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Medicina interna e consumo di alcol: Un problema sottovalutato. Il ruolo della SIA per la prevenzione

Appendici: etanolo

ETANOLO

Coordinatore: Andrea Ghiselli

Alessandro Casini, Mauro Ceccanti, Carlo La Vecchia, Valentino Patussi, Emanuele Scafato, Francesco Violi

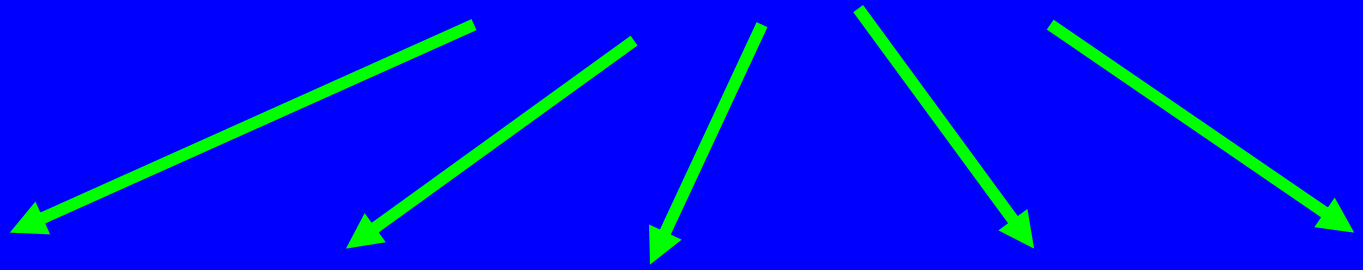
SICS

Etanolo

Concetti guida

- L'etanolo (alcol etilico) è una sostanza non nutriente d'interesse nutrizionale che – pur apportando energia (7 kcal/g) – non ha finalità funzionali e/o metaboliche specifiche.
- La principale fonte di etanolo nella dieta della popolazione italiana è rappresentata dal gruppo "Vino e sostituti" (84%), seguito dal gruppo "Birra, sidro e sostituti" (9%) e dalle altre bevande alcoliche (vino dolce, spumanti, aperitivi e liquori, per il 7%).
- È una molecola potenzialmente tossica per l'organismo, di elevata pericolosità sociale che può causare – nel caso di abuso – importanti danni organici e psicologici; elevate assunzioni sono associate ad un aumento del rischio di malattie cardio-cerebrovascolari, di epatopatie e malattie gastrointestinali, nonché di alcune forme di tumori.

CONSUMO DI ALCOL



Fegato
Pancreas

Sistema Nervoso

-App. Cardio-Vascolare
-App. Digerente
-Sist. Emopoietico

-Stato Nutrizionale
-App. Immunitario
-Cancerogenesi
-Sist. Endocrino
-App. Riproduttivo
-App. Respiratorio
-S. Feto-Alcolica

-< Performance
-< Qualità di vita
-<Aspettativa di vita

ALCOLOGIA COINVOLTA IN NUMEROSE DISCIPLINE MEDICHE INTERNISTICHE

Ricoveri ospedalieri

Complicanze post-chirurgiche

Importante fattore di trapianto d'organo

- **Non percepito il problema alcologico**

- **Se percepito non affrontato in modo adeguato**

- **Etica**

PATOLOGIA ALCOL CORRELATA ED OSPEDALIZZAZIONE

- 7-24% prevalenza ricoveri in ambiente internistico (Kennel-Webb et al, QJM 1999; Smothers et al, Arch Intern Med 2003)
- 18.6% dei ricoveri (Cameron et al, Scott Med J 2006)
- 16% dei ricoveri in degenza ordinaria (Salvagnini et al., Intern Emerg Med 2008)
- 10% dei ricoveri in terapia intensiva (Moss and Burnham, Lancet 2006)

Table 1. The fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria for the framing of patients with alcohol use disorder (AUD).

1.	Alcohol is often taken in larger amounts or over a longer period than was intended.
2.	There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.
3.	A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.
4.	Craving, or a strong desire or urge to use alcohol.
5.	Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.
6.	Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
7.	Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
8.	Recurrent alcohol use in situations in which it is physically hazardous.
9.	Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.
10.	Tolerance, as defined by either of the following: (a) A need for markedly increased amounts of alcohol to achieve intoxication or desired effect; (b) A markedly diminished effect with continued use of the same amount of alcohol.
11.	Withdrawal, as manifested by either of the following: (a) The characteristic withdrawal syndrome for alcohol (refer to criteria A and B of the criteria set for alcohol withdrawal); (b) Alcohol is taken to relieve or avoid withdrawal symptoms.

all the criteria in Table 1). The presence of two or three symptoms indicate a mild disorder, four or five symptoms a moderate one, and six or more symptoms a severe disorder. Notably, DSM-5 removes "legal problems" between the diagnostic criteria adding the craving [11].

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed.; American Psychiatric Association: Washington, DC, USA, 2013; pp. 154–196.

