Section 2. Cancer in humans

Section 2 *summarizes* all of the pertinent epidemiological studies and *identifies tumour sites* for which there is *sufficient, limited***,** or *inadequate evidence* of carcinogenicity in humans.

Instructions at a glance

1. Section 2 is a systematic review of original research. Generally only analytical epidemiological studies (typically cohort and case–control studies) are included.
2. The literature search will be conducted using the HAWC Literature Search tool (a collaborative workspace for conducting risk assessments for human health; https://hawcproject.org/). Initial searches will be provided by the IARC secretariat and further refined by the Working Group.
3. Text is written in Word and submitted electronically via the IARC Monographs Online Publication System (IOPS).
4. Included studies are described individually**,** providing essential details about the study and the key results. Information given in the tables does not need to be repeated in the text.
5. Tables for Section 2 are constructed using the IARC Table Builder online tool linked to IOPS.
6. Your assignment *should be prepared before the meeting* according to the deadline provided to you.

The Working Group conducts a systematic review of original research. Normally only analytical epidemiological studies (typically cohort and case–control studies) are included. When *multiple publications* are available for a single study, only the most recent or most informative publication is described in detail. Well-conducted quantitative meta-analyses may also be reviewed. *Case reports and descriptive studies* (correlation or ecological studies) should be reviewed only when they are the only information available or when they add materially to other evidence. *Narrative reviews, commentaries and letters* that do not provide relevant original data are not reviewed or cited.

Identifying the relevant information

Searching the literature

The Working Group identifies relevant peer-reviewed literature through comprehensive searches of relevant databases (e.g. PubMed). Additional studies may be identified by hand searching or from past Monographs, government documents, authoritative reviews or, expert knowledge of the literature. The HAWC Literature Search tool documents the search topics, terms, sources, and identified studies. Search terms are drafted by the IARC secretariat and further refined by the Working Group. Further detail on these topics and associated search terms is available at https://hawcproject.org/.

Instructions on how to use the HAWC Literature Search tool can be found in this video.

Screening and organizing the results

The Working Group screens the retrieved literature for relevance. The IARC secretariat can assist with the initial screen focused on exclusion of studies that do not address the agent or cancer in humans. Other exclusion criteria (e.g. ecological studies and case reports) used by the Working Group are documented in HAWC using tags.

The Working Group considers all included studies. Using the literature tagging function in HAWC, the Working Group organizes the studies by cancer site and/or study design, and by additional subtopics according to the monograph outline. Studies may fall into more than one topic or category. Default tags for included and excluded studies are provided by the IARC secretariat and if necessary may be further refined by the Working Group.

Literature trees in HAWC document the number of studies identified, screened, excluded and categorized per category of evidence.

See page 8 of the Preamble to the IARC Monographs for further guidance about the types of studies included.

Summarizing the evidence

Once tagging is complete, the IARC secretariat reviews the results and may refine the outline and writing assignments, considering the extent of relevant evidence and needed expertise.

Text

Text is *written in Word and uploaded electronically* via the IARC Monographs Online Publication System (IOPS). Included studies are described individually**,** providing essential details about the study such as:

- the reference (first author et al., year)
- design
- location
- number of subjects
- exposure assessment method
- key results with the risk estimate (95% confidence interval, CI)

The level of detail should be proportional to the importance of the study and give only the minimum detail needed to evaluate the particular study in the context of all of the studies presented. Information given in the tables does not need to be repeated in the text unless it is especially important for interpreting the results. It is not necessary to cite study features such as response rates or covariates controlled in the

text, unless they are notable as limitations or strengths. Risk estimates and 95% CIs should be provided for the main results without descriptions of statistical significance. *P*-values for trend may be reported when available. When there are multiple publications on a single study, previous papers may be briefly indicated in the text as Working Group comments, or in the Comments field of the table.

Less informative studies may be either described in a brief, summary style giving key characteristics and results of the studies or in the aggregate.

For each study or group of studies, it is important to include an expert assessment of the strengths and limitations as well as important points of interpretation, which should be indicated in square brackets [ ]. Study strengths and limitations are noted in the tables (see below).

Subsections describing a number of studies may have a brief introduction describing the included literature, the reasons for exclusions, if any, and highlighting important issues of interpretation.

Tables

Tables for Section 2 are constructed using the IARC Table Builder online tool. Please fill in all of the fields provided for descriptive information and results for each study.

Example of description of an individual study

Pesticide use and cancer of the breast (excluding prevalent and in-situ cancers) was investigated among 30 454 wives of farmers enrolled in the AHS (Engel et al., 2005). At enrolment, famers' wives were given a questionnaire to investigate personal ever versus never use of specific pesticides, while information on potential indirect exposure to pesticides was obtained from their husbands' responses concerning use of specific pesticides; 309 cases of cancer of the breast were identified. No elevation in risk was observed when considering wives' use of malathion in the entire cohort (RR, 0.9; 95% CI, 0.7–1.2), while an increase was observed when restricting the analysis to wives who had never used pesticides themselves, but whose husband had used malathion (RR, 1.4; 95% CI, 1.0–2.0), after adjusting for age, race, and state of residence. There was no apparent trend in relation to husband's use of malathion [data not shown]. [The Working Group noted inconsistency in the results in that there was no elevation in risk for personal use of malathion, but an increase was noted only for husband's use. The strengths of this study included its large sample size, comprehensive exposure assessment, extent of potential confounder control, and exploration of potential effect modulation, such as by family history. Because of the small number of cases in North Carolina, these were excluded from the analyses.]

