

2018	DIET, NUTRITION, PHYSICAL ACTIVITY AND CANCERS OF THE MOUTH, PHARYNX AND LARYNX		
		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing		Alcoholic drinks
	Probable		Body fatness ¹
LIMITED EVIDENCE	Limited – suggestive	Non-starchy vegetables Healthy dietary patterns ² Coffee	Mate ³
	Limited – no conclusion	Cereals (grains) and their products; starchy roots, tubers, and plantains; fruits; pulses (legumes); dietary fibre; total meat; red meat; processed meat; poultry; fish; eggs; dairy products; total fat; animal fats; plant oils; tea; soft drinks; fruit juices; frying, grilling (broiling) and barbecuing (charbroiling); cooked food-acrylamide; protein; vitamin A; thiamin; riboflavin; niacin; vitamin C, iron, selenium; energy intake, carotenoids; retinol; folate; vitamin D; vitamin E; calcium; other patterns of diet (not related to healthy dietary indices); physical activity; height	
STRONG EVIDENCE	Substantial effect on risk unlikely		

- 1 Body fatness marked by body mass index (BMI), waist circumference and waist-hip ratio.
- 2 Judgements relate to healthy dietary patterns as marked by greater healthy dietary indices. These indices produce an integrated score to assess adherence to healthy eating or lifestyle recommendations or patterns. They are characterised by factors such as healthy weight management, engagement in physical activity, limiting intake of foods and drinks that promote weight gain, limiting intake of red and processed meat, limiting intake of alcoholic drinks, higher intake of plant foods, and breastfeeding (in women).
- 3 Mate, an infusion prepared from dried leaves of *Ilex paraguariensis*, is drunk traditionally in parts of South America, through a metal straw.

Summary of cohort studies – non-starchy vegetables. Dose-response analyses from individual studies identified in the CUP

Cancer type	Study	Increment	No. Cases	RR (95% CI)
Oral cavity	Netherlands Cohort Study [24]	Per 25 g/day	131	0.95 (0.89–1.02)
	NIH-AARP [25]	Per serving/ 1,000 kcal	319	0.84 (0.73–0.95)
Oro- and hypo-pharyngeal combined	Netherlands Cohort Study [24]	Per 25 g/day	88	0.94 (0.85–1.04)
	NIH-AARP [25]	Per serving/ 1,000 kcal	142	0.90 (0.74–1.09)
Laryngeal	Netherlands Cohort Study [24]	Per 25 g/day	193	0.98 (0.92–1.04)
	NIH-AARP [25]	Per serving/ 1,000 kcal	279	0.91 (0.79–1.05)
Head and neck	Netherlands Cohort Study [24]	Per 25 g/day	415	0.96 (0.92–1.01)
	NIH-AARP [25]	Per serving/ 1,000 kcal	787	0.89 (0.82–0.97)
Upper aerodigestive tract	European Prospective Investigation into Cancer and Nutrition [27]	Per 40 g/day	352	0.89 (0.78–1.02)

Note: All studies in men and women.

Summary of published pooled analysis of head and neck cancer, case-control studies – vegetables (excluding potatoes)

Analysis	Contrast	RR (95% CI)	P trend	No. studies	No. cases
Chuang, 2012 [23]	Highest vs. lowest				
	All	0.66 (0.49–0.90)	0.01		12,968
	Never smokers and light drinkers (≤3 drinks a day)	0.85 (0.60–1.19)	0.15	22	1,015

Summary of categorical analyses from studies reporting on healthy dietary indices and cancers of the mouth, pharynx and larynx

Diet index/ Cancer type	Study	Contrast	No. Cases	RR (95% CI)	P trend
American Cancer Society Guidelines score					
Oral cavity	NIH-AARP [35]	Quintile 5 vs. Quintile 1	862 M, 292 W	0.79 (0.64–0.97) 0.71 (0.48–1.06)	0.06 0.03
Laryngeal			620	0.82 (0.64–1.05)	0.06
Healthy Eating Index-2005					
Oral cavity	NIH-AARP [36]	Quintile 5 vs. Quintile 1	572 M, 208 W	0.84 (0.63–1.14) 0.58 (0.36–0.96)	0.25 0.004
Orophypo- pharyngeal			263 M, 74 W	0.64 (0.41–1.01) 0.42 (0.17–1.08)	0.008 0.054
Laryngeal			526 M, 96 W	0.70 (0.51–0.96) 0.40 (0.17–0.93)	0.098 0.0007
Head and neck		Quintile 5 vs. Quintile 1	1,466 M, 402 W	0.74 (0.61–0.89) 0.48 (0.33–0.70)	0.0008 <0.0001
aMED (Mediterranean) score					
Oral	NIH-AARP [36]	7-9 vs. 0-2	572 M, 208 W	0.95 (0.66–1.37) 0.47 (0.24–0.93)	0.31 <0.0001
Orophypo- pharyngeal		7-9 vs. 0-2 5-6 vs. 0-2	263 M, 74 W	0.91 (0.54–1.52) 0.68 (0.35–1.32)	0.046 0.079
Laryngeal		7-9 vs. 0-2	526 M, 96 W	0.68 (0.45–1.03) 0.59 (0.18–2.01)	0.059 0.075
Head and neck		7-9 vs. 0-2	1,466 M, 402 W	0.80 (0.64–1.01) 0.42 (0.24–0.74)	0.002 <0.0001
WCRF/AICR score					
Upper aerodigestive tract	European Prospective Investigation into Cancer and Nutrition [34]	Quintile 5 vs. Quintile 1	602	0.69 (0.50–0.95)	<0.0001

