COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Bagnardi et al., (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose–response meta-analysis. British Journal of Cancer 112, 580-593

1. As part of the strategy proposed to consider the role of alcohol consumption and cancer risk, it was suggested that the COC review the epidemiological data on alcohol consumption and cancer published since the last IARC review in 2009. Members considered the IARC reviews at the time. In 2007 (published IARC 2010), IARC reviewed the epidemiological evidence on the possible association between alcoholic beverage consumption and cancer at 27 anatomical sites (cancers of the oral cavity and the pharynx, larynx, oesophagus, liver, breast stomach, colon and/or rectum, pancreas, lung, urinary bladder, endometrium, ovary, uterine cervix, prostate, kidney, lymphatic and haematopoietic system, testis, brain, thyroid, melanoma and other female cancers (vulva and vagina)). They re-affirmed their previous conclusion (IARC, 1988) that cancers of the upper digestive tract (oral cavity, pharynx, larynx, and oesophagus) and the liver are causally related to the consumption of alcoholic beverages. In addition, IARC considered that there was now sufficient evidence to conclude that cancer of the colo-rectum and female breast are causally related to the consumption of alcoholic beverages (IARC, 2007). Following another IARC review in 2009 (IARC 2012), IARC reaffirmed their position for the aforementioned cancers and also reported an association between alcohol consumption and cancer of the pancreas, although they were unable to reach a conclusion on whether this was causal. COC agreed that an update review of the causal cancer sites and pancreas would be an appropriate strategy to help in its future calculation of burden of cancer attributable to alcohol consumption.

2. To date, COC has considered alcohol and the risk of pancreatic cancer, liver cancer, colorectal cancer and breast cancer. Alcohol and the risk of the upper aero-digestive cancers will be brought to forthcoming COC meetings. COC has also considered evidence on the effect of alcohol cessation on cancer risk. Additionally, COC has reviewed recent meta-analyses on the inverse association between alcohol consumption and Hodgkin's lymphoma, non-Hodgkin's lymphoma, kidney and extra-hepatic bile system cancer risk.

3. The Secretariat has identified a recently published meta-analysis by Bagnardi et al. (2015) on alcohol consumption and the risk of 23 site-specific cancers. Tables outlining the findings for each of the 23 site specific cancers from the meta-analysis are attached as Annex A. The tables also include details of the IARC opinion for each of the sites and comparative details of the studies included in the Bagnardi et al (2015) analysis and those reviewed by the COC where relevant. The Bagnardi et al (2015) paper is attached as Annex B.

4. Bagnardi et al. (2015) performed their meta-analysis of data on alcohol drinking (light, moderate and heavy drinking) and cancer risk using data from 572 studies published between 1956 and 2012 (409 case-control and 163 cohort studies).

Criteria set for inclusion in the meta-analysis were a) case-control studies, nested case-control studies or cohort studies published as original articles; b) studies that reported findings as odds ratios (ORs), relative risks (RRs) or hazard ratios (HRs) for at least two levels of alcohol consumption versus non-drinkers or occasional drinkers; c) studies that reported confidence intervals (CI) or standard errors of the risk estimates or sufficient data to calculate them. Criteria set for exclusion from the meta-analysis were studies reporting on specific alcohol beverage only as the non-drinkers in those studies could be drinkers of another alcoholic beverage type. For the purposes of the analysis and to have unity in the expression of consumption, they used g per day as a standard measure of ethanol intake using the following assumptions: 0.8 g/ml, 28 g/ounce and 12.5 g/drink. For studies where the levels of consumption were reported in a range, the exposure was assigned as the midpoint of the range for the reported categories of alcohol intake. They considered as light, moderate and heavy drinking every interval whose midpoint was ≤12.5, ≤50 and > 50g per day of alcohol. Depending on the study and, if the data were available, the Bagnardi et al analysis used RR adjusted for the main site specific confounders or they calculated the unadjusted RRs from the raw data. The reference category was non-drinker. A pooled RR was estimated of each site-specific cancer for light drinkers versus non-drinkers, moderate drinkers versus non-drinkers and heavy drinkers versus non-drinkers using random-effects models. Statistical heterogeneity among studies was assessed using I^2. Subgroup analyses were also performed on cancer sites where 10 or more studies were available and considered study design, gender and geographical area.

