	385(35)	Community	Self-reported exposure to welding arc; probably occupational but not clear	0.99 (0.48-2.05)
Holly <i>et al.</i> 1996	US	221(40)	447(47)	Community	'Welding' (self or in proximity to): could include non-occupational	2.2 (1.3-3.5)
Guénel <i>et al.</i> 2001	France	50(7)	479(14)	Community	Worked for 6 months or more as a welder or sheet metal worker	7.3 (2.6-20.1)
Monárrez-Espino <i>et al.</i> 2002	Germany	118 (13)	475 (101)	Community or hospital	Worked for 6 months or more as welder, brazer or solderer	0.9 (0.43-1.75)
Vajdic <i>et al.</i> 2004	Australia	246(43)	893(144)	Community	'Own welding'(could include non-occupational)	1.1 (0.8-1.7)
Lutz <i>et al.</i> 2005	Europe	m: 164(15)	2089 (79)	Community or hospital	Welders and sheet-metal workers	2.18 (1.18-4.04)
		f: 128 (1)	1067 (7)		Welders and sheet-metal workers	1.95 (1.08-3.52)

Notes: m – male; f - female

140 cases overlap in Seddon *et al.* (1990) and Lischko *et al.* (1990).

Ajani *et al.* (1992) used the same cases and controls as Seddon *et al.* (1990) but included more other variables in analysis.

17. None of the studies in Table 1 reported the ages of the cases at the time of their diagnoses.
18. In addition there is a published meta-analysis of much of the above evidence (Shah *et al.*, 2005). The summary risk estimate of developing the disease from the exposure was 2.05 (95% confidence interval (95% CI) 1.20-3.51). This analysis did not include the findings of Siemiatycki (1991) or Lutz *et al.* (2005), both of which indicated risks that were more than doubled, or of Lischko *et al.* (1990) or Monárrez-Espino *et al.* (2002) in each of which the risk was not increased.¹
19. Three of the studies reported estimates of risk after stratification by duration of work as a welder. Their findings are summarised in Table 2: the second group of estimates from Holly *et al.* (1996) are based on the time from start of work as a welder to diagnosis.

Table 2. Summary of case control evidence showing risks of welding according to duration of work as a welder.

Study	Years welding	Odds ratio (95% confidence interval)
Holly <i>et al.</i> 1996	≤1	2.2 (0.7-7.0)
	2-10	1.8 (0.88-3.6)
	≥11	1.9 (1.0-3.6)
Holly <i>et al.</i> 1996	≤10	1.2 (0.2-6.6)
	11-29	1.5 (0.7-3.0)
	≥30	2.1 (1.1-4.0)
Guénel <i>et al.</i> 2001	<20	5.7 (1.6-19.8)
	≥20	11.5 (2.4-55.5)
Vajdic <i>et al.</i> 2004	0.1-4.0	0.8 (0.4-1.4)
	4.1-22	1.2 (1.0-2.7)
	>22	1.7 (1.0-2.7)

20. Finally, an examination of the UK Decennial Supplement covering the years 1991-2000 revealed that there were no cancers of the eye reported in male welders (whereas 2.6 cancers of the eye would have been 'expected' according to statistical estimates).

¹ The IARC review claimed to include the findings from Ajani *et al.* (1992) but this appears not to have been the case.

Cooking

21. There has recently been an interest in professional 'cooking' as a risk factor for ocular melanoma, prompted in part by the finding, in one of the population-based case-control studies above (Guénel *et al.*, 2001), of a non-significantly increased risk of ocular melanoma, based on two cases, in male cooks.
22. The nature of any risk associated with cooking is not understood but may relate to high exposures to non-ionising radiation.
23. An IAC literature search has revealed several case-control studies that examine this issue. Their findings are summarised in Table 3; some of the studies use overlapping populations and it can be difficult to be sure that their findings are truly independent.

Table 3. Summary of evidence from case control studies about ocular melanoma in cooks.