NIH-AARP dose-response analysis results by dietary index and head and neck cancer stratified by smoking

	Per increment of 10-score of the HEI-2005		Per increment of 1-score of the aMED score	
	Men	Women	Men	Women
Never smokers	1.00 (0.87–1.15)	0.80 (0.62–1.04)	1.00 (0.91–1.10)	0.91 (0.76–1.09)
Former smokers	0.91 (0.84–0.99)	0.79 (0.65–0.97)	0.93 (0.89–0.99)	0.75 (0.65–0.86)
Current smokers	0.87 (0.78–0.98)	0.74 (0.62–0.88)	0.91 (0.84–0.99)	0.87 (0.77–0.98)

Summary of case-control studies – mate

Cancer type	Study	Contrast	No. Cases, Controls	OR (95% CI)	P trend
Oral cavity	Deneo-Pellegrini, 2013, M [39]	Ever vs. never drinkers	696 cases, 696 controls	1.05 (0.70–1.55)	-
		Hot or very hot vs. never		1.11 (0.74–1.66)	0.37
	Franco, 1989 [41]	30 cups/month vs. <1 cup/month	232 cases, 464 controls	1.6 (0.8–3.3)	-
Oral cavity and pharyngeal combined	De Stefani 1988, M [42]	>2 L/day vs. <1 L/day	108 cases, 286 controls	5.2 (2.1–13.1)	-
Mouth	Pintos, 1994 [43]	>3 gourds/day vs. never	169 cases, 338 controls	2.82 (1.2–6.6)	0.038
Oral cavity and oropharyngeal combined	Szymanska, 2010 [40]	Ever vs. never	628 cases, 1,026 controls	1.48 (1.05–2.08)	-
		Hot or very hot vs. never		1.15 (0.79–1.66)	0.72
Hypo-pharyngeal and laryngeal combined	Szymanska, 2010 [40]	Ever vs. never drinkers	410 cases, 1,026 controls	1.51 (1.05–2.18)	-
		Hot or very hot vs. never		1.28 (0.87–1.9)	0.72
Upper aerodigestive tract	Szymanska, 2010 [40]	Ever vs. never drinkers	37 cases,* 1,026 controls	2.29 (0.58–9.07)	0.12
		Hot or very hot vs. never		2.50 (0.93–6.74)	0.095

* Never drinkers, never smokers

Summary of cohort studies – coffee. Dose-response analyses from individual studies identified in the CUP

Cancer type	Study	Contrast/ Increment	No. Cases	RR (95% CI)	P trend
Oral cavity	NIH-AARP [46]	>3 vs. <1 cups/ day	392	0.85 (0.62–1.16)*	0.14
Oral cavity and pharyngeal combined	Cancer Prevention Study II (mortality) [47]	>4 cups/day vs. no coffee/tea	299	0.58 (0.37–0.92)*	0.01
	Miyagi Cohort Study [48]	≥1 cup/day vs. never	48	0.35 (0.16–0.77)*	0.009
	Norwegian cohort [50]	≥7 cups/day vs. ≤2 cups/day ≥5 cups/day vs. <5 cups/day	33 M,	M: 0.5	-
			12 W	W: 0.7	
Pharyngeal	NIH-AARP [46]	>3 vs. <1 cups/ day	177	1.23 (0.75–2.01)*	0.34
Laryngeal	NIH-AARP [46]	>3 vs. <1 cups/ day	306	1.01 (0.71–1.44)*	0.95
Head and neck	Prostate, Lung, Colorectal, Ovarian cancer screening trial [49]	Per 1 cup/day	145	0.99 (0.91–1.09)*	
Upper aerodigestive tract	Miyagi Cohort Study [48]	≥1 cup/day vs. never	157	0.51 (0.33–0.77)*	0.002
	Hawaiian Prospective UADT Study M [51]	≥5 cups/week vs. ≤1 cup/week	92	1.44 (0.63–3.32)	0.441

* Hazard ratios

Summary of published pooled analysis of cancers of the mouth, pharynx and larynx, case-control studies – coffee*

Analysis		Increment	OR (95% CI)	No. Studies	No. Cases
Galeone, 2010 [52]	Oral cavity and pharyngeal combined	Per 1 cup/day	0.96 (0.94–0.98)	9	3,745
	Oral cavity		0.96 (0.92–0.99)		1,130
	Oro- and hypo-pharyngeal		0.95 (0.93–0.98)		2,023
	Laryngeal		0.99 (0.95–1.04)		1,178

* Results shown are for caffeinated coffee.

