



# **Update on alcohol and cancer epidemiology**

**Is the evidence getting clearer?**

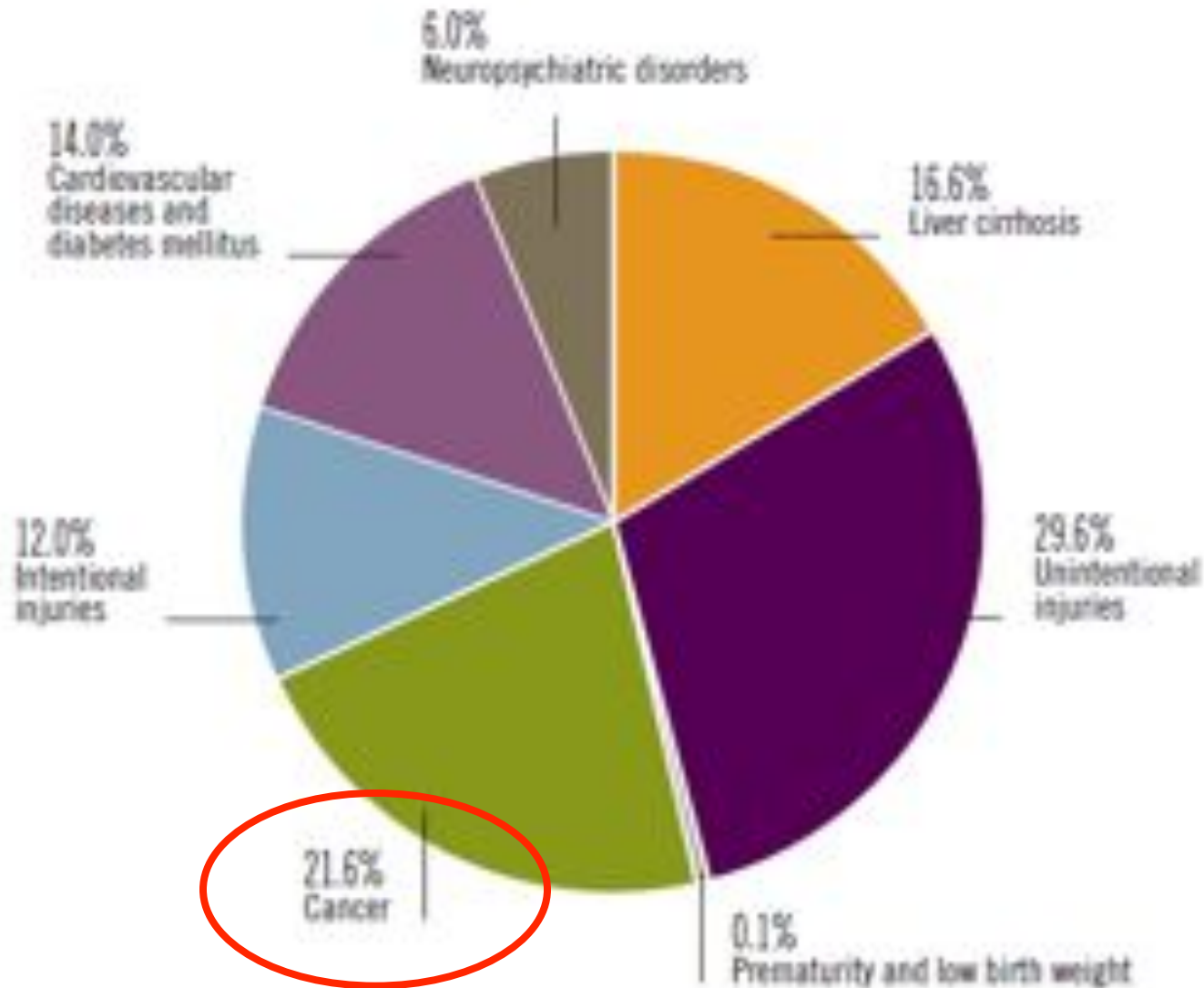
International Agency for Research on Cancer  
Lyon, France