5. Results for each site are presented in the attached tables. In brief, they observed a dose response relationship for oral and pharyngeal cancer, oesophageal squamous cell carcinoma, colorectal cancer, laryngeal cancer and female breast cancer. They reported that heavy drinkers had a higher risk of cancers of the gallbladder, liver, stomach, pancreas and lung compared to non-drinkers. They also indicated a positive association with prostate cancer and malignant melanoma. Inverse associations were observed for Hodgkin's lymphoma and non-Hodgkin's lymphoma.

Questions for the Committee

1) What are Members' general views on this meta-analysis?

2) Do Members have any specific comments on this analysis?

3) Do Members have any comment on the sites where the outcomes of the Bagnardi et al (2015) analysis are different to the IARC conclusions?

4) For completeness, do Members think the other sites need reviewing in light of this publication?

Secretariat
April 2015

References

Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, Scotti L, Jenab M, Turati F, Pasquali E, Pelucchi C, Galeone C, Bellocco R, Negri E, Corrao G, Boffetta P, La Vecchia C. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. Br J Cancer. 112, 580-593

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Table of data from Bagnardi et al with comparison to findings of IARC and papers assessed by COC.

Secretariat
April 2015

Latest IARC opinion - Vol 100e	Total Number of papers used by Bagnardi et al (2015) (cohort / case-control)	Number of papers published since 2009 used by Bagnardi et al (2015)	Number of papers in current review by COC	Has COC reviewed all studies published since 2009 in Bagnardi et al (2015)	List of studies not yet reviewed by COC	Bagnardi et al (2015) results												Bagnardi et al (2015) conclusions
						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Oral cavity and pharynx																		
Sufficient	52 (5/47)	4	10 Meta- or pooled analyses 10 Cohort 6 Case-Control 4 others	Yes			All			Cohort			Men			European		Dose-response relationship observed
						Light	1.13 (1.00-1.26)	26	4	0.86 (0.60-1.23)	68	12	1.20 (1.06-1.35)	0	5	0.95 (0.80-1.12)	0	
						Moder-ate	1.83 (1.62-2.07)	72	5	1.25 (1.02-1.53)	16	26	2.01 (1.69-2.40)	73	16	1.51 (1.22-1.89)	67	
						Heavy	5.13 (4.31-6.10)	77	3	3.13 (1.59-6.19)	69	21	5.33 (4.28-6.63)	71	14	5.41 (3.79-7.72)	81	
										Case-Control			Women			North-American		
						Light			22	1.22 (1.10-1.35)	0	8	1.00 (0.78-1.27)	51	11	1.09 (0.92-1.29)	38	
						Moder-ate			47	1.91 (1.69-2.16)	70	9	1.67 (1.25-2.22)	52	15	2.02 (1.74-2.34)	46	
						Heavy			35	5.34 (4.46-6.39)	77	3	5.70 (3.75-8.66)	0	12	5.58 (4.35-7.15)	71	
																Asian		
						Light									7	1.33 (1.06-1.68)	21	
						Moder-ate									12	2.18 (1.64-2.91)	78	
						Heavy									4	3.02 (1.93-4.73)	62	

Latest IARC opinion - Vol 100e	Total Number of papers used by Bagnardi et al (2015) (cohort / case-control)	Number of papers published since 2009 used by Bagnardi et al (2015)	Number of papers in current review by COC	Has COC reviewed all studies published since 2009 in Bagnardi et al (2015)	List of studies not yet reviewed by COC	Bagnardi et al (2015) results												Bagnardi et al (2015) conclusions
						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Laryngeal Cancer																		
Sufficient	41 (3/38)	1	6 Meta- or pooled analyses 4 Cohort 2 Case-Control	Yes			All			Cohort			Men			European		Dose-response relationship observed
						Light	0.87 (0.68-1.11)	39	3	0.81 (0.61-1.07)	21	8	0.85 (0.61-1.19)	51	4	0.83 (0.41-1.67)	54	
						Moder-ate	1.44 (1.25-1.66)	61	3	1.09 (0.70-1.72)	46	21	1.50 (1.23-1.83)	66	16	1.36 (1.12-1.65)	64	
						Heavy	2.65 (2.19-3.19)	77	3	1.12 (0.75-1.67)	0	22	2.77 (2.15-3.57)	83	18	2.71 (2.02-3.63)	82	
										Case-Control			Women			North-American		
						Light			11	0.88 (0.61-1.27)	45	3	0.89 (0.62-1.29)	0	7	0.90 (0.67-1.21)	37	
						Moder-ate			34	1.48 (1.28-1.73)	62	3	1.59 (1.06-2.38)	0	15	1.54 (1.20-1.98)	57	
						Heavy			33	2.81 (2.33-3.39)	76	1	1.55 (0.45-5.34)	0	13	2.74 (2.15-3.48)	60	
																Asian		
						Light									4	0.72 (0.34-1.50)	52	
						Moder-ate									4	1.57 (0.78-3.16)	69	
						Heavy									3	1.63 (0.70-3.79)	81	

