

NON-ALCOHOLIC DRINKS AND THE RISK OF CANCER					
WCRF/AICR GRADING		DECREASES RISK		INCREASES RISK	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing			Arsenic in drinking water ¹	Lung 2017
	Probable	Coffee	Liver 2015 Endometrium 2013 ²	Arsenic in drinking water ¹	Bladder 2015 Skin (unspecified) 2017
				Mate ³	Oesophagus (squamous cell carcinoma) 2016
LIMITED EVIDENCE	Limited – suggestive	Coffee	Mouth, pharynx and larynx 2018	Arsenic in drinking water ¹	Kidney 2015
			Skin (basal cell carcinoma [men and women] / malignant melanoma [women]) 2017	Mate ³	Mouth, pharynx and larynx 2018
		Tea	Bladder 2015		
STRONG EVIDENCE	Substantial effect on risk unlikely	None identified			

- 1 The International Agency for Research on Cancer (IARC) has judged arsenic and inorganic arsenic compounds to be carcinogenic to humans (Group 1) [2]. Drinking water contaminated with arsenic is also classed separately as a human carcinogen (Group 1) [2]. Water can become contaminated by arsenic as a result of natural deposits present in the earth, volcanic activity, or agricultural, mining and industrial practices. Countries particularly affected by higher levels of arsenic in drinking water include Bangladesh, China and India.
- 2 The effect of coffee on the risk of endometrial cancer is observed with both caffeinated and decaffeinated coffee so cannot be attributed to caffeine.
- 3 Mate, an aqueous infusion prepared from dried leaves of the plant *Ilex paraguariensis*, is traditionally drunk scalding hot through a metal straw in parts of South America. In 2016, an IARC Working Group declared that drinking very hot beverages, including mate, above 65°C is probably carcinogenic to humans (Group 2A) [3].

Summary of published cohort studies for consumption of arsenic in drinking water¹ and the risk of cancer

Cancer	Total no. of studies	Exposure level	Total no. of studies	No. of studies showing statistically significant increased risk	No. of studies showing no statistically significant association	No. of studies showing statistically significant decreased risk	Conclusion ²	Date of CUP cancer report ³
Lung	4 ⁴	High	3	3	0	0	Convincing: Increases risk	2017
		Low	1	0	1	0		
Bladder	7	High	3	2	1	0	Probable: Increases risk	2015
		Low	4	0	4	0		
Skin ⁵	3	High	1	1	0	0	Probable: Increases risk	2017
		Low	2	0	2	0		
Kidney	4	High	1	1	0	0	Limited – suggestive: Increases risk	2015
		Low	3	0	3	0		

1 The International Agency for Research on Cancer (IARC) has judged arsenic and inorganic arsenic compounds to be carcinogenic to humans (Group 1) [2]. Drinking water contaminated with arsenic is also classed separately as a human carcinogen (Group 1) [2]. Water can become contaminated by arsenic as a result of natural deposits present in the earth, volcanic activity, or agricultural, mining and industrial practices. Countries particularly affected by higher levels of arsenic in drinking water include Bangladesh, China and India.

2 See Definitions of WCRF/AICR grading criteria (**Section 1:** Non-alcoholic drinks and the risk of cancer: a summary matrix) for explanations of what the Panel means by ‘convincing’, ‘probable’ and ‘limited – suggestive’.

3 Throughout this Third Expert Report, the year given for each cancer site is the year the CUP cancer report was published, apart from for nasopharynx, cervix and skin, where the year given is the year the SLR was last reviewed. Updated CUP cancer reports for nasopharynx and skin will be published in the future.

4 A fifth study reported on dietary arsenic intake from foods (see CUP lung cancer report 2017: Section 7.1 and CUP lung cancer SLR 2015: Section 4.1.2.7.2).

5 Evidence from a published IARC review of case-control and ecological studies on consumption of arsenic in drinking water and skin cancer [2] was also considered by the Panel. Four out of six case-control studies and most ecological studies reported a statistically significant increased risk for skin cancer (histological type not specified).