**Dr. Isabelle Romieu**

# Key Facts

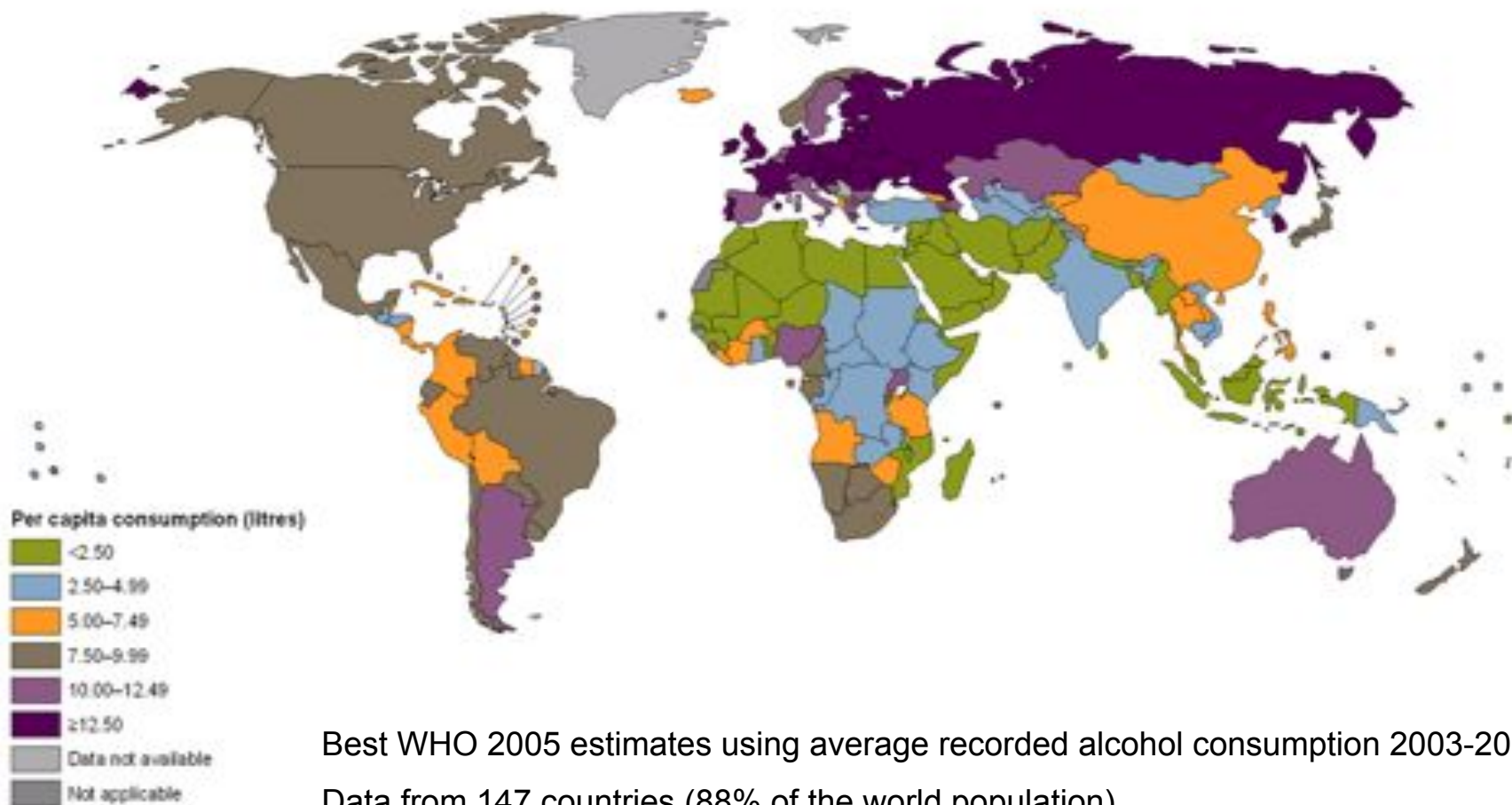
- Alcohol is the world's third largest risk factor for disease burden
- More than 1.9 billion adults ( $\geq 15$  years old) are regular alcohol consumers, with an average daily consumption of 13 g of ethanol (~one drink).
- There are around 2.5 million alcohol-related deaths each year
- 320 000 (12.8%) of alcohol-related deaths are among young people (15-29 years old)

# Global distribution of all alcohol-attributable deaths by disease



# Total adult *per capita* consumption

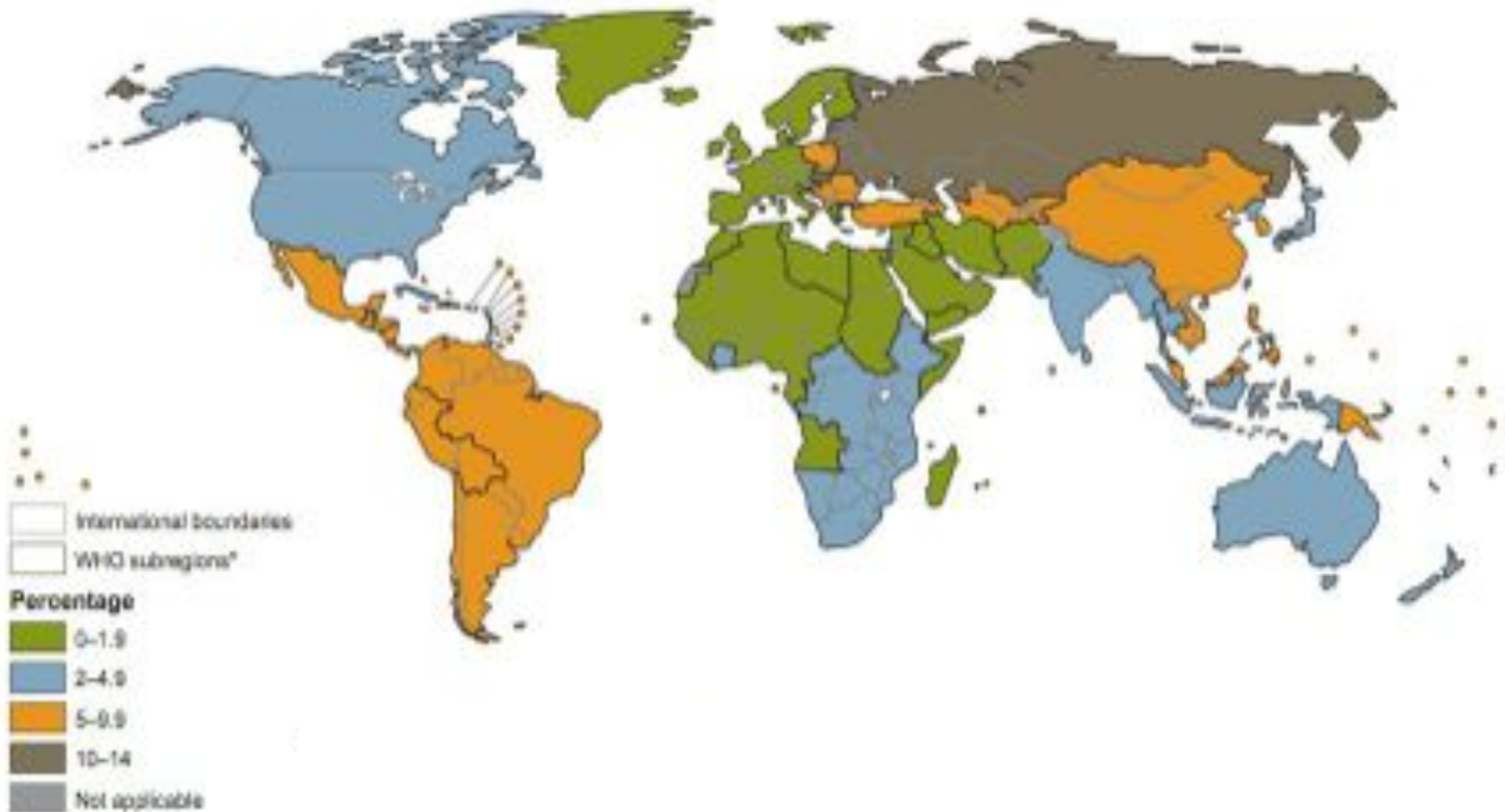
Global Information System on Alcohol and Health



Best WHO 2005 estimates using average recorded alcohol consumption 2003-2005.  
Data from 147 countries (88% of the world population).