Example of description when there are a several independent publications from a single study

Three population-based case–control studies conducted in the 1980s by the National Cancer Institute in Nebraska (Hoar Zahm et al., 1990), Iowa and Minnesota (Brown et al., 1990; Cantor et al., 1992), and Kansas (Hoar et al., 1986) provided information on several pesticides. All three studies assessed the risk for non-Hodgkin lymphoma (NHL). NHL cases and controls were combined from these studies to create a pooled data set to increase study precision to enable analyses for specific pesticides (Waddell et al., 2001; De Roos et al., 2003).

These studies also assessed other cancer sites. The study in Iowa and Minnesota included leukaemia (Brown et al., 1990) and NHL (Cantor et al., 1992), the study in Iowa included multiple myeloma (Brown et al., 1993b), the study in Nebraska included NHL, Hodgkin lymphoma, multiple myeloma, and chronic lymphocytic leukaemia (Hoar Zahm et al., 1990), and the study in Kansas included NHL, soft tissue sarcoma, and Hodgkin lymphoma (Hoar et al., 1986). In Iowa and Minnesota, 622 cases of NHL (Cantor et al., 1992), and 669 cases of leukaemia (Brown et al., 1990) among white men aged ≥ 30 years were identified from the Iowa state cancer registry and from a surveillance system of hospital and pathology laboratory records in Minnesota. In Iowa, cases of multiple myeloma (n = 173) were identified from the state cancer registry (Brown et al., 1993b).

Example of description in summary style

Two recent hospital-based case–control studies (Gousias et al., 2009; Spinelli et al., 2010), one conducted in Greece and the other in France, examined associations between glioma and mobile-phone use. Neither was informative due to small numbers and unclear exposure assessment methods.

Example of subsection introduction

Case–control studies investigating the association of air pollution and cancer of the lung are presented below according to the main type of exposure under study. Studies focused on all sources of air pollution have been divided according to the methodology, qualitative or quantitative, used for exposure assessment. The main development in the design of the studies is the evolution of exposure assessment methods from rather crude classification of urban areas and air pollution zones (Vena, 1982; Samet et al., 1987), proximity to industry (Brown et al., 1984; Pershagen, 1985), proximity to traffic (Vineis et al., 2006), to more advanced use of fixed monitors data (Jedrychowski et al., 1990), exposure modeling (Nyberg et al., 2000), and national spatio-temporal air pollution maps (Hystad et al., 2012, 2013).

Examples of tables

2.1 Cancer in humans: cohort studies

Actions

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Reference, location, follow-up/enrollment period, study-design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
van Amelsvoort et al. (2009) Pernis, The Netherlands 1954-2006 Cohort	570; Men employed ≥1 year in a pesticide production plant 1954-1970. **Exposure assess. method:** modelling; Exposure modelled from blood measures in subgroup (n = 343) to produce total dose for each worker. Range 11mg - 7755 mg dieldrin and aldrin combined.	All cancers combined	Estimated intake of aldrin+dieldrin				Earlier publications from this study are Swaen et al, 2002; Sielken et al, 1999; de Jong et al, 1997; Ribbens 1985. **Strengths:** Biomonitoring data modelled to give quantitative exposure assessment. **Limitations:** No internal comparisons made. Unable to separate exposure to dieldrin and aldrin. Small numbers
			All	82	0.76 (0.61–0.95)	Age, time	
			Low	27	1 (0.66–1.46)		
			Moderate	27	0.75 (0.5–1.09)		
			High	28	0.66 (0.44–0.96)		
		All cancers combined: Mortality	SMR				
			Assistant operator	28	0.86 (0.58–1.25)	age, time	
			Maintenance	11	0.66 (0.33–1.19)		
			Operator	41	0.78 (0.56–1.05)		
			Supervisor	2	0.45 (0.06–1.65)		
		Oesophagus	Estimated intake of aldrin+dieldrin				
			All	4	1.59 (0.43–4.08)	Age, time	
			Low	2	2.87 (0.35–10.35)		
			Moderate	1	1.17 (0.03–6.49)		
			High	1	1.08 (0.03–5.99)		

2.2 Cancer in humans: case-control studies

Actions

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Reference, location, follow-up/enrollment period, study-design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Lee et al. (2004) Iowa, Minnesota, Nebraska, USA 1980-86 Case-Control	**Cases:** 872; State Health Registry, hospitals and Nebraska Lymphoma Study Group **Controls:** 2336; population-based and matched on age, race and state **Exposure assess. method:** questionnaire; Telephone or personal interviews with subjects or next of kin in Nebraska	NHL (Non-hodgkin's lymphoma)	Ever use of aldrin				**Strengths:** Pooled study so larger numbers **Limitations:** Use of proxy respondents may have led to nondifferential misclassification. No adjustment for co-exposures.
			Aldrin among asthmatics	10	2.1 (0.9–5.1)	age, vital status, state	
			Aldrin among non-asthmatics	66	1 (0.7–1.5)		