2019 DIET, NUTRITION, PHYSICAL ACTIVITY AND SKIN CANCER

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	**Convincing**		
	Probable		**Arsenic in drinking water[1] (unspecified skin cancer)** **Adult attained height[2] (MM)**
LIMITED EVIDENCE	**Limited – suggestive**	Coffee (BCC; MM [women])	Alcoholic drinks (BCC; MM) Adult attained height[2,3] (BCC) Birthweight[3,4] (MM)
	Limited – no conclusion	Potatoes, non-starchy vegetables, fruits, milk, coffee (MM [men], SCC), decaffeinated coffee, tea, alcoholic drinks (SCC), total fat, cholesterol, protein, retinol in the diet and/or supplements, beta-carotene in the diet (MM; NMSC), vitamin D, selenium, caffeine physical activity, body fatness, adult attained height (SCC), patterns of diet, meat, processed meat, fish, oily fish, offal, poultry, eggs, all vegetables, multivitamin supplements, folate, pyridoxine B_6, cobalamin B_{12}, lycopene, lutein and zeaxanthin, vitamin A, vitamin C, vitamin E, carotenoids, alpha-carotene, energy intake	
STRONG EVIDENCE	**Substantial effect on risk unlikely**	**High-dose beta-carotene supplements[5] (NMSC)**	

BCC, basal cell carcinoma; MM, malignant melanoma; NMSC, non-melanoma skin cancer; SCC, squamous cell carcinoma.

1 The International Agency for Research on Cancer (IARC) has judged arsenic and inorganic arsenic compounds to be carcinogenic to humans (Group 1) [5]. Drinking water contaminated with arsenic is also classed separately as a human carcinogen (Group 1) [5]. 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 Adult attained height is unlikely to directly influence the risk of cancer. It is a marker for genetic, environmental, hormonal and nutritional factors affecting growth during the period from preconception to completion of growth in length.

3 The evidence shows that, in general, the taller people are during adulthood and the more people weighed at birth, the higher their risk of some cancers. A better understanding of the developmental factors that underpin the associations between greater growth and cancer risk is needed.

4 Birthweight is a marker for prenatal growth, reflecting a combination of factors including foetal nutrition, and is also a predictor of later growth and maturation.

5 The evidence for beta-carotene and non-melanoma skin cancer is derived from one study on plasma levels, as well as two studies on high-dose supplement use (50 milligrams per day and 50 milligrams per day on alternate days).

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

Study	Increment/ contrast	Sex	RR (95% CI)	No. of cases (No. of participants)
High-exposure area				
South-western Taiwan cohort, 1989–1992 [40]	0.71 to 1.1 vs 0 mg per litre	Men and women	Skin cancer 8.69 (1.08-65.50)	26 (654)
Low-exposure area				
Danish Diet, Cancer and Health cohort [39]	Per 1 µg per litre Time-weighted average exposure	Men and women	**MM** IRR 0.80 (0.59-1.08)	147 (56,378)
	Per 1 µg per litre Time-weighted average exposure		**NMSC** IRR 0.99 (0.94-1.06)	1,010 (56,378)
Cohort of Mormons, USA[1] [41]	≥ 5,000 vs < 1,000 ppb-years	Men	**MM** SMR 0.83 (0.17-2.43)	3 (2,092)
		Women	**MM** SMR 1.82 (0.50-4.66)	4 (1,966)

[1]The Lewis Cohort study [41] is a retrospective cohort study of mortality.

Abbreviations: IRR, incident rate ratio; MM, malignant melanoma; NMSC, non-melanoma skin cancer; ppb, parts per billion; SMR, standardised mortality ratio.

Summary of CUP 2018 stratified dose–response meta-analyses of coffee consumption and risk of malignant melanoma

Analysis	Increment	Sex	RR (95% CI)	I^2	No. studies	No. cases
CUP 2018 analysis	Per cup of coffee per day	All	0.96 (0.92-1.00)	50%	7	6,401
		Men	1.03 (0.97-1.10)	0%	2	818
		Women	0.91 (0.86-0.96)	36%	4	1,830

Summary of published meta-analyses of coffee consumption and the risk of malignant melanoma

Study	Increment/ contrast	RR (95% CI)	I^2, p value	No. studies	No. cases
Liu et al. 2016[1] [52]	Caffeinated coffee per one cup per day	0.96 (0.91-1.00)	-	Cohort: 7	5,737
	Highest versus lowest categories of consumption	0.84 (0.71-0.99)	57%		
Wang et al. 2016[2] [53]	Total coffee intake per one cup per day	0.97 (0.93-1.00)	-	Cohort: 6 Case-control: 1	6,094
	Highest versus lowest categories of consumption	0.83 (0.72-0.97)	51%, 0.048	Cohort: 7	5,660

Specific adjustments for skin sensitivity or sun exposure

1. In this meta-analysis, two studies did not adjust for any measures of skin sensitivity or sun exposure, three studies adjusted for multiple measures of skin sensitivity and sun exposure, and one study adjusted for 'July erythermal exposure'. For full details, please see the original papers.
2. In this meta-analysis, two studies did not adjust for any measures of skin sensitivity or sun exposure, four studies adjusted for multiple measures of skin sensitivity and sun exposure, and one study adjusted for 'July erythermal exposure'. The case-control study adjusted for multiple measures of skin sensitivity and sun exposure. For full details, please see the original papers.