International Agency for Research on Cancer

# Alcohol-attributable deaths



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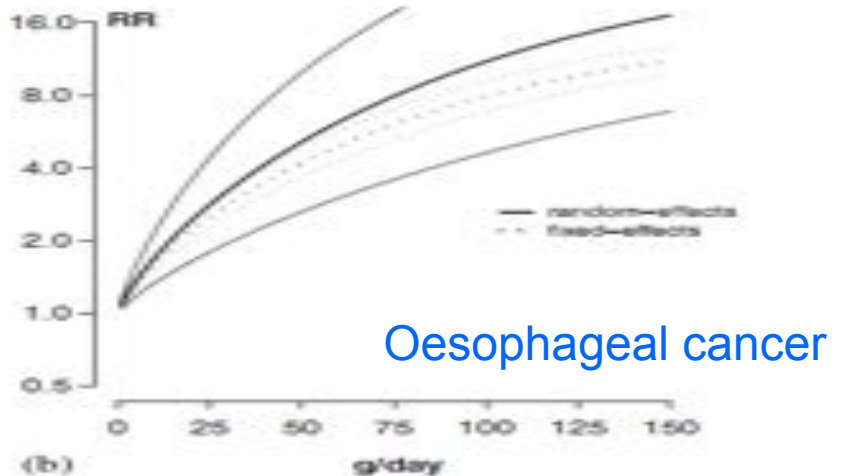
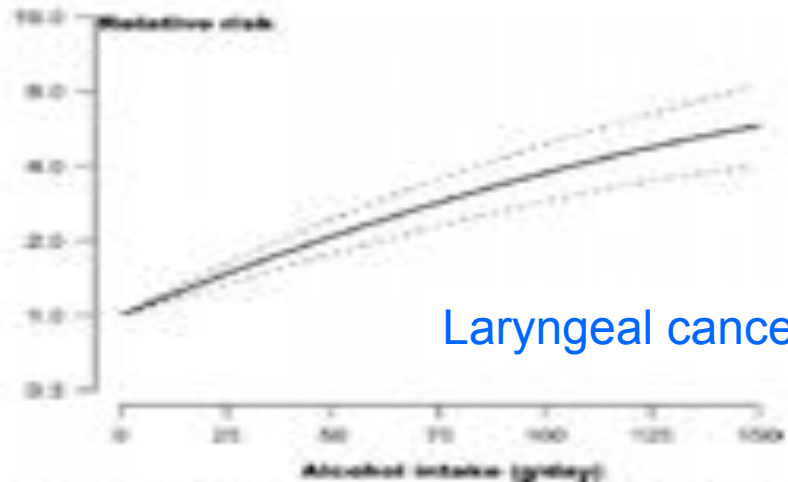
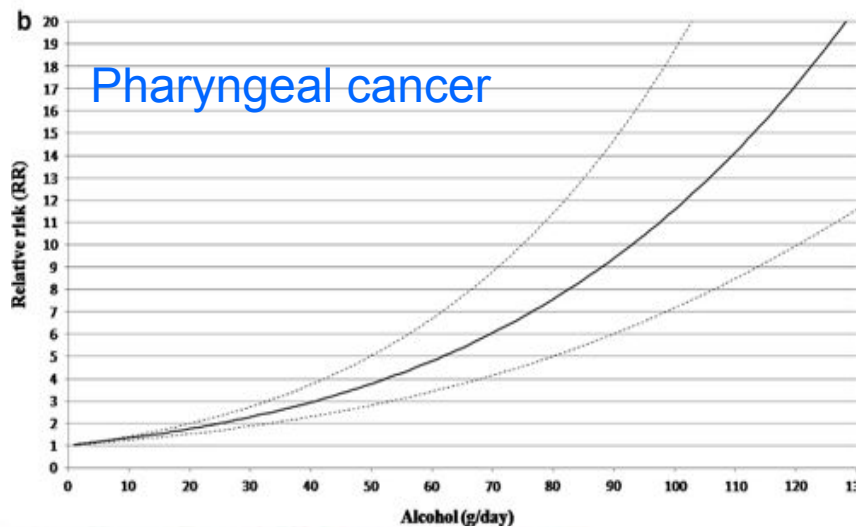
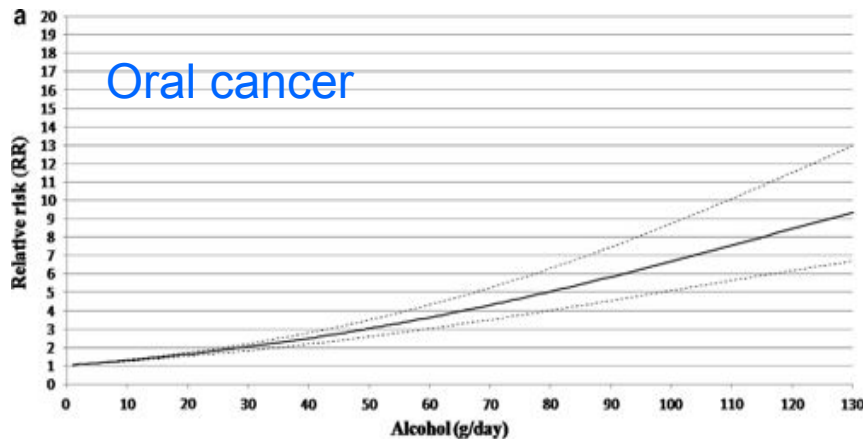
# IARC evaluation (Vol. 100E)