Latest IARC opinion - Vol 100e	Total Number of papers used by Bagnardi et al (2015) (cohort / case-control)	Number of papers published since 2009 used by Bagnardi et al (2015)	Number of papers in current review by COC	Has COC reviewed all studies published since 2009 in Bagnardi et al (2015)	List of studies not yet reviewed by COC	Bagnardi et al (2015) results												Bagnardi et al (2015) conclusions
						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Oesophageal Squamous Cell Carcinoma																		
Sufficient	54 (13/41)	7	13 Meta- or pooled analyses 13 Cohort 18 Case-Control 6 others	Yes			All			Cohort			Men			European		Dose-response relationship observed
						Light	1.26 (1.06-1.50)	68	10	1.20 (0.84-1.71)	84	16	1.39 (1.11-1.74)	61	7	1.05 (0.79-1.38)	22	
						Moder-ate	2.23 (1.87-2.65)	85	13	1.92 (1.44-2.58)	83	28	2.25 (1.78-2.85)	85	10	1.91 (1.32-2.77)	71	
						Heavy	4.95 (3.86-6.34)	91	9	3.56 (2.25-5.64)	91	24	4.69 (3.49-6.31)	88	8	4.76 (2.69-8.41)	85	
										Case-control			Women			North-American		
						Light			24	1.29 (1.07-1.55)	49	8	1.14 (0.87-1.49)	43	12	1.07 (0.84-1.37)	32	
						Moder-ate			40	2.34 (1.87-2.92)	86	8	2.18 (1.42-3.35)	72	13	2.95 (2.38-3.67)	37	
						Heavy			32	5.43 (4.04-7.32)	91	3	8.32 (2.95-23.45)	72	10	7.63 (5.34-10.91)	59	
																Asian		
						Light									11	1.54 (1.18-2.00)	71	
						Moder-ate									23	2.20 (1.65-2.94)	91	
						Heavy									18	4.24 (2.93-6.14)	93	

Latest IARC opinion - Vol 100e	Total Number of papers used by Bagnardi et al (2015) (cohort / case-control)	Number of papers published since 2009 used by Bagnardi et al (2015)	Number of papers in current review by COC	Has COC reviewed all studies published since 2009 in Bagnardi et al (2015)	List of studies not yet reviewed by COC	Bagnardi et al (2015) results												Bagnardi et al (2015) conclusions
						Alcohol intake	All		Study Type			Sex			Population groups			
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Oesophageal adenocarcinoma & gastric cardia																		
	25 (4/21)	4		Yes			All			Cohort			Men			European		No association observed
						Light	0.86 (0.76-0.98)	32	4	0.88 (0.74-1.03)	6	3	0.94 (0.42-2.08)	78	7	0.79 (0.68-0.93)	0	
						Moder-ate	0.97 (0.78-1.22)	72	4	0.82 (0.62-1.07)	50	5	0.92 (0.46-1.86)	76	5	0.90 (0.60-1.36)	61	
						Heavy	1.15 (0.95-1.39)	36	1	1.11 (0.48-2.56)	0	6	1.17 (0.72-1.88)	57	4	1.52 (0.80-2.88)	65	
										Case-Control			Women			North-American		
						Light			17	0.88 (0.74-1.04)	38	2	0.85 (0.63-1.14)	0	10	0.95 (0.78-1.16)	41	
						Moder-ate			17	1.06 (0.78-1.43)	75	2	0.62 (0.42-0.93)	0	10	0.99 (0.78-1.25)	56	
						Heavy			17	1.16 (0.95-1.41)	40	1	3.80 (0.89-16.32)	0	9	1.23 (0.93-1.63)	38	
																Asian		
						Light									2	1.18 (0.24-5.79)	82	
						Moder-ate									4	0.97 (0.24-3.83)	91	
						Heavy									3	0.89 (0.49-1.64)	36	