Summary of CUP 2016 meta-analysis and published pooled analysis of case-control studies, oral cavity cancer – alcohol

Analysis	Increment/ Contrast	RR (95% CI)	I ² /P trend	No. Studies	No. Cases
CUP Mouth, Pharynx and Larynx SLR 2016	Per 10 g/day	1.15 (1.09–1.22)	88%	6	5,617
Lubin 2011 [70]	5–10 drinks/ day vs. 0.01–0.9 drinks/day				
	M	1.75 (1.1–2.8)	<0.01	15	1,333
	W	2.37 (0.8–7.5)	<0.01		

Summary of CUP 2016 meta-analysis and published meta-analysis of cohort studies, oral cavity and pharyngeal cancers combined – alcohol

Analysis	Increment/Contrast	RR (95% CI)	I ²	No. Studies	No. Cases
CUP Mouth, Pharynx and Larynx SLR 2016	Per 10 g/day	1.19 (1.10–1.30)	83%	5	954
Bagnardi, 2015 [79]	Moderate drinkers (≤50 g/day) vs. non-drinkers	1.25 (1.02–1.53)	16%	5	993
	Heavy drinking (>50 g per day) vs. non-drinker	3.13 (1.59–6.19)	69%	3	

Summary of published pooled analysis of case-control studies, pharyngeal cancer – alcohol

Analysis	Cancer types	Contrast	OR (95% CI)	P trend	No. Studies	No. Cases
Lubin 2011 [70]	Oropharyngeal cancer	5–10 drinks/day vs. 0.01–0.9 drinks/day M	2.82 (1.8–4.3),	<0.01	15	1,528
		W	7.63 (2.8–21.0)	<0.01		404
	Hypo-pharyngeal cancer	5–10 drinks/day vs. 0.01–0.9 drinks/day M	7.03 (2.6–19.0),	<0.01		395
		W	19.6 (1.8–217.0)	<0.01		77

Summary of CUP 2016 meta-analysis and published meta-analysis of cohort studies, upper aerodigestive tract cancer – alcohol

Analysis	Increment/Contrast	RR (95% CI)	I ²	No. Studies	No. cases
CUP Mouth, Pharynx and Larynx SLR 2016	Per 10 g/day	1.18 (1.10–1.26)	95%	9	1,826
Jayasekara, 2016 [89]	Highest vs. lowest	2.83 (1.73–4.62)	0%	3	595

Summary of CUP dose-response meta-analyses, per 10 grams per day – other alcohol exposures, by cancer type

Analysis	Cancer type	RR (95% CI)	I² (%)	No. studies
CUP 2016 Beer	Oral cavity	1.14 (0.96–1.36)	74	2
	Pharyngeal	1.12 (1.02–1.24)	0	2
	Laryngeal	1.05 (0.98–1.13)	0	2
	Head and neck	1.09 (1.01–1.18)	49	2
CUP 2016 Wine	Oral cavity	0.90 (0.77–1.06)	18	2
	Pharyngeal	0.99 (0.83–1.17)	0	2
	Laryngeal	0.93 (0.80–1.07)	0	3
	Head and neck	0.92 (0.83–1.02)	0	2
CUP 2016 Spirits	Oral cavity	1.11 (1.02 –1.21)	0	2
	Pharyngeal	1.08 (0.89–1.31)	55	2
	Laryngeal	1.04 (0.96–1.13)	0	2
	Head and neck	1.09 (1.02–1.15)	15	2

Summary of results from published pooled analysis [100] – BMI and head and neck cancer

	No. Cases	HR (95% CI) Obese (≥ 30.0) vs. 21 to <23 kg/m ²	HR (95% CI) Underweight (15.0 to 20.9) vs. 21.0 to <23 kg/m ²	HR (95% CI) Per 5 kg/m ²	P trend
All	3,760	0.85 (0.76–0.96)	1.28 (1.11–1.46)	0.94 (0.90–0.98)	0.003
Never smokers	796	1.40 (1.08–1.81)	1.17 (0.85–1.61)	1.15 (1.06–1.24)	0.0006
Former smokers	1,508	0.96 (0.79–1.18)	1.24 (0.94–1.63)	0.99 (0.93–1.06)	0.79
Current smokers	1,367	0.58 (0.47–0.72)	1.30 (1.08–1.57)	0.76 (0.71–0.82)	<0.0001