Summary of published cohort studies for consumption of arsenic in drinking water and the risk of lung cancer

Study description	Total no. of cases	Sex	RR (95% CI)	Increment/contrast
High-exposure areas				
Chung, 2013 South-western Taiwan cohort, 1989–1996 [66]	71	Men and women	1.47 (0.66–3.31)	≥ 19.5 vs < 9.1 µg/litre/year
	43	Men	SMR 6.05 (4.38–8.15)	
	28	Women	SMR 7.18 (4.77–10.38)	
Chen, 2010 North-eastern Taiwan cohort [68]	178	Men and women	2.08 (1.33–3.27)	≥ 10,000 vs < 400 µg/litre/year
Tsuda, 1995 Japanese cohort, 1959–1992 [67]	9	Men and women	SMR 15.69 (7.38–31.02)	≥ 1 ppm
Low-exposure areas				
Baastrup, 2008 Danish Diet, Cancer and Health cohort [69]	402	Men and women	IRR 0.99 (0.90–1.08)	Per 1 µg/litre
			IRR 1.00 (0.98–1.03)	Per 5 mg/litre

Summary of published cohort and nested case-control studies for consumption of arsenic in drinking water and the risk of bladder cancer

Publication	Total no. of cases	Sex	RR (95% CI)	Increment/contrast
High-exposure areas				
Chung, 2013 South-western Taiwan cohort, 1989–1996 [66]	43	Men and women	7.74 (0.97–61.51)	≥ 19.5 vs 9.1 µg /litre/year
Chen, 2010 North-eastern Taiwan cohort, 1991/1994–2006 [72]	45	Men and women	12.6 (3.40–46.8)	≥ 10,000 vs < 400 µg/litre
Tsuda, 1995 Japanese cohort, 1959–1992 [67]	3	Men and women	SMR 31.18 (8.62–91.75)	≥ 1 ppm
Low-exposure areas				
Baastруп, 2008 Danish Diet, Cancer and Health cohort [69]	214	Men and women	1.00 (0.91–1.11)	Per µg/litre
Michaud, 2004 ATBC study ¹ [73]	280	Men	1.13 (0.70–1.81)	Toenail arsenic level > 0.161 vs < 0.05 µg/gram
Lewis, 1999 Cohort of Mormons, USA ² [75]	–	Men	SMR 0.42 (0.08–1.22)	≥ 5,000 ppb-year
		Women	SMR 0.81 (0.10–2.93)	
Kurttio, 1999 Finnish cohort, 1981–1995 [74]	61	Men and women	1.00 (0.91–1.11)	3 to 9 years before cancer diagnosis ≥ 2.0 vs < 0.5 mg

Abbreviations: SMR, standardised mortality ratio.
¹ The ATBC study [73] is a nested case-control study.
² The Lewis Cohort study [75] is retrospective cohort study of mortality.

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Summary of published cohort studies for consumption of arsenic in drinking water and the risk of skin cancer

Study description	Total no. of cases	Sex	RR (95% CI)	Increment/contrast
High-exposure areas				
Hsueh, 1997 South-western Taiwan cohort 1989–1992 [78]	26	Men and women	Skin cancer 8.69 (1.08–65.50)	0.71–1.1 vs 0 mg/litre
Low-exposure areas				
Baastrup, 2008 Danish Diet, Cancer and Health cohort [69]	147	Men and women	Malignant melanoma IRR 0.80 (0.59–1.08)	Per 1 µg/litre Time-weighted average exposure
			Non-melanoma skin cancer IRR 0.99 (0.94–1.06)	Per 1 µg/litre Time-weighted average exposure
Lewis, 1999 Cohort of Mormons, USA ¹ [75]	3	Men	Malignant melanoma SMR 0.83 (0.17–2.43)	≥ 5,000 vs <1,000 ppb-years
	4	Women	Malignant melanoma SMR 1.82 (0.50–4.66)	

Abbreviations: IRR, incident rate ratio; SMR, standardised mortality ratio.

¹ The Lewis Cohort study [75] is retrospective cohort study of mortality.