Latest IARC opinion - Vol 100e	Total Number of papers used by Bagnardi et al (2015) (cohort / case-control)	Number of papers published since 2009 used by Bagnardi et al (2015)	Number of papers in current review by COC	Has COC reviewed all studies published since 2009 in Bagnardi et al (2015)	List of studies not yet reviewed by COC	Bagnardi et al (2015) results												Bagnardi et al (2015) conclusions
						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Colorectal cancer																		
Sufficient	66 (33/33)	6	9 Meta-or pooled analyses 8 Cohort 9 Case-Control	No	Breslow et al 2011, Yi et al, 2010, Yamamoto et al, 2010 Mortia et al 2009		All			Cohort			Men			European		Dose-response relationship observed
						Light	0.99 (0.95-1.04)	40	33	1.01 (0.95-1.06)	22	29	1.05 (0.95-1.16)	44	13	1.03 (0.97-1.10)	21	
						Moder-ate	1.17 (1.11-1.24)	52	33	1.20 (1.12-1.29)	45	36	1.21 (1.11-1.32)	40	13	1.17 (1.07-1.29)	57	
						Heavy	1.44 (1.25-1.65)	69	14	1.41 (1.23-1.63)	46	20	1.53 (1.30-1.80)	70	7	1.22 (0.98-1.52)	61	
										Case-Control			Women			North-American		
						Light			32	0.97 (0.89-1.06)	53	23	0.95 (0.89-1.01)	27	27	0.96 (0.90-1.03)	44	
						Moder-ate			33	1.14 (1.05-1.25)	58	20	1.07 (0.99-1.16)	32	27	1.14 (1.05-1.24)	48	
						Heavy			15	1.46 (1.15-1.86)	78	4	1.24 (0.68-2.25)	69	9	1.29 (1.01-1.66)	65	
																Asian		
						Light									22	1.03 (0.91-1.18)	38	
						Moder-ate									24	1.24 (1.08-1.42)	56	
						Heavy									13	1.73 (1.39-2.16)	67	

Latest IARC opinion - Vol 100e	Total Number of papers used by Bagnardi et al (2015) (cohort / case-control)	Number of papers published since 2009 used by Bagnardi et al (2015)	Number of papers in current review by COC	Has COC reviewed all studies published since 2009 in Bagnardi et al (2015)	List of studies not yet reviewed by COC	Bagnardi et al (2015) results												Bagnardi et al (2015) conclusions
						Alcohol intake	All		Study Type			Sex			Population groups			
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Small Intestine cancer																		
	5 (1/4)	1	N/A	Not reviewed by COC to date	N/A		All											
						Light	1.05 (0.77-1.44)	8										
						Moder-ate	1.00 (0.81-1.25)	0										
						Heavy	1.07 (0.67-1.68)	21										
Gallbladder Cancer																		
	8 (4/4)	1	N/A	Not reviewed by COC to date	N/A		All											
						Light	1.23 (0.84-1.83)											
						Moder-ate	0.88 (0.68-1.13)											
						Heavy	2.64 (1.62-4.30)											

Latest IARC opinion - Vol 100e	Total Number of papers used by Bagnardi et al (2015) (cohort / case-control)	Number of papers published since 2009 used by Bagnardi et al (2015)	Number of papers in current review by COC	Has COC reviewed all studies published since 2009 in Bagnardi et al (2015)	List of studies not yet reviewed by COC	Bagnardi et al (2015) results												Bagnardi et al (2015) conclusions
						Alcohol intake	All		Study Type			Sex			Population groups			
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Liver Cancer																		
Sufficient	36 (9/27)	6	5 Meta- or pooled analyses 12 Cohort 4 Case-Control	No	Hassan et al. 2009 Yun et al. 2010		All			Cohort			Men			European		Significantly higher risk of liver cancer among heavy drinkers
						Light	1.00 (0.85-1.18)	47	9	0.85 (0.74-0.97)	32	10	1.05 (0.84-1.32)	53	6	0.92 (0.58-1.46)	31	
						Moder-ate	1.08 (0.97-1.20)	49	9	1.00 (0.87-1.17)	58	16	1.08 (0.88-1.32)	57	9	0.83 (0.70-0.97)	0	
						Heavy	2.07 (1.66-2.58)	79	7	1.12 (1.02-1.23)	0	11	1.59 (1.21-2.09)	69	8	2.00 (1.07-3.74)	85	
										Case-Control			Women			North-American		
						Light			12	1.31 (0.97-1.78)	23	6	0.81 (0.59-1.12)	26	3	1.24 (0.73-2.10)	0	
						Moder-ate			27	1.15 (0.97-1.35)	40	8	1.24 (0.88-1.75)	39	8	1.23 (0.97-1.56)	33	
						Heavy			24	2.79 (2.00-3.87)	76	3	3.89 (1.60-9.48)	10	7	3.40 (2.54-4.55)	0	
																Asian		
						Light									12	1.02 (0.83-1.26)	58	
						Moder-ate									18	1.14 (0.97-1.33)	59	
						Heavy									15	1.59 (1.27-2.00)	69	