CONSUMATORI ALCOL: Caratterizzazione del RISCHIO

Minor rischio	**Low risk level** **MINOR RISCHIO**	MASCHI	**età 18-64 anni**: 1-2 bicchieri e **NO** *Binge drinking*
			età>=65 anni: 1 bicchiere e **NO** *Binge drinking*
		FEMMINE	**età >=18anni:** 1 bicchieri e **NO** *Binge drinking*
Consumatori a rischio	**Low risk level** **<u>BUT</u>** **binge drinker**	MASCHI	**età 18-64 anni**: 1-2 bicchieri **MA** *Binge drinking*
			età>=65 anni: 1 bicchiere **MA** *Binge drinking*
		FEMMINE	**età >=18anni**: 1 bicchieri **MA** *Binge drinking*
	Medium risk level **RISCHIOSO**	MASCHI	**Età 18-64 anni** : 3-5 bicchieri **e/o** *Binge drinking*
		FEMMINE	**età 18-64 anni**: 2-4 bicchieri **e/o** *Binge drinking*
		MASCHI E FEMMINE	**età>= 65 anni**: 2-4 bicchieri **e/o** *Binge drinking*
	High risk level **DANNOSO**	MASCHI	**età >=18 anni**: 6+ bicchieri **e/o** *Binge drinking*
		FEMMINE	**età >=18 anni**: 4+ bicchieri **e/o** *Binge drinking*

CONSUMO DI BEVANDE ALCOLICHE IN SOGGETTI SANI

Donna < 10 gr/die — ***Basso rischio***
Uomo < 20 gr/die

one in 1000 deaths *

Donna 11-40 gr/die — ***Consumo Rischioso***
Uomo 21-60 gr/die — **one in 100 deaths ***
> 65 anni e fra i 16-18 anni >12/die

Donna > 40 gr/die — ***Consumo Dannoso***
Uomo > 60 gr/die
Binge Drinking

Scafato E et al, Istituto Superiore di Sanità 2010
Italian Society on Alcohol (SIA), 2018

Rehm et al, BMC 2014
higher than the usually accepted involuntary risk of one in one million !!! *

ACCEPTABLE DAILY INTAKE (ADI) FOR LIVER CIRRHOSIS MORBIDITY AND MORTALITY

ADI= BMDL/UF

2.6 g/day

IPCS: international Programme on Chemical Safety
BMD: brenchmark dose
BMDL: lower one-sided confidence limit of BMD
UF: uncertainly factor

Lachenmeier et al, Int J Epidemiol, 2011

US Environmental Protection Agenct, 1995
EFSA. EFSA J 2005
Bi J, J Food Sci 2010

Sovrappeso/ Obesità

Patologie Odontoiatriche

Patologie gastroenterologiche
- Alterazioni ghiandole salivari (parotidi in particolare)
- Malattia da reflusso gastro-esofageo
- Esofagite
- Alterazioni della motilità esofago-gastro-duodenale
- Dispepsia (cattiva digestione)
- Gastrite cronica
- Duodenite cronica
- Favorita l'ulcera peptica (?)
- Epatopatia cronica/ cirrosi epatica
- Alterazioni dell'assorbimento e dell'alvo
- Neoplasie benigne
- Neoplasie maligne

Patologie neurologiche
- Cafelea
- Alterazioni ritmo sonno-veglia
- Vasculopatia
- Declino cognitivo
- Demenza
- Epilessia
- Neoplasie maligne

Patologie apparato cardio-vascolare
- Ipertensione arteriosa
- Aritmie
- Ictus emorragico

Apparato endocrino-riproduttivo (ritardo pubertà, riduzione fertilità)

Patologie dermatologiche (psoriasi)

Problemi perinatali (aborto spontaneo, disturbi fetali da alcol, nascita prematura, ritardo crescita)

Tumori (cavità orale, faringe, laringe, esofago, colon, retto, fegato, mammella)

Consumo Rischioso

Patologie Psichiatriche
Disturbi dell'umore
Disturbi dello spettro schizofrenico
Disturbo antisociale di personalità
Disturbo borderline di personalità
Suicidio
Peggioramento di altre comorbilità

Patologie Neurologiche
Intossicazione acuta: ubriachezza, coma, amnesie
Sindrome da astinenza: epilessia (convulsioni), tremori, allucinazioni, delirium tremens
Malattie da carenze nutrizionali (soprattutto vitamina B1, B6, B12 e folati)
- Sindrome di Wenicke-Korsakoff
- Polineuropatia
- Neuropatia ottica (ambliopia alcolica o alcol-tabagica)
- Pellagra

Altre malattie:
- Degenerazione cerebellare
- Malattia di Marchifava-Bignami
- Demenza alcolica
- Idrocefalo normoteso
- Encefalopatia Porto-Sistemica
- Trauma cranico
- Tumori

Patologie Cardio-Vascolari
Ipertensione ateriosa
Aritmie
Cardipatia ischemica coronarica
Ictus (ischemico, emorragico)
Cardiomiopatia dilatativa

Patologie Epato-Gastroenterologiche

Patologie Dismetaboliche (dislipidemie, diabete mellito)