Summary of CUP dose–response meta-analyses from case-control studies for consumption of mate¹ and the risk of cancer

Cancer	Total no. of studies	No. of studies in meta-analysis	Total no. of cases	Risk estimate (95% confidence interval [CI])	Increment	I ² (%)	Conclusion ²	Date of CUP cancer report ³
Oesophagus (squamous cell carcinoma)	8	5 ⁴	1,162	1.16 (1.07–1.25)	Cup per day	89	Probable: Increases risk	2016 ⁵
Mouth, pharynx and larynx⁶	5	0	–	Statistically significant increased risk in 3 studies	–	–	Limited – suggestive: Increases risk	2018

- 1 Mate, an aqueous infusion prepared from dried leaves of the plant *Ilex paraguariensis*, is traditionally drunk scalding hot through a metal straw in parts of South America. In 2016, an IARC Working Group declared that drinking very hot beverages, including mate, above 65°C is probably carcinogenic to humans (Group 2A) [3].
- 2 See Definitions of WCRF/AICR grading criteria (**Section 1**: Non-alcoholic drinks and the risk of cancer: a summary matrix) for explanations of what WCRF means by ‘probable’ and ‘limited – suggestive’.
- 3 Throughout this Third Expert Report, the year given for each cancer site is the year the CUP cancer report was published, apart from for nasopharynx, cervix and skin, where the year given is the year the SLR was last reviewed. Updated CUP cancer reports for nasopharynx and skin will be published in the future.
- 4 Four of the studies on consumption of mate and oesophageal cancer reported on oesophageal squamous cell carcinoma and the fifth did not specify a cancer subtype.
- 5 Data presented are from the 2005 oesophageal cancer SLR (see CUP Oesophageal cancer SLR 2015, Appendix 3). No analysis was conducted in the CUP.
- 6 A dose–response meta-analysis of cohort studies could not be conducted in the CUP. Three of five studies identified on consumption of mate and cancers of the mouth, pharynx and larynx reported a statistically significant increased risk for people who had ever consumed mate compared with those who had never consumed mate, or for people who consumed greater amounts of mate compared with those who had consumed the least (see CUP mouth, pharynx and larynx report 2018, Table 5).

Summary of published pooled analyses for consumption of mate and the risk of oesophageal squamous cell carcinoma

Publication	Contrast	RR (95% CI)	No. of studies (case-control)	No. of cases
Lubin, 2014 ¹ [84]	Ever vs never	1.60 (1.2–2.2)	2	1,391
	Warm vs never	1.20 (0.8–1.7)		168
	Hot vs never	1.61 (1.2–2.2)		929
	Very hot vs never	2.15 (1.5–3.1)		213

¹ In the Lubin, 2014 study [84] the *odds ratios* increased linearly with cumulative mate consumption.

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Summary of CUP dose–response meta-analyses for consumption of coffee and the risk of cancer

Cancer	Type	Total no. of studies	No. of studies in meta-analysis	Total no. of cases	Risk estimate (95% CI)	Increment	I ² (%)	Conclusion ²	Date of CUP cancer report ³
Liver	Coffee	8	6	1,582	0.86 (0.81–0.90)	Cup per day	18	Probable: Decreases risk	2015
Endometrium ³	Coffee	8	7	3,571	0.93 (0.91–0.96)	Cup per day	10	Probable: Decreases risk	2013
	Decaf- feinated coffee	3	3	2,585	0.92 (0.87–0.97)	Cup per day	0		
Mouth, pharynx and larynx ⁴	Coffee	6	0	–	Statistically significant increased risk in 3 studies	–	–	Limited – suggestive: Decreases risk	2018
Skin (basal cell carcinoma [men and women] / malignant melanoma [women])	Coffee	5	3	23,109	0.96 (0.94–0.97)	Cup per day	0	Limited – suggestive: Decreases risk	2017
		4	4	1,830	0.91 (0.86–0.96)		36		

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- 3 The effect of coffee on the risk of endometrial cancer is observed with both caffeinated and decaffeinated coffee so cannot be attributed to caffeine.
- 4 A dose–response meta-analysis of cohort studies could not be conducted in the CUP. Three of six studies identified on consumption of coffee and cancers of the mouth, pharynx and larynx reported a statistically significant decreased risk for people who consumed the highest compared with the lowest level of coffee consumed or when conducting a dose–response analysis per cup per day (see CUP mouth, pharynx and larynx report 2018, Table 6).

CUP dose–response meta-analysis for consumption of tea and the risk of bladder cancer

Cancer	Total no. of studies	No. of studies in meta-analysis	Total no. of cases	Risk estimate (95% CI)	Increment	I ² (%)	Conclusion ¹	Date of CUP cancer report ²
Bladder	4	4	1,446	0.94 (0.89–0.98)	Cup per day	0	Limited – suggestive: Decreases risk	2015

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