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						Alcohol intake	All		Study Type			Sex			Population groups			
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Stomach cancer																		
Data difficult to interpret	39 (19/20)	7	N/A	Not reviewed by COC to date	N/A		All			Cohort			Men			European		Significantly higher risk of stomach cancer among heavy drinkers Could be biased by unaccounted confounders and misclassifi-cation of exposure. Should be investigated more.
						Light	0.99 (0.92-1.06)	55	19	0.94 (0.87-1.03)	55	14	1.00 (0.92-1.10)	17	12	0.98 (0.84-1.15)	66	
						Moder-ate	0.97 (0.90-1.04)	46	19	0.96 (0.88-1.06)	62	20	1.07 (1.00-1.14)	2	11	0.90 (0.79-1.04)	46	
						Heavy	1.21 (1.07-1.36)	41	9	1.15 (1.03-1.28)	0	12	1.20 (0.99-1.45)	63	5	1.21 (1.04-1.42)	0	
										Case-Control			Women			North-American		
						Light			16	1.08 (0.93-1.26)	57	6	1.08 (0.76-1.54)	73	6	0.95 (0.75-1.22)	50	
						Moder-ate			20	0.98 (0.89-1.08)	11	5	0.90 (0.66-1.22)	62	7	0.90 (0.76-1.06)	1	
						Heavy			11	1.22 (0.97-1.54)	65	1	3.23 (0.80-13.07)	0	3	1.42 (0.86-2.34)	21	
																Asian		
						Light									15	1.01 (0.94-1.08)	25	
						Moder-ate									16	1.01 (0.91-1.12)	59	
						Heavy									10	1.08 (0.93-1.26)	35	

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						Alcohol intake	All		Study Type			Sex			Population groups			
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Pancreatic Cancer																		
Association observed	39 (18/21)	13	3 Meta- and pooled analyses 6 Cohort 2 Case-Control	No	Heinen et al. 2009 Jiao et al. 2009 Kim et al. 2010 Rohrmann et al. 2009 Sonoyana et al. 2011		All			Cohort			Men			European		Significantly higher risk of pancreatic cancer among heavy drinkers (more studies needed)
						Light	0.95 (0.89-1.01)		18	0.95 (0.89-1.01)	40	15	0.98 (0.86-1.11)	46	11	0.90 (0.85-0.96)	0	
						Moder-ate	1.03 (0.97-1.09)		18	1.06 (0.99-1.13)	28	20	1.08 (1.00-1.15)	0	11	0.97 (0.90-1.04)	0	
						Heavy	1.19 (1.11-1.28)		9	1.18 (1.08-1.28)	0	12	1.16 (1.06-1.27)	0	4	0.79 (0.50-1.24)	0	
										Case-Control			Women			North-American		
						Light			18	0.97 (0.84-1.13)	42	13	0.93 (0.86-1.01)	39	16	0.99 (0.89-1.09)	52	
						Moder-ate			21	0.97 (0.88-1.06)	8	11	1.04 (0.93-1.17)	51	16	1.03 (0.95-1.12)	13	
						Heavy			13	1.16 (0.98-1.37)	17	4	1.17 (0.98-1.40)	2	9	1.17 (1.08-1.28)	0	
																Asian		
						Light									8	1.01 (0.71-1.45)	45	
						Moder-ate									9	1.19 (0.97-1.46)	30	
						Heavy									8	1.18 (0.96-1.44)	0	