Problemi perinatali (aborto spontaneo, sindrome feto-alcolica)

Neoplasie

Tabella XIII – Patologie psico-fisiche correlate all'alcoldipendenza

ALCOHOL

Fatty Liver

Alcohol Hepatitis/Fibrosis

Cirrhosis

Hepatocellular Carcinoma

Chronic Pancreatitis

Parotid Hypertrophy

Glossitis

Stomatitis

Gastro-Esophageal Reflux

Mallory-Weiss Syndrome

Chronic Gastritis

Erosive Hemorrhagic Gastritis

Delayed Gastric Emptyimg

Malabsorption

Reduce Transit Time

Carcinogenesis*

***Upper Aero-Digestive Tract, Colon, Rectum, Breast, Liver, Pancreas**

Testino G, Hepatogastroenterology 2008

Popolazione italiana
≥18 anni (stima)
50.001.556

Consumatori	Astemi ed astinenti	Mancata risposta
34.247.747	15.119.878	633.931
(68,5%)	(30,2%)	(1,3%)

Consumatori giornalieri	Consumatori occasionali
13.892.563	20.355.184
(27,8%)	(40,7%)

BASSO RISCHIO
M=1-3 UA ; F=1-2 UA
11.546.644

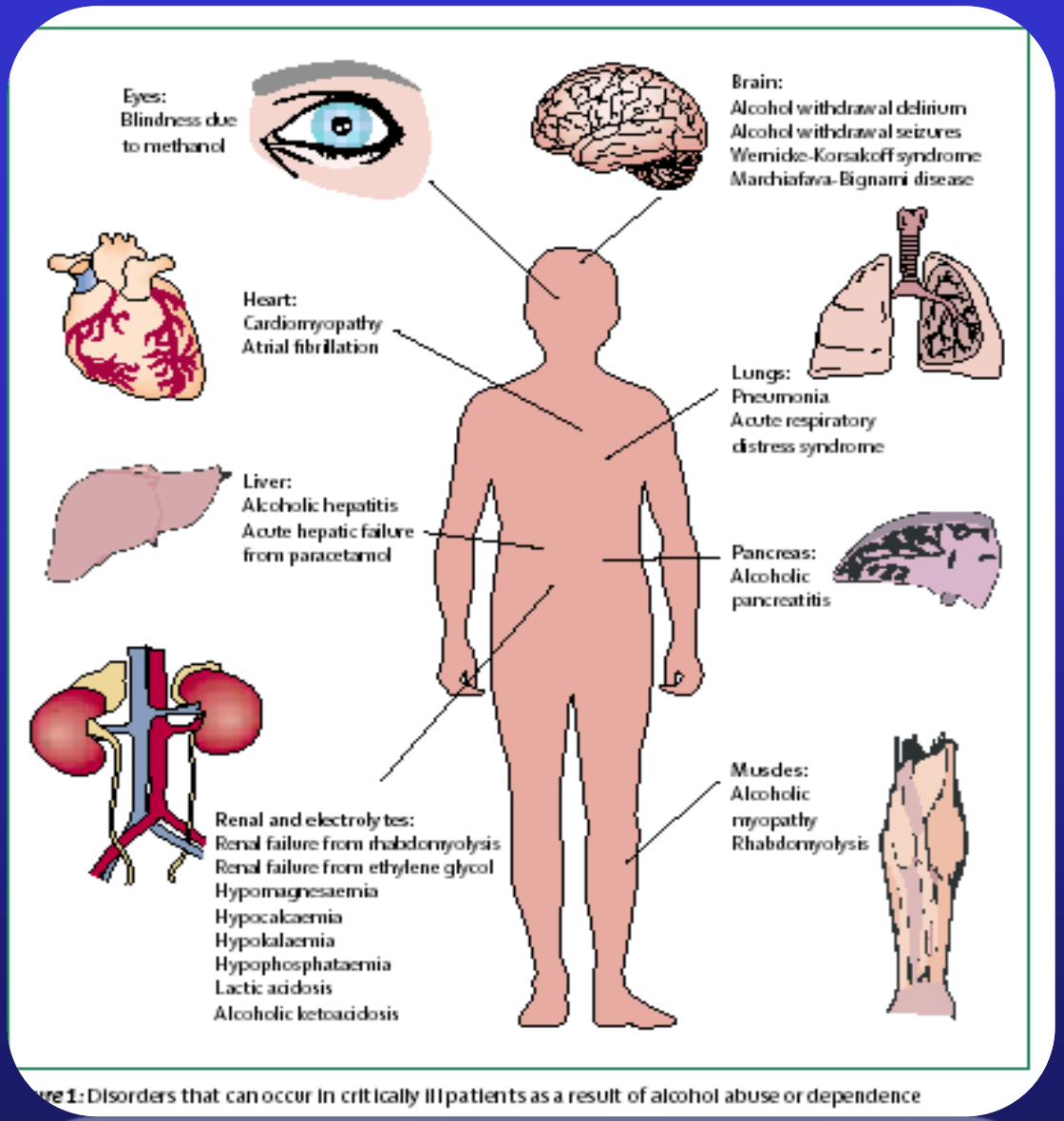
HCV
HBV
SM
ecc

MEDIO RISCHIO
M=4-5 UA ; F=3 UA
1.529.976

ALTO RISCHIO
M>5 UA ; F>3 UA
815.943

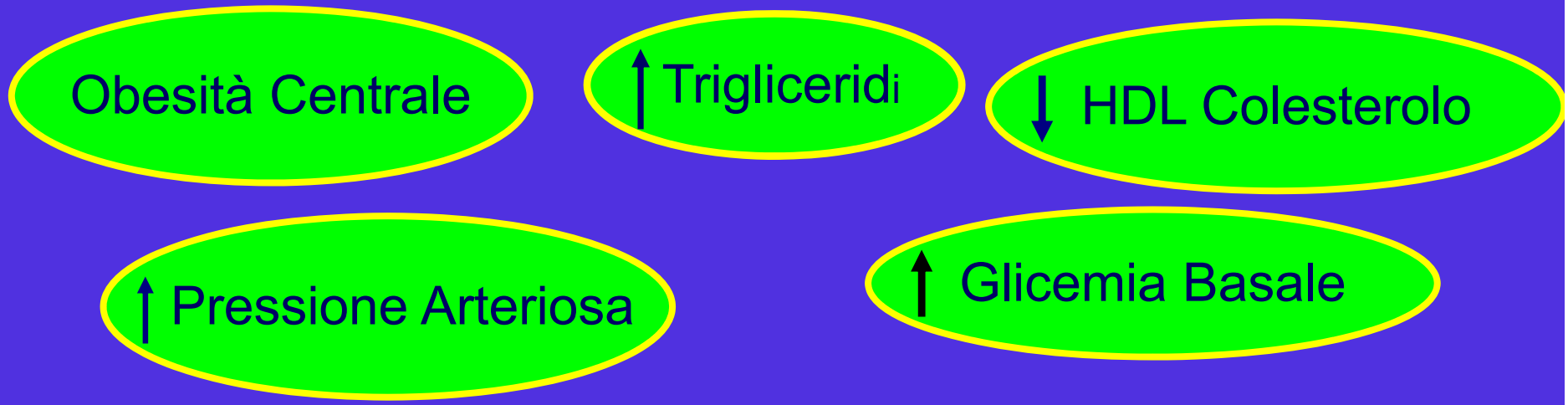
SM: Sindrome Metabolica

Modified by E. Scafato, ISS



re 1: Disorders that can occur in critically ill patients as a result of alcohol abuse or dependence

Moss M. and Burnham E. L., The Lancet 2006



Sindrome metabolica

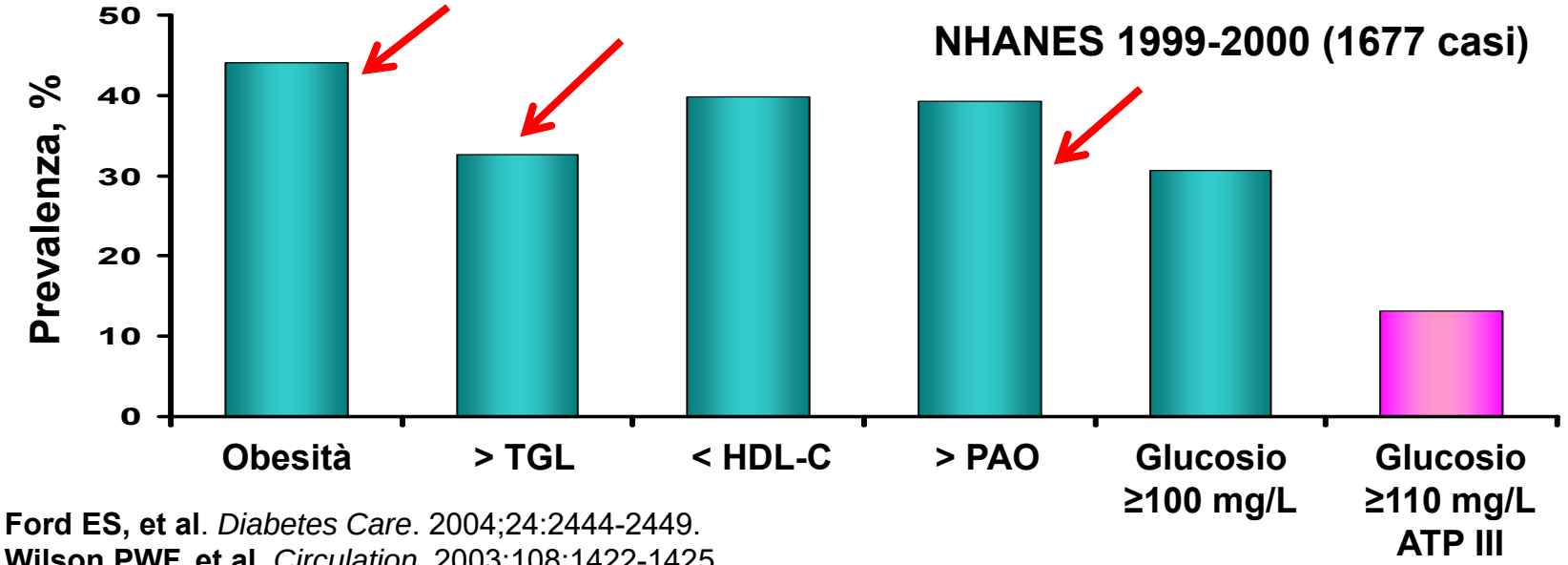
Insieme di fattori di rischio di origine metabolica, tra loro correlati, che inducono lo sviluppo di una malattia cardiovascolare aterosclerotica