- The Working Group confirmed previous conclusion (Vol. 44, 1988):
  - Cancers of the oral cavity, pharynx, larynx, oesophagus and liver are causally related to the consumption of alcoholic beverages.
  - There is sufficient evidence for breast cancer in women and colorectal cancer

## Overall evaluations: Group 1

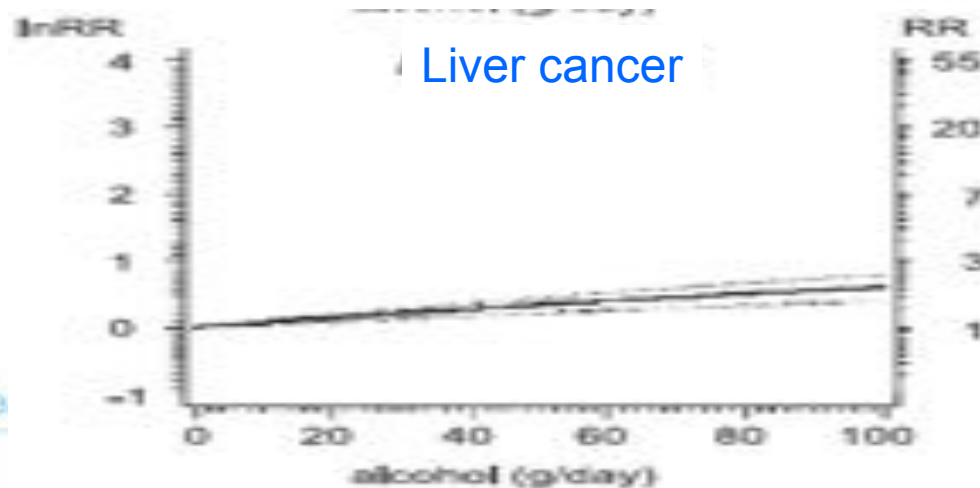
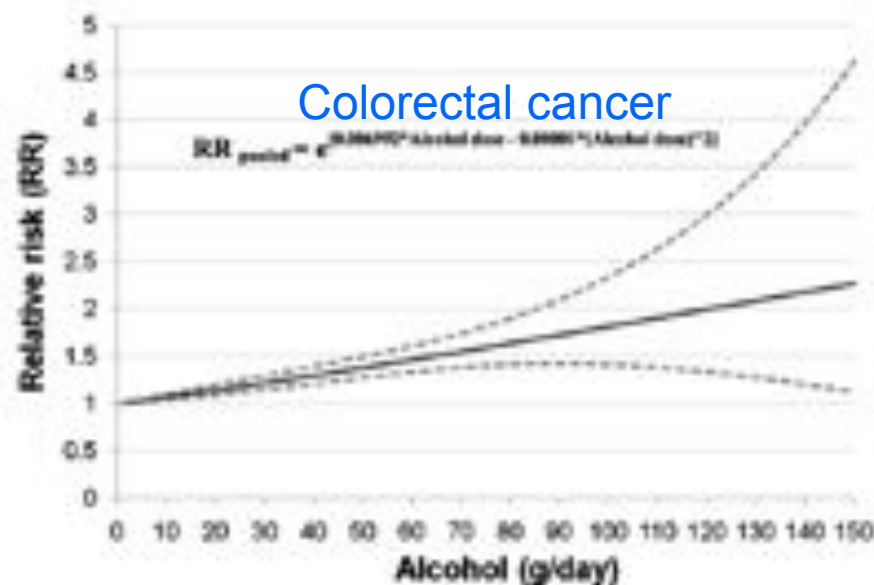
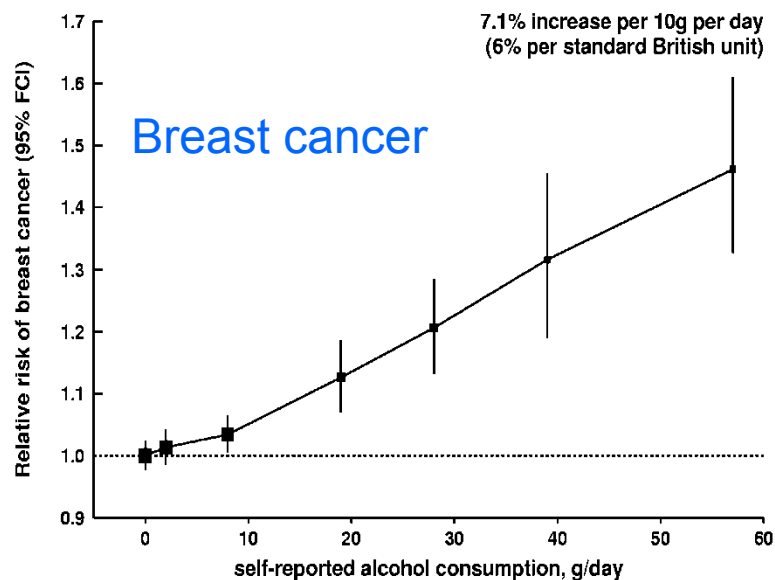
- Alcoholic beverages are carcinogenic to humans
- Ethanol in alcoholic beverages is carcinogenic to humans
- Acetaldehyde is carcinogenic to humans