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						Alcohol intake	All		Study Type			Sex			Population groups			
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Lung Cancer																		
Available data were inadequate	34 (18/16)	5	N/A	Not reviewed by COC to date	N/A		All			Cohort			Men			European		Significantly higher risk of lung cancer among heavy drinkers. Could be biased by unaccounted confounders and misclassifi-cation of exposure. Should be investigated more.
						Light	0.84 (0.79-0.88)	44	18	0.85 (0.82-0.89)	26	17	0.86 (0.82-0.91)	0	4	0.80 (0.76-0.85)	0	
						Moder-ate	0.98 (0.92-1.05)	57	18	0.97 (0.91-1.04)	60	22	0.98 (0.89-1.08)	60	4	0.88 (0.83-0.94)	0	
						Heavy	1.15 (1.02-1.30)	73	13	1.07 (0.93-1.25)	75	14	1.14 (1.00-1.31)	78	4	0.96 (0.74-1.26)	40	
										Case-Control			Women			North-American		
						Light			11	0.71 (0.57-0.89)	57	11	0.85 (0.77-0.93)	59	14	0.87 (0.80-0.94)	44	
						Moder-ate			14	1.03 (0.87-1.21)	51	11	1.01 (0.89-1.15)	70	14	1.06 (0.98-1.15)	45	
						Heavy			7	1.33 (1.07-1.66)	51	4	1.20 (0.75-1.92)	65	6	1.26 (1.10-1.45)	53	
																Asian		
						Light									9	0.81 (0.69-0.94)	45	
						Moder-ate									12	0.93 (0.80-1.08)	51	
						Heavy									6	0.92 (0.87-0.98)	0	

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						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Female Breast Cancer																		
Sufficient	118 (43/75)	21	7 Meta- or pooled analyses 15 Cohort 14 Case-Control 15 other	No	Barnes et al 2011 Brown et al. 2010 Buck et al. 2011 Hines et al. 2010 Kim et al. 2010 Suzuki et al. 2010		All			Cohort			Men			European		Dose-response relationship observed
						Light	1.04 (1.01-1.07)	63	42	1.06 (1.03-1.10)	41				41	1.03 (0.98-1.10)	67	
						Moder-ate	1.23 (1.19-1.28)	54	37	1.22 (1.17-1.27)	31				33	1.19 (1.10-1.28)	60	
						Heavy	1.61 (1.33-1.94)	10	6	1.50 (1.19-1.89)	0				5	1.82 (1.14-2.89)	43	
									Case-Control			Women			North-American			
						Light			73	1.04 (0.99-1.09)	69				55	1.06 (1.03-1.10)	55	
						Moder-ate			58	1.23 (1.16-1.32)	62				46	1.25 (1.20-1.31)	51	
						Heavy			5	1.78 (1.27-2.50)	28				4	1.67 (1.33-2.09)	0	
																Asian		
						Light									8	0.89 (0.72-1.11)	75	
						Moder-ate									8	1.44 (1.21-1.71)	20	
						Heavy									1	3.44 (0.47-25.14)	0	

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						Alcohol intake	All		Study Type			Sex			Population groups			
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Cervical Cancer																	
Weak and difficult to draw any conclusions	5 (2/3)	1	N/A	Not reviewed by COC to date	N/A		All										
						Light	0.87 (0.75-1.01)										
						Moder-ate	0.90 (0.73-1.11)										
						Heavy	n.e										

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						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Endometrial Cancer																		
Inconsistent	21 (8/13)	3	N/A	Not reviewed by COC to date	N/A		All			Cohort			Men			European		No association observed
						Light	0.97 (0.92-1.01)	6	8	0.97 (0.92-1.02)	4				8	1.00 (0.93-1.07)	10	
						Moder-ate	0.99 (0.84-1.16)	73	5	1.06 (0.89-1.26)	67				4	1.15 (0.84-1.57)	86	
						Heavy	n.e.	–	–	n.e.	–				–	n.e.	–	
									Case-Control				Women		North-American			
						Light			13	0.95 (0.87-1.03)	14				11	0.93 (0.86-1.00)	13	
						Moder-ate			8	0.87 (0.64-1.18)	78				7	0.97 (0.80-1.18)	60	
						Heavy			–	n.e.	–				–	n.e.	–	
																Asian		
						Light									2	0.93 (0.68-1.26)	0	
						Moder-ate									2	0.43 (0.25-0.74)	0	
						Heavy									–	n.e.	–	

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						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Ovarian Cancer																		
Little evidence of an association	20 (4/16)	2	N/A	Not reviewed by COC to date	N/A		All			Cohort			Men			European		
						Light	0.98 (0.93-1.03)	16	4	1.02 (0.96-1.08)	0				7	0.96 (0.89-1.05)	23	
						Moder-ate	1.03 (0.95-1.12)	39	4	1.08 (0.99-1.19)	20				5	1.02 (0.93-1.11)	22	
						Heavy	n.e.	–	–	n.e.	–				–	n.e.	–	
									Case-Control				Women		North-American			
						Light			16	0.94 (0.87-1.01)	17				11	1.00 (0.92-1.09)	0	
						Moder-ate			13	0.99 (0.88-1.12)	43				10	1.09 (0.95-1.24)	27	
						Heavy			–	n.e.	–				–	n.e.	–	
																Asian		
						Light									–	n.e.	–	
						Moder-ate									–	n.e.	–	
						Heavy									–	n.e.	–	