Study (Country)	Number exposed		Source of controls	Exposure	Odds ratio (95% confidence interval)
	Cases	Controls			
Guénel <i>et al.</i> 2001 (France)	2	6	Community	Ever worked as a 'cook' for 6 months or more	3.8 (0.7-19.7)
Monárrez-Espino <i>et al.</i> 2002 (Germany)	6 (m)	8 (m)	Hospital and community	Ever worked in 'cooking' for 6 months or more	5.6 (1.66-19.1)
	11 (f)	29 (f)			1.1 (0.40-3.30)
Stang <i>et al.</i> 2003 (Germany)	9	12	Community	Ever worked as a 'cook' for 6 months or more	3.5 (1.2-9.7)
	6	8		Author-ratings of actual 'cooking'	7.0 (1.8-27.6)
Lutz <i>et al.</i> 2005 (6 European countries)	14	None	Community or hospital	Ever worked as a 'cook' for 6 months or more	3.24 (1.58-6.62)
Schmidt-Pokrzywniak <i>et al.</i> 2010 (Germany, 'RIFA' study)	13	25	Community	Ever worked as a 'cook' for 6 months or more	1.1 (0.5-2.1)
	8	19		Author-ratings of actual 'cooking'	0.9 (0.4-2.1)
Behrens 2012 (9 European countries)	28	215	Hospital and community	Ever worked in 'cooking' for 6 months or more	1.53 (0.95-2.47)

Note: Guénel *et al.* (2001), Stang *et al.* (2003), Lutz *et al.* (2005) and Behrens *et al.* (2012) used data from the nine-country European Rare Cancer Study; the data in Lutz *et al.* (2005) and Behrens *et al.* (2012) overlap. Furthermore, there was overlap in the data used by Stang *et al.* (2003) and Monárrez-Espino *et al.* (2002).

24. A meta-analysis of what are probably independent data was published in 2013. The summary risk estimate of developing the disease from the exposure from four studies was 2.1 (95% CI 1.2-3.7). No sex-specific analyses were reported.
25. In addition, Vågerö *et al.* (1990) from an analysis of cancer registration data in England and Wales (1971-1978) and on the basis of six cases, reported a relative risk of 3.19 (1.17-6.95) in female 'kitchen hands'.
26. Stang *et al.* (2003) reported a positive exposure-response relationship with duration of work as a cook in which the risks were more than doubled after just six months employment; no such relationship was found by Schmidt-Pokrzywniak *et al.* (2010). No other information on the relationship between duration of work and risk is available.

Conclusions

27. There is consistent evidence that the risks of ocular melanoma are increased by occupational welding, but in only half of the published studies were the risks more than doubled. Furthermore, uncertainty over the definitions of 'welding' in these studies, and the absence of robust exposure-response relationships, make prescription at this time impossible.
28. There may be an increase in risk of ocular melanoma in cooks but the evidence base is limited and again there is a lack of clarity over the definitions of exposure and very little information on the duration of exposure that would confer an increase in risk.
29. The Council will continue to monitor emerging research evidence on these suspected associations.

Diversity and equality

30. IIAC seeks to promote equality and diversity as part of its values. The Council has resolved to seek to avoid unjustified discrimination on equality grounds, including age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender and sexual orientation. During the course of this review no diversity and equality issues were apparent.

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Glossary of terms used in this report

Study design

Case-control study: A study which compares people who have a given disease (cases) with people who do not (controls) in terms of exposure to one or more risk factors of interest. Have cases been exposed more than non-cases? The outcome is expressed as an **Odds Ratio**, a form of **Relative Risk**.

Measures of association

Relative Risk (RR): A measure of the strength of association between exposure and disease. RR is the ratio of the risk of disease in one group to that in another. Often the first group is exposed and the second unexposed or less exposed. *A value greater than 1.0 indicates a positive association between exposure and disease.* (This may be causal, or have other explanations, such as bias, chance or confounding.)

Odds Ratio (OR): A measure of the strength of association between exposure and disease. It is the odds of exposure in those with disease relative to the odds of exposure in those without disease, expressed as a ratio. For rare exposures, odds and risks are numerically very similar, so the OR can be thought of as a **Relative Risk**. *A value greater than 1.0 indicates a positive association between exposure and disease.* (This may be causal, or have other explanations, such as bias, chance or confounding.)

Other epidemiological terms

Confidence Interval (CI): The **Relative Risk** reported in a study is only an *estimate* of the true value in the underlying population; a different sample may give a somewhat different estimate. The CI defines a plausible range in which the true population value lies, given the extent of statistical uncertainty in the data. The commonly chosen 95% CIs give a range in which there is a 95% chance that the true value will be found (in the absence of bias and confounding). *Small studies generate much uncertainty and a wide range, whereas very large studies provide a narrower band of compatible values.*

Meta-analysis: A statistical process of pooling quantitative information across studies to produce an overall summary risk estimate, taking account of their differing sizes.