# Dose-cancer risk relationship (UADT)



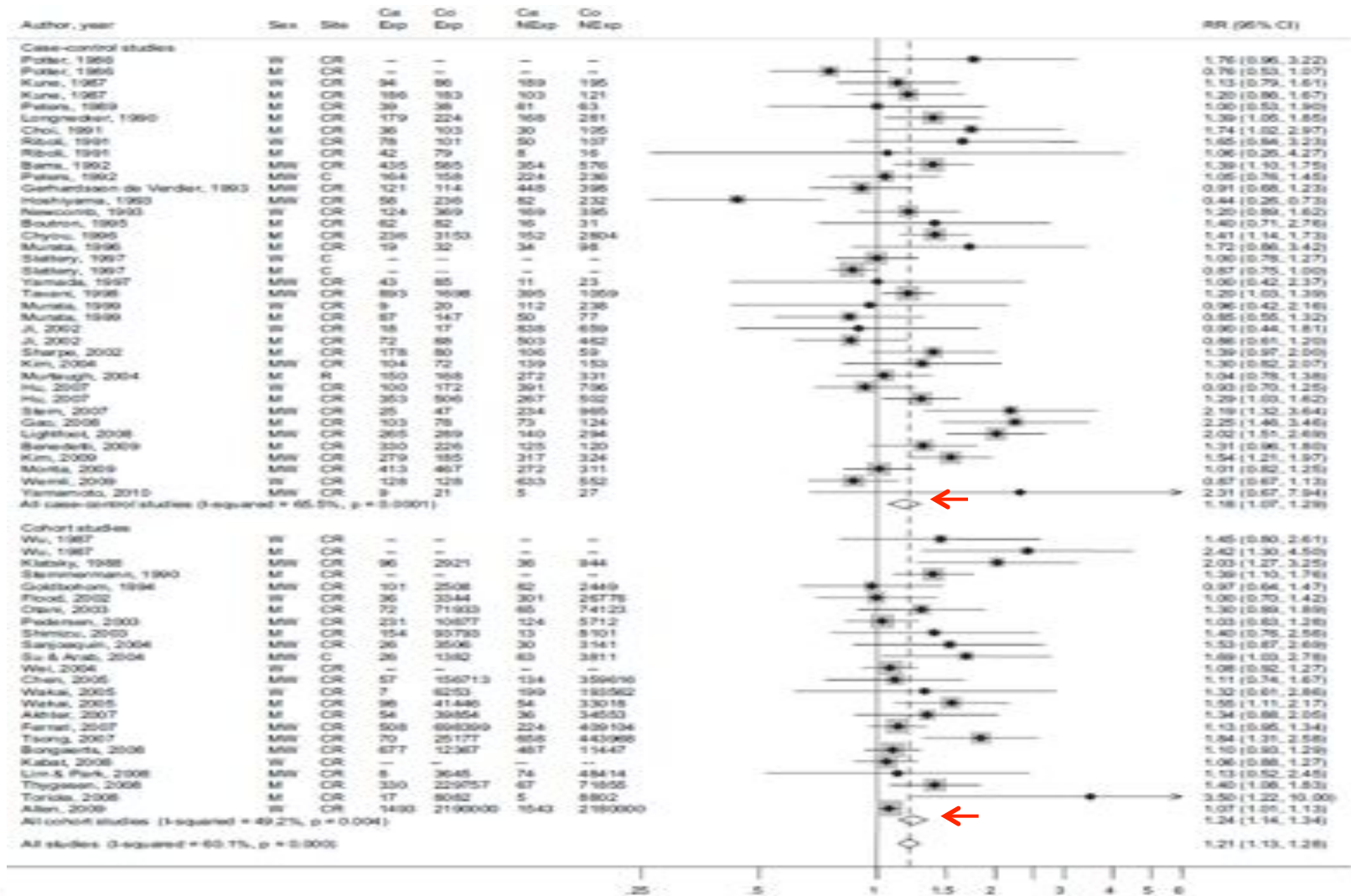


# Dose-cancer risk relationship





# Alcohol drinking and colorectal cancer



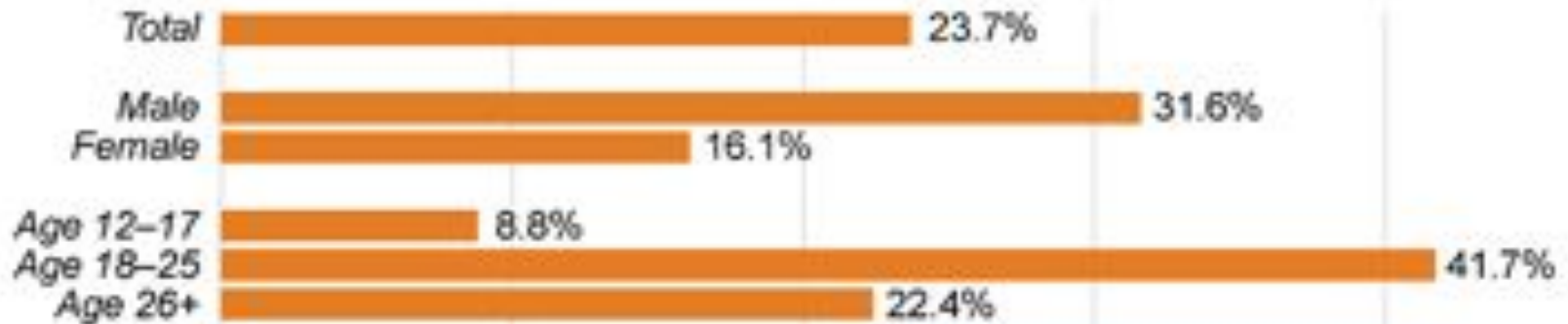
# Alcohol Attributable Burden of Cancer Incidence-EPIC

	Men	Women
Total	10% (7% to 13%)	3% (1% to 5%)
UADT	44% (31% to 56%)	25% (5% to 46%)
Liver	33% (11% to 54%)	18% (-3% to 38%)
Colorectal	17% (10% to 25%)	4% (-1% to 10%)
Breast	-	5% (2% to 8%)