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						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Prostate Cancer																		
Little evidence for an association	43 (20/23)	7	N/A	Not reviewed by COC to date	N/A		All			Cohort			Men			European		Indication of a positive association
						Light	1.04 (1.01-1.08)	0	19	1.04 (1.01-1.08)	0				11	1.02 (0.94-1.11)	0	
						Moder-ate	1.06 (1.01-1.11)	17	20	1.06 (0.99-1.13)	24				11	1.00 (0.90-1.11)	18	
						Heavy	1.09 (0.98-1.21)	37	8	1.04 (0.90-1.21)	45				4	0.95 (0.75-1.21)	36	
										Case-Control			Women			North-American		
						Light			17	1.04 (0.97-1.11)	0				21	1.05 (1.01-1.09)	5	
						Moder-ate			21	1.06 (0.99-1.14)	15				22	1.09 (1.02-1.16)	29	
						Heavy			10	1.12 (0.95-1.33)	37				7	1.20 (1.09-1.31)	13	
																Asian		
						Light									3	0.91 (0.70-1.19)	0	
						Moder-ate									5	1.05 (0.85-1.31)	0	
						Heavy									4	1.00 (0.58-1.72)	50	

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						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Kidney Cancer																		
No causal association	17 (6/11)	2	N/A	Not fully reviewed by COC to date NB - one meta-analysis reviewed	N/A		All			Cohort			Men			European		No association observed
						Light	0.92 (0.86-0.99)	34	6	0.93 (0.85-1.02)	37	10	0.99 (0.87-1.11)	30	7	1.01 (0.86-1.17)	32	
						Moder-ate	0.79 (0.72-0.86)	38	6	0.74 (0.64-0.86)	46	10	0.83 (0.71-0.97)	46	7	0.81 (0.69-0.94)	34	
						Heavy	0.80 (0.57-1.14)	49	2	0.88 (0.16-4.92)	81	3	0.88 (0.29-2.63)	65	2	0.75 (0.60-0.93)	0	
										Case-Control			Women			North-American		
						Light			11	0.92 (0.82-1.03)	36	9	0.85 (0.78-0.92)	0	6	0.89 (0.80-1.00)	41	
						Moder-ate			11	0.82 (0.72-0.94)	32	6	0.65 (0.52-0.81)	42	6	0.80 (0.69-0.92)	38	
						Heavy			3	0.81 (0.67-0.98)	0	–	n.e.	–	1	0.98 (0.68-1.41)	0	
																Asian		
						Light									1	0.63 (0.35-1.13)	0	
						Moder-ate									2	1.07 (0.18-6.41)	84	
						Heavy									2	0.88 (0.16-4.92)	81	

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						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Bladder Cancer																		
No association was observed	19 (3/16)	0	N/A	Not reviewed by COC to date	N/A		All			Cohort			Men			European		No association observed
						Light	0.99 (0.89-1.10)	39	3	1.10 (0.87-1.41)	49	9	1.13 (0.97-1.32)	32	8	1.09 (0.85-1.40)	51	
						Moder-ate	1.01 (0.91-1.12)	41	3	1.03 (0.76-1.40)	56	12	1.07 (0.95-1.22)	23	8	1.07 (0.89-1.28)	43	
						Heavy	0.95 (0.75-1.20)	65	–	n.e.	–	5	1.24 (0.87-1.78)	70	4	1.23 (0.76-1.99)	81	
										Case-Control			Women			North-American		
						Light			16	0.96 (0.85-1.09)	37	7	0.88 (0.70-1.12)	52	9	0.95 (0.84-1.09)	41	
						Moder-ate			16	1.01 (0.90-1.13)	42	6	0.93 (0.72-1.20)	44	9	0.96 (0.84-1.09)	40	
						Heavy			10	0.95 (0.75-1.20)	65	1	0.81 (0.38-1.73)	0	4	0.80 (0.56-1.14)	68	
																Asian		
						Light									2	1.00 (0.64-1.56)	0	
						Moder-ate									2	1.49 (0.54-4.09)	65	
						Heavy									2	0.89 (0.51-1.54)	0	