Patogenesi: Insulinoresistenza

LA SINDROME METABOLICA

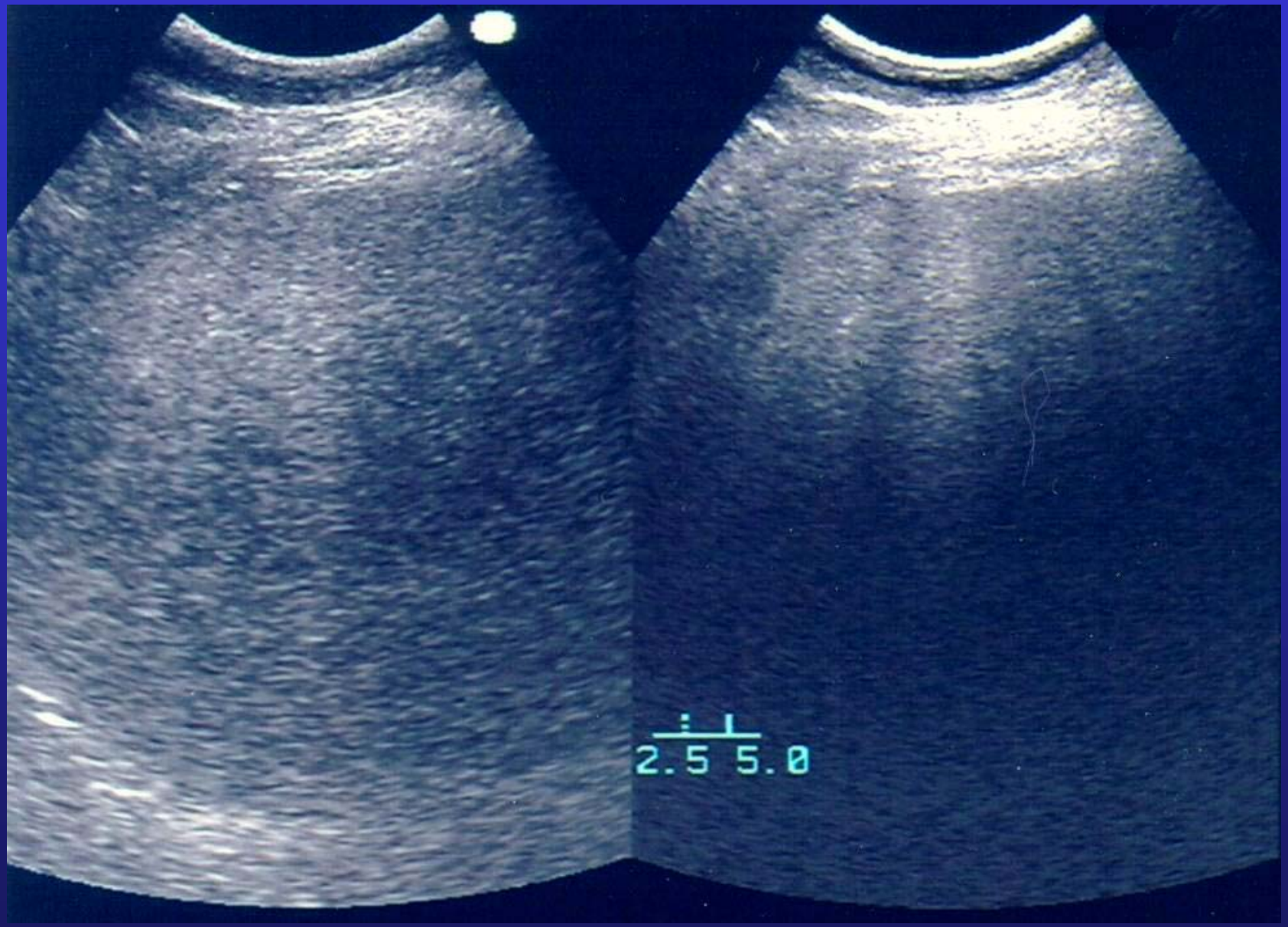
La sindrome metabolica è un fattore prognostico per lo sviluppo di diabete mellito T2, aterosclerosi e malattie cardiovascolari e si definisce con la presenza di almeno 3 delle seguenti alterazioni:

- ✓ **Circonferenza vita:** > 102 cm per l'uomo, > 88 cm per la donna
- ✓ **Trigliceridi plasmatici:** ≥150 mg/dL
- ✓ **Colesterolo-HDL:** < 40 mg/dL per l'uomo, 50 mg/dL per la donna
- ✓ **Pressione arteriosa:** ≥ 130 sistolica e/o ≥85 diastolica mmHg
- ✓ **Glicemia a digiuno:** ≥ 110 mg/dL

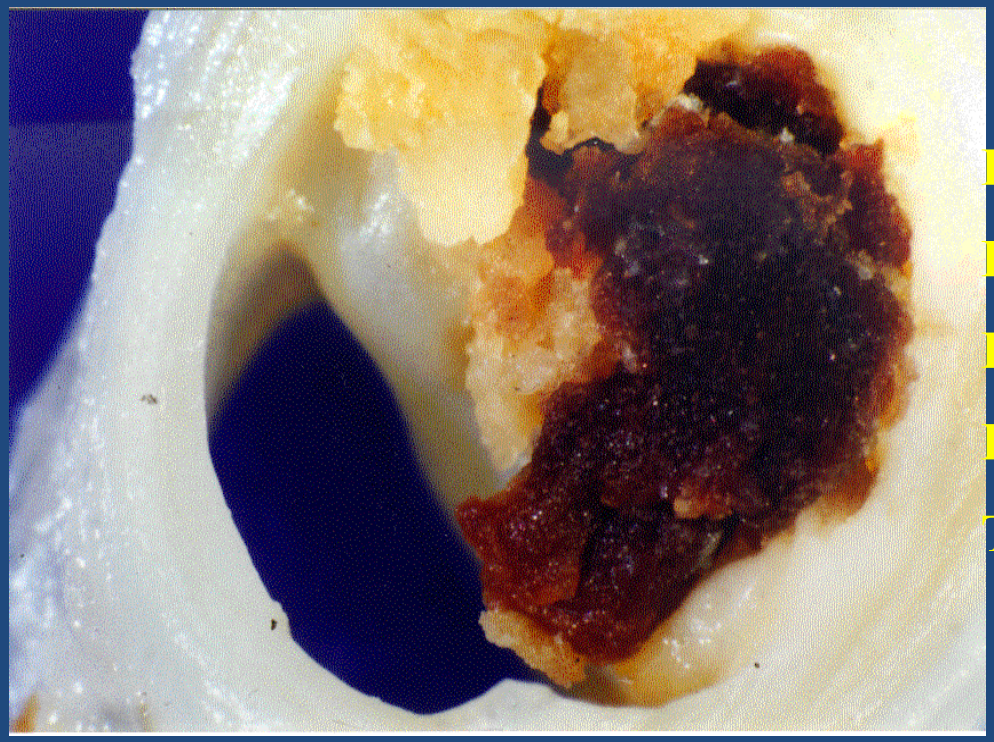


Ford ES, et al. *Diabetes Care*. 2004;24:2444-2449.
Wilson PWF, et al. *Circulation*. 2003;108:1422-1425.

From F. Bonino, Liver Day, Genova 2017


2.5 5.0

L' instabilità della placca, più che la severità della stenosi determina la progressione della malattia coronarica



IL –6

IL-1

IL-2

IL-8

TNF-a

La stratificazione del rischio potrebbe essere basata non solo sull' anatomia ma anche su marker di attività della malattia e sulla possibile vulnerabilità della placca

Alcohol intake increases the risk of HCC in hepatitis C virus-related compensated cirrhosis: A prospective study

Background & Aims: Whether alcohol intake increases the risk of complications in patients with HCV-related cirrhosis remains unclear. The aim of this study was to determine the impact of alcohol intake and viral eradication on the risk of hepatocellular carcinoma (HCC), decompensation of cirrhosis and death.

Methods: Data on alcohol intake and viral eradication were prospectively collected in 192 patients with compensated HCV-related cirrhosis.

Results: 74 patients consumed alcohol (median alcohol intake: 15 g/day); 68 reached viral eradication. During a median follow-

Conclusions: Light-to-moderate alcohol intake increases the risk of HCC in patients with HCV-related cirrhosis. Patient care should include measures to ensure abstinence.

HCC

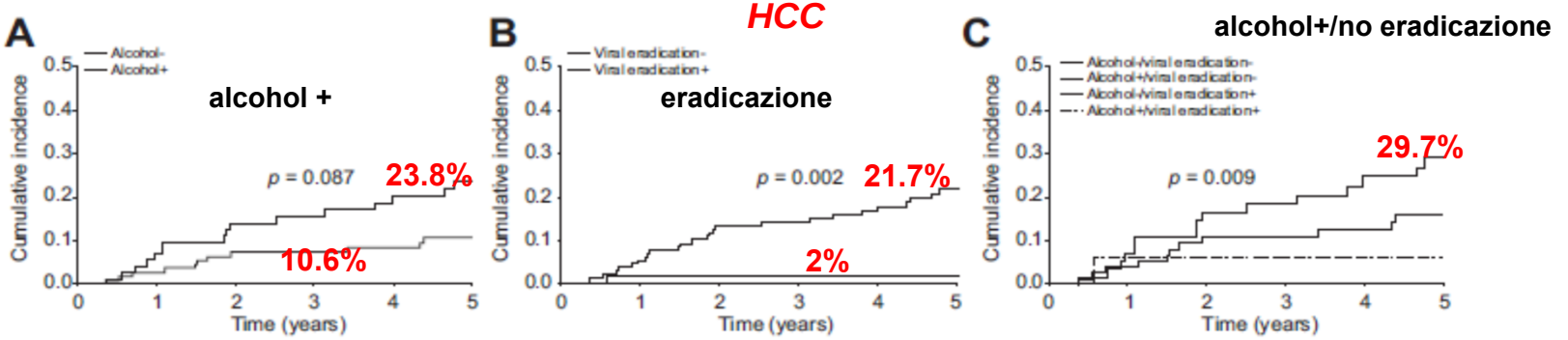
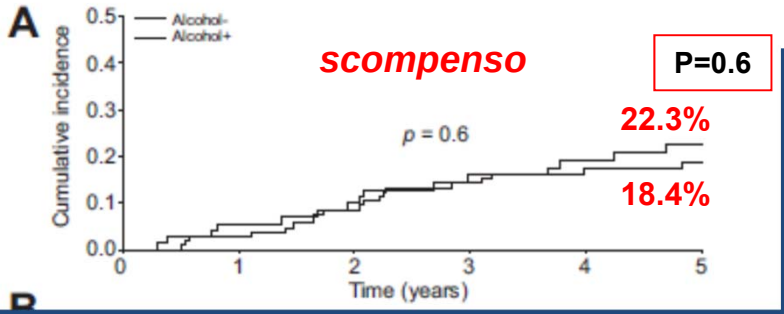
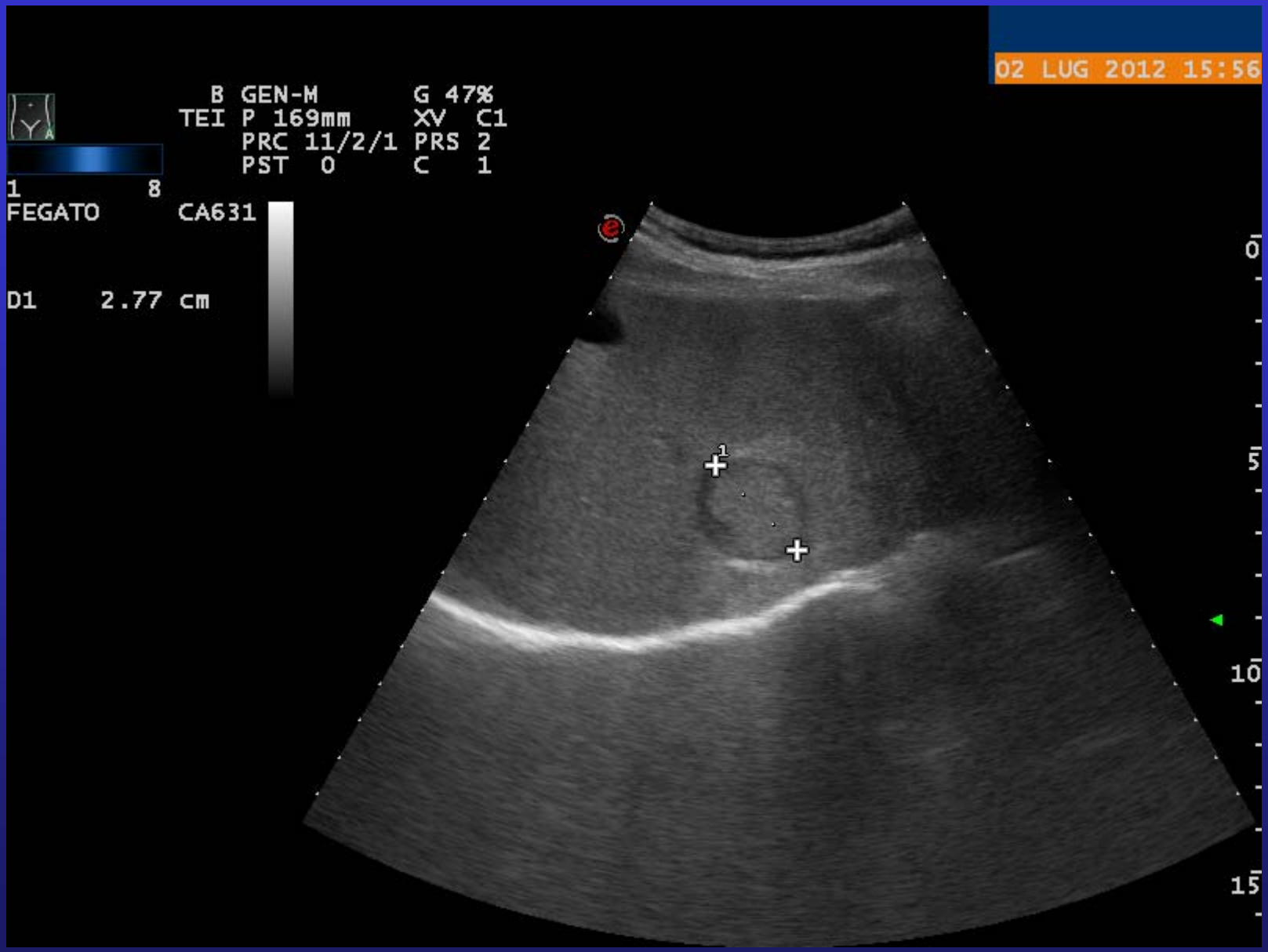


Fig. 1. 5-year cumulative incidence rate of HCC. (A) 5-year cumulative incidence rate of HCC according to alcohol intake. (B) 5-year cumulative incidence rate of HCC according to viral eradication. (C) 5-year cumulative incidence rate of HCC according to alcohol intake and viral eradication. HCC, hepatocellular carcinoma.



Vandenbulcke et al, J Hepatol 2016



Centro Alcologico Regionale – Regione Liguria

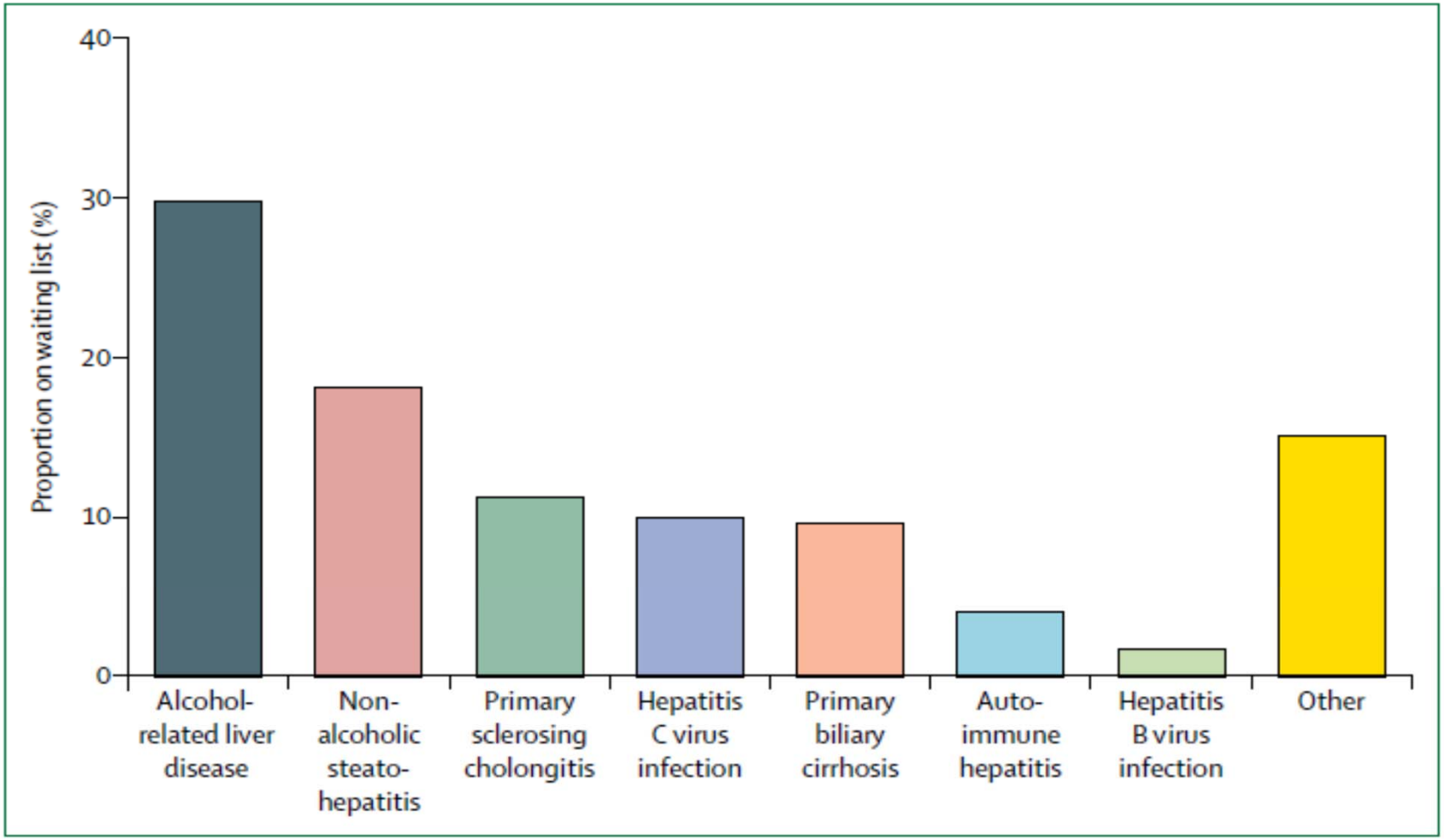