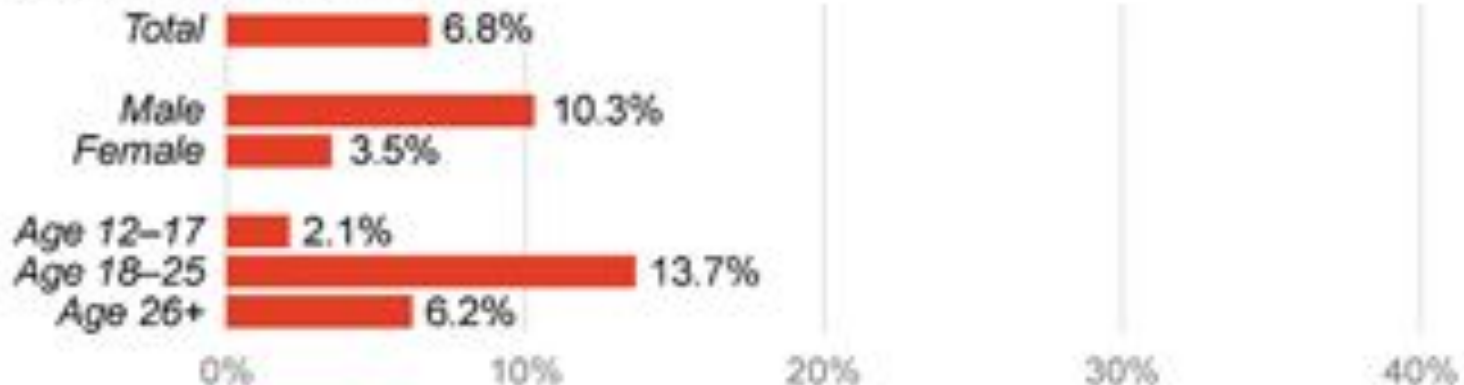
Based on 8 countries: France, Italy, Spain, UK, the Netherlands, Greece, Germany, Denmark ( env. 350,000 individuals)

# Binge drinking by age (USA)

## Binge Drinking



## Heavy Alcohol Use



Note: The survey defines "binge drinking" as five or more drinks on the same occasion at least one day in the last month, and "heavy use" as the same amount on at least five days in the last month.

# Alcohol intake and BC by drinking pattern

Days Alcohol Consumed in Typical Week					Largest No. of Alcoholic Drinks Consumed in 1 Day in Typical Month				
Days, No.	Cases/ Person-Years, No.	Incidence Rate <sup>a</sup>	Multivariate RR (95% CI) <sup>b</sup>		Drinks, No.	Cases/ Person-Years, No.	Incidence Rate <sup>a</sup>	Multivariate RR (95% CI) <sup>b</sup>	
			Model 1	Model 2				Model 1	Model 2
0	2382/654 064	364	1 [Reference]	1 [Reference]	0	1735/476 522	364	1 [Reference]	1 [Reference]
1-2	1441/385 233	373	1.05 (0.99-1.13)	1.03 (0.95-1.11)	1-2	2559/653 056	392	1.08 (1.02-1.16)	1.07 (0.99-1.15)
3-4	500/132 420	378	1.05 (0.95-1.16)	0.97 (0.86-1.09)	3-5	905/233 786	387	1.16 (1.07-1.27)	1.08 (0.97-1.20)
5-7	961/217 546	442	1.20 (1.11-1.30)	1.05 (0.93-1.18)	≥6	131/31 614	414	1.33 (1.11-1.59)	1.21 (0.99-1.47)
P for trend	5284/1 390 704	380	<.001	.29		5331/1 394 978	382	<.001	.04

Abbreviation: RR, relative risk.

<sup>a</sup>Per 100 000 person-years.

<sup>b</sup>Covariates listed in footnote to Table 2. Analyses begin in 1988 when drinking patterns were first assessed. Model 1 does not control for cumulative alcohol intake. Model 2 does control for cumulative alcohol intake.

# Alcohol intake and BC by age at consumption

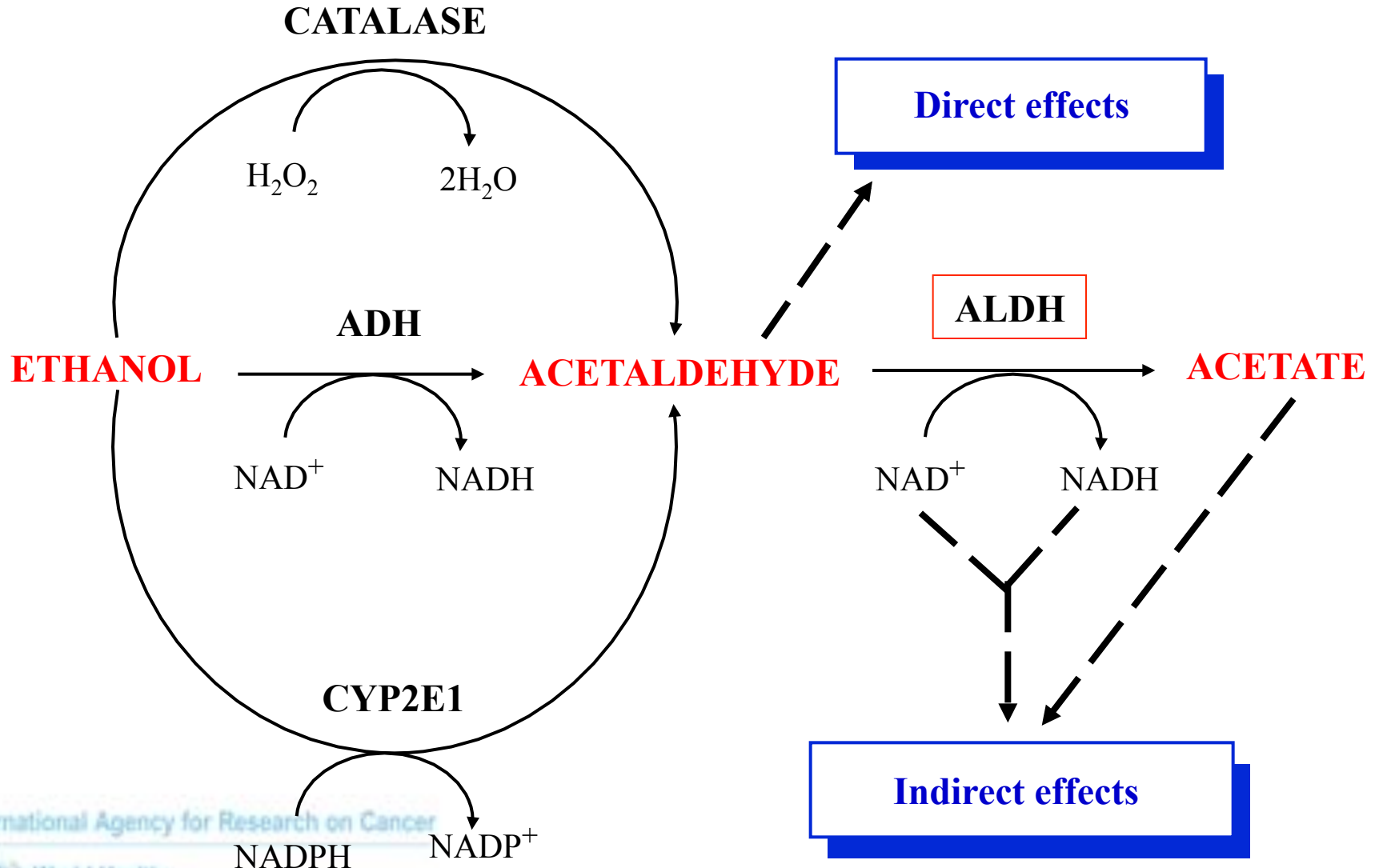
All Invasive Breast Cancers								
Cumulative Alcohol Intake, g/d	Ages 18-40 y				Age >40 y			
	Cases/ Person-Years, Incidence No.	Rate <sup>a</sup>	RR (95%CI)		Cases/ Person-Years, Incidence No.	Rate <sup>a</sup>	RR (95%CI)	
			Model 1 <sup>b</sup>	Model 2 <sup>c</sup>			Model 1 <sup>b</sup>	Model 2 <sup>c</sup>
0	816/235246	347	1 (Reference)	1 (Reference)	976/283346	344	1 (Reference)	1 (Reference)
0.1-4.9	3028/828044	366	1.06 (0.97-1.14)	1.02 (0.93-1.12)	2162/606120	357	1.03 (0.95-1.11)	1.02 (0.93-1.10)
5-9.9	748/189544	395	1.13 (1.02-1.26)	1.05 (0.93-1.18)	704/185852	379	1.09 (0.99-1.20)	1.07 (0.96-1.19)
10-19.9	322/74250	434	1.25 (1.09-1.43)	1.15 (0.99-1.33)	690/162162	426	1.20 (1.09-1.33)	1.17 (1.04-1.31)
≥20	42/9128	429	1.33 (0.97-1.82)	1.21 (0.88-1.67)	424/98732	429	1.23 (1.09-1.39)	1.18 (1.03-1.34)
RR per 10-g increase			1.16 (1.08-1.25)	1.08 (1.00-1.18)			1.08 (1.05-1.12)	1.07 (1.03-1.10)
P for trend	4956/1336212	371	<.001	.05	4956/1336212	371	<.001	<.001



# Genetic susceptibility

- Role of polymorphisms in enzymes involved in ethanol and acetaldehyde metabolism ( ADH, ALDH)
- May explain inter-individual differences of susceptibility to alcohol
- Role of polymorphism of genes involved in nutrient metabolism  
e.g. MTHFR that acts on folate metabolism