Summary of results in never smokers from published pooled analysis [100] – BMI and cancers of the mouth, pharynx and larynx, by cancer type

Cancer type	Increment	No. Cases	HR (95% CI)	P trend
Oral cavity	per 5 kg/m ² BMI in never smokers	298	1.10 (0.97–1.25)	0.14
Oral cavity and pharyngeal (not otherwise specified) combined		93	1.36 (1.11–1.66)	0.003
Oropharyngeal		241	0.98 (0.84–1.14)	0.77
Hypo-pharyngeal		22	0.96 (0.55–1.67)	0.88
Laryngeal		142	1.42 (1.19–1.70)	0.0001

Summary of studies identified in the CUP but not included in the pooled analysis – BMI

Cancer type	Study	Contrast/ increment	No. Cases	RR (95% CI)	P trend
Oral cavity	CPRD [95]	Per 5 kg/m ² All Never smokers	7,976	0.81 (0.74–0.89) 1.07 (0.91–1.26)	-
Laryngeal	Cohort from Sweden, M [98]	Obese vs. normal weight	263	0.94 (0.57–1.56)	>0.35
Oropharyngolar- yngeal	JAMS, M [86]	≥23.2 kg/m ² vs. ≤18.9 kg/m ²	29	0.31 (0.08–1.11)*	-
Upper aerodigestive tract	Cohort from China, M [99]	Per 5 kg/m ² 15 –<23.5 kg/m ² 23.5 –<35 kg/m ²	706	1.06 (0.83–1.37) 0.87 (0.51–1.50)	-
	JAMS, M [86]	≥23.2 kg/m ² vs. ≤18.9 kg/m ²	52	0.28 (0.09–0.85)*	-

* Not adjusted for smoking.

Summary of other published pooled analyses of cancers of the mouth, pharynx and larynx – BMI

Analysis	Cancer type	Contrast/ Increment	RR (95% CI)	I ² /P trend	No. Studies	No. Cases
Parr, 2010 [101]	Oropharyngeal and laryngeal combined, mortality	Per 5 kg/m ²	0.66 (0.46–0.95)*	-	39 cohort studies	159
	Upper aerodigestive tract, mortality	Per 5 kg/m ²	0.78 (0.62–0.98)*	-		388
Lubin, 2011 [70]	Oral cavity	BMI ≥ 35 kg/m ² vs. BMI 18.5–24.9 kg/m ² M	0.65 (0.4–1.1)**	<0.01	15 Case-control studies	1,516
		W	0.92 (0.5–1.6)**	<0.01		925
	Oropharyngeal	BMI ≥ 35 kg/m ² vs. BMI 18.5–24.9 kg/m ² M	0.48 (0.3–0.7)**	<0.01		1,733
		W	0.35 (0.2–0.7)**	<0.01		564
	Hypo-pharyngeal	BMI 30.0–34.9 kg/m ² vs. BMI<18.5 kg/m ² M	0.24 (0.1–0.5)**	0.10		412
		W	0.24 (0.1–0.8)**	<0.01		96
	Laryngeal	BMI ≥ 35 kg/m ² vs. BMI 18.5–24.9 kg/m ² M	0.77 (0.4–1.4)**	<0.01		1,503
		W	0.27 (0.1–0.8)**	<0.01		237

* Hazard ratios ** Odds ratios

Summary of results for waist circumference from published pooled analysis [100] – head and neck cancer

	No. Cases	HR (95% CI) highest vs. lowest	RR (95% CI) Per 5 cm*	P trend
All	1,931	1.08 (0.93–1.25)	1.04 (1.03–1.05)	<0.0001
Never smokers	441	1.51 (1.09–2.08)	1.07 (1.01–1.14)	0.022
Former smokers	706	1.21 (0.94–1.55)	1.06 (1.01–1.11)	0.01
Current smokers	745	0.80 (0.62–1.04)	1.04 (1.02–1.05)	<0.0001

* controlling for BMI

Summary of results from published pooled analysis (NCI consortium [100]) reviewing waist-hip ratio and head and neck cancer

	No. Cases	RR (95% CI) Highest vs. lowest	RR (95% CI) Per 0.1 unit	P trend
All	1,677	1.30 (1.12–1.50)	1.06 (1.04–1.09)	<0.0001
Never smokers	382	1.23 (0.89–1.69)	1.08 (0.96–1.22)	0.2013
Former smokers	577	1.25 (0.98–1.59)	1.10 (1.01–1.20)	0.0351
Current smokers	685	1.38 (1.09–1.75)	1.06 (1.02–1.10)	0.0017