Summary of CUP 2018 meta-analysis and published meta-analyses of alcohol consumption and the risk of malignant melanoma

Analysis	Increment/contrast	RR (95% CI)	I^2, p value	No. of studies	No. of cases
CUP Skin SLR 2018	Per 10 grams of alcohol (as ethanol) per day	1.08 (1.03-1.13)	66%	6	7,367
Bagnardi *et al.* 2015[1,2] [70]	Light drinking (≤ 12.5 grams per day) vs no or occassional drinking	1.25 (1.13-1.38	0%	2	2,666
	Moderate drinking (12.5–50 grams per day) vs no or occasional drinking	1.27 (1.13-1.42)	0%		
Rota *et al.* 2014[2,3] [71]	Any alcohol drinking vs no or occasional drinking	1.26 (1.19-1.35)	0%, 0.657	2	2,666
	Light alcohol drinking (≤ 1 drink per day) vs no or occasional drinking	1.25 (1.15-1.35)	0%, 0.847		
	Moderate to heavy alcohol drinking (> 1 drink per day) vs no or occasional drinking	1.29 (1.17-1.43)	0%, 0.370		

Specific adjustments for skin sensitivity or sun exposure

1. The meta-analysis reported that one study adjusted for measures of skin sensitivity and sun exposure. For details, please see original paper.
2. The same two cohorts were used for Bagnardi *et al.* 2015 [70] and Rota *et al.* 2014 [71].
3. The meta-analysis reported that one study adjusted for measures of sun exposure. For details, please see original paper.

Summary of published randomised controlled trials for beta-carotene supplements and the risk of non-melanoma skin cancer

Study	Contrast	Sex	RR (95% CI)	Length of intervention (years)	No. of cases treatment/placebo (No. of participants)
Physicians Health Study [82]	50 mg every other day vs placebo	Men	0.98 (0.92-1.05)	12	1,786/1,821 (22,071)
Beta Carotene Trial 1983–89 [83]	50 mg/day vs placebo	Men and women	1.04 (0.89-1.21)	5	362/340 (1,805)

Summary of published meta-analyses for high-dose beta-carotene supplements and the risk of non-melanoma skin cancer

Analysis	Contrast	RR (95% CI)	Heterogeneity p-value	No. of studies	No. of cases
Druesne-Pecollo *et al.* 2010[1] [84]	Supplemented with beta-carotene (no upper limit) vs placebo	0.99 (0.93-1.05)	0.52	4	4,447
	Supplemented with beta-carotene (alone) vs placebo	0.99 (0.93-1.06)	0.17	2	3,870
	Supplemented with beta-carotene (combined with other antioxidants) vs placebo	0.98 (0.83-1.15)	0.55	2	577
	Supplemented with beta-carotene (with doses of 20 to 30 miligrams per day) vs placebo	0.99 (0.93-1.05)	0.36	3	4,315
	Supplemented with beta-carotene (in populations with majority men) vs placebo	0.97 (0.91-1.03)	0.46	3	4,119
	Supplemented with beta-carotene (in populations with majority women) vs placebo	1.18 (0.97-1.45)	0.53	2	395

Specific adjustments for skin sensitivity or sun exposure

1. The review article did not provide information on adjustments made in each trial. For details please see original trials.

Note: All four RCTs included in this meta-analysis [84] were identified as part of the CUP: one [82] is included in the evidence summary above, two [85, 86] are included in the CUP Skin SLR 2017 in section 5.5.18 under *Multivitamin supplements* and one [87] disaggregated the outcome of non-melanoma skin cancer into basal cell carcinoma and squamous cell carcinoma and so is not included in the evidence summary above (see table 28 in the CUP Skin SLR 2017).

Summary of published pooled analyses of height and malignant melanoma mortality

Publication	Outcome	Increment	Sex	RR (95% CI)	I^2	No. of studies	No. of cases
Emerging Risk Factors Collaboration[1] [101]	Malignant melanoma mortality	Per 6.5 cm	Men and women	1.26 (1.12-1.42)	43%	121	679
Asia-Pacific Cohort Studies Collaboration[1] [102]	Malignant melanoma mortality	Per 6 cm	Men	1.44 (1.15-1.79)	-	44	63
			Women	1.04 (0.71-1.52)	-		25
The Metabolic Syndrome and Cancer Project (Me-Can)[1] [91]	Malignant melanoma mortality	Per 5 cm	Men	1.10 (0.99-1.21)	-	7	246
			Women	1.09 (0.92-1.29)	-		102

Specific adjustments for skin sensitivity or sun exposure

1. In this meta-analysis, the authors did not add confounding variables relating to skin sensitivity or sun exposure to the multivariate model used. For details of adjustments made please see original studies.

Summary of prospective cohort studies of height and the risk of basal cell carcinoma

Study	Contrast	Sex	RR (95% CI)	No. of cases
Nambour Skin Cancer Study [88]	Highest quartile vs lowest quartile	Men and women	1.28 (1.01-1.62) P-trend = 0.015	344
United States Radiologic Technologists cohort [95]	≥67 vs ≤62 inches	Women	1.64 (1.40-1.93) P-trend < 0.0001	1,786
	≥73 vs ≤67 inches	Men	1.34 (0.94-1.89) P-trend = 0.05	481