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						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Non-Hodgkins Lymphoma																		
No or inverse associations with consumption of alcoholic beverages	24 (9/15)	3	N/A	Not fully reviewed by COC to date NB – one meta-analysis reviewed	N/A		All			Cohort			Men			European		Inverse associated. Could be biased by unaccounted confounders and misclassifi-cation of exposure. Should be investigated more.
						Light	0.88 (0.80-0.97)	65	9	1.02 (0.93-1.12)	39	7	0.96 (0.78-1.18)	50	9	0.97 (0.83-1.12)	35	
						Moder-ate	0.87 (0.81-0.95)	35	9	0.87 (0.77-0.97)	36	9	0.91 (0.76-1.08)	47	9	0.95 (0.82-1.12)	53	
						Heavy	0.75 (0.64-0.88)	10	3	0.74 (0.59-0.92)	0	2	0.87 (0.52-1.43)	0	2	0.97 (0.71-1.34)	0	
										Case-Control			Women			North-American		
						Light			15	0.78 (0.69-0.88)	46	8	0.90 (0.78-1.04)	62	10	0.87 (0.77-0.99)	66	
						Moder-ate			15	0.88 (0.78-0.99)	37	5	0.86 (0.72-1.03)	44	9	0.84 (0.76-0.94) 0.77 (0.59-1.00)	32	
						Heavy			4	0.82 (0.60-1.13)	50	–	n.e.	–	1		0	
																Asian		
						Light									2	0.75 (0.41-1.36)	88	
						Moder-ate									3	0.77 (0.61-0.98)	0	
						Heavy									3	0.62 (0.50-0.78)	0	

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						Alcohol intake	All		Study Type			Sex			Population groups			
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Hodgkins Lymphoma																		
No or inverse associations with consumption of alcoholic beverages	9 (2/7)	2	N/A	Not fully reviewed by COC to date NB – one meta-analysis reviewed	N/A		All											Inverse association Could be biased by unaccounted confounders and misclassifi-cation of exposure. Should be investigated more.
						Light	0.73 (0.59-0.89)											
						Moder-ate	0.73 (0.60-0.87)											
						Heavy	0.63 (0.41-0.97)											
Brain Cancer																		
Not possible to draw any conclusions	6 (4/2)	2	N/A	Not reviewed by COC to date	N/A		All											
						Light	1.01 (0.86-1.18)											
						Moder-ate	1.10 (0.84-1.43)											
						Heavy	1.45 (0.69-3.08)											

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						Alcohol intake	All		Study Type			Sex			Population groups			
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Thyroid Cancer																	
Not possible to draw any conclusions	9 (6/3)	3	N/A	Not reviewed by COC to date	N/A		All										
						Light	0.81 (0.74-0.88)										
						Moder-ate	0.81 (0.71-0.94)										
						Heavy	n.e.										

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						Alcohol intake	All		Study Type			Sex			Population groups				
							RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	
Malignant Melanoma																		
Not possible to draw any conclusions	14 (2/12)	0	N/A	Not reviewed by COC to date	N/A		All			Cohort			Men			European		Indication of a positive association (more studies needed)
						Light	1.11 (0.97-1.27)	36	2	1.25 (1.13-1.38)	0	3	1.19 (0.82-1.72)	0	5	0.97 (0.74-1.28)	76	
						Moder-ate	1.20 (1.03-1.41)	38	2	1.27 (1.13-1.42)	0	3	1.32 (0.90-1.92)	0	5	1.01 (0.75-1.36)	68	
						Heavy	n.e.	–	–	n.e.	–	–	n.e.	–	–	n.e.	–	
										Case-Control			Women			North-American		
						Light			12	1.06 (0.90-1.25)	32	4	1.25 (1.13-1.38)	0	6	1.32 (1.11-1.59)	0	
						Moder-ate			10	1.16 (0.92-1.45)	47	3	1.27 (1.14-1.43)	0	5	1.47 (1.14-1.88)	0	
						Heavy			–	n.e.	–	–	n.e.	–	–	n.e.	–	
																Asian		
						Light									–	n.e.	–	
						Moder-ate									–	n.e.	–	
						Heavy									–	n.e.	–	

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Bagnardi et al., (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose–response meta-analysis. British Journal of Cancer 112, 580-593

Full paper: Bagnardi et al., (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose–response meta-analysis. British Journal of Cancer 112, 580-593

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