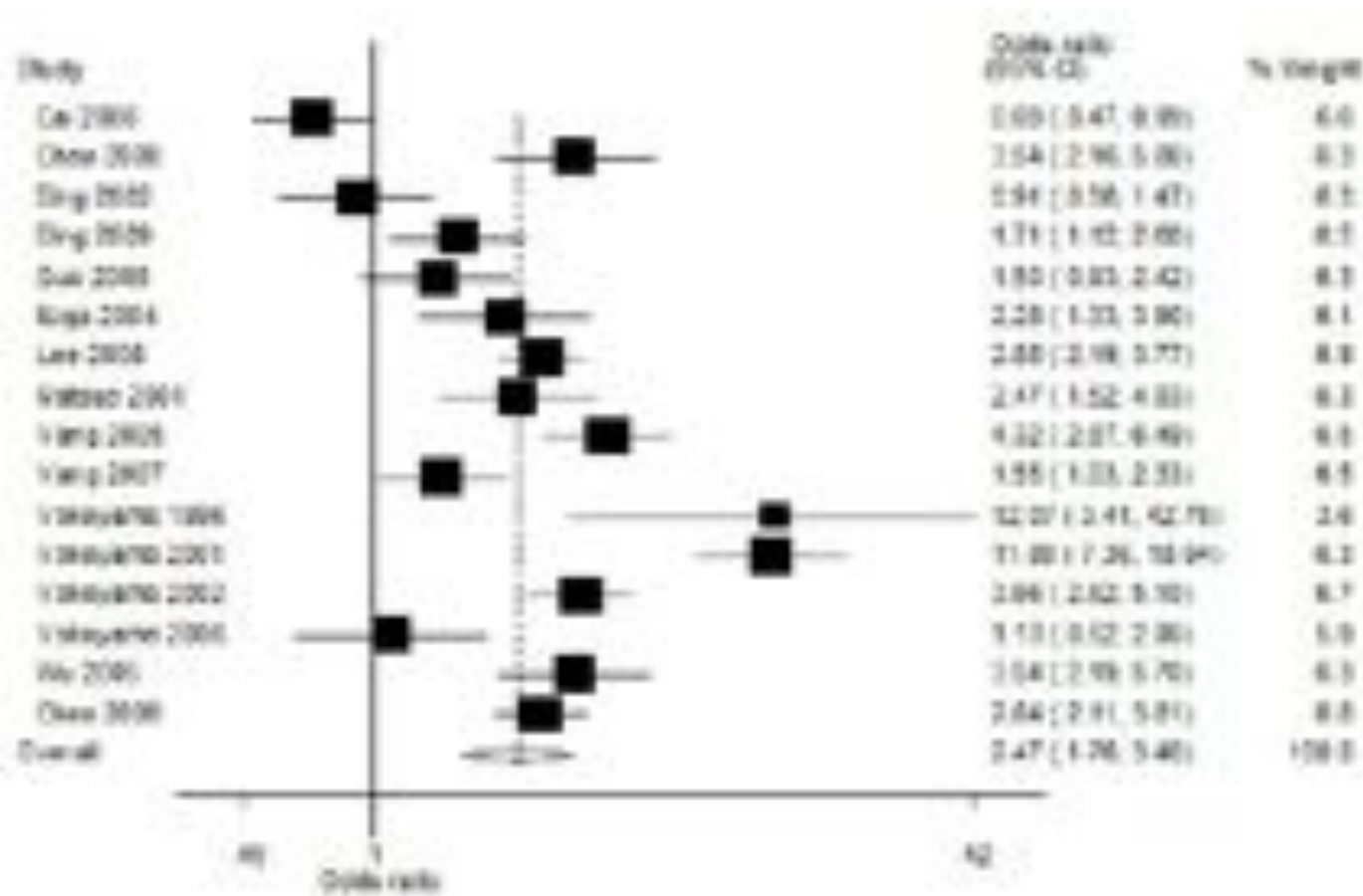
# Alcohol metabolism





# Alcohol and Oesophageal cancer

## ALDH2\*1/\*2 vs ALDH2\*1/\*1



# Alcohol-folate interaction and BC

Quintile intake*	Alcohol $\geq 15$ g/d				Alcohol $< 15$ g/d			
	ER <sup>+</sup>		ER <sup>-</sup>		ER <sup>+</sup>		ER <sup>-</sup>	
	Cases	RR (95% CI)	Cases	RR (95% CI)	Cases	RR (95% CI)	Cases	RR (95% CI)
Total folate ( $\mu\text{g}/\text{d}$ )								
$< 228$	83	1.00	36	1.00	399	1.00	170	1.00
228-294	95	1.09 (0.81-1.47)	25	0.73 (0.43-1.22)	474	1.05 (0.91-1.20)	201	1.10 (0.90-1.36)
294-381	90	1.08 (0.80-1.47)	28	0.89 (0.54-1.48)	496	1.03 (0.90-1.18)	144	0.76 (0.60-0.95)
381-534	90	1.05 (0.77-1.43)	26	0.81 (0.48-1.35)	511	1.06 (0.93-1.21)	177	0.93 (0.75-1.15)
$\geq 534$	80	1.00 (0.73-1.37)	14	0.46 (0.25-0.86)	494	1.01 (0.88-1.15)	164	0.88 (0.71-1.10)
$P_{\text{trend}}$		0.81		0.03		0.94		0.15
Dietary folate ( $\mu\text{g}/\text{d}$ )								
$< 206$	85	1.00	36	1.00	368	1.00	163	1.00
206-246	103	1.21 (0.90-1.62)	30	0.89 (0.55-1.45)	453	1.11 (0.97-1.28)	176	1.04 (0.84-1.29)
246-284	86	1.03 (0.76-1.40)	32	1.00 (0.61-1.63)	480	1.10 (0.96-1.27)	174	1.00 (0.80-1.24)
284-332	95	1.22 (0.91-1.65)	15	0.52 (0.28-0.96)	517	1.13 (0.98-1.29)	157	0.88 (0.70-1.10)
$> 332$	69	1.06 (0.77-1.47)	16	0.66 (0.36-1.21)	556	1.16 (1.02-1.33)	186	1.04 (0.83-1.28)
$P_{\text{trend}}$		0.74		0.06		0.04		0.85

# MTHFR-alcohol interaction

	Alcohol consumption (tertiles)		P-trend	P-interaction
	Medium	High		
<b>Colorectal cancer</b>				
				0.31
CC/CT (cases/controls)	96/124	80/175		
Adjusted OR (95% CI)	1.12 (0.78, 1.60)	1.87 (1.29, 2.71)	<0.001	
TT (cases/controls)	25/26	33/33		
Adjusted OR (95% CI)	1.01 (0.55, 1.85)	0.89 (0.51, 1.54)	0.700	
<b>Colon cancer</b>				
				0.70
CC/CT (cases/controls)	96/68	80/85		
Adjusted OR (95% CI)	1.75 (1.12, 2.72)	2.60 (1.63, 4.12)	<0.001	
TT (cases/controls)	25/11	33/16		
Adjusted OR (95% CI)	1.28 (0.58, 2.79)	1.20 (0.60, 2.42)	0.282	
<b>Rectal cancer</b>				
				0.40
CC/CT (cases/controls)	96/43	80/73		
Adjusted OR (95% CI)	0.80 (0.50, 1.30)	1.78 (1.13, 2.82)	0.001	
TT (cases/controls)	25/9	33/14		
Adjusted OR (95% CI)	0.84 (0.36, 1.95)	0.84 (0.41, 1.72)	0.581	

# Conclusions and Perspectives

- Alcohol causes several cancers: oral cavity, pharynx, larynx, oesophagus, and colorectal, liver and female breast.
- The adverse effect is observed even with light (  $\leq 1$  drink/day) alcohol consumption.
- Increasing alcohol consumption increases risk in a dose-dependent manner
- No specific difference in alcoholic beverages and ethanol content and acetaldehyde appears the common factor related to the increased risk of cancer
- Alcohol carcinogenesis may be modulated by the activity of several polymorphisms in enzymes involved in ethanol and/or acetaldehyde and some nutrient metabolism.

# Conclusions and Perspectives (2)

Further epidemiological studies should:

- Used standardized drinking exposure (g of ethanol vs volume of alcoholic beverage).
- Focus on **drinking pattern** ( e.g Binge drinking) and determine the effect of cumulative vs current intake
- Explore the possibility of a **susceptibility window** during adolescence and the role of age-started dinking?
- Explore **modulators** of effects: nutrient intake such as folate and genetic susceptibility
- Explore **epigenetic changes** related to alcohol intake



International Agency for Research on Cancer

# Thank you

Dr. Isabelle Romieu  
Head Nutrition and Metabolism Section  
at IARC

[iromieu@iarc.fr](mailto:iromieu@iarc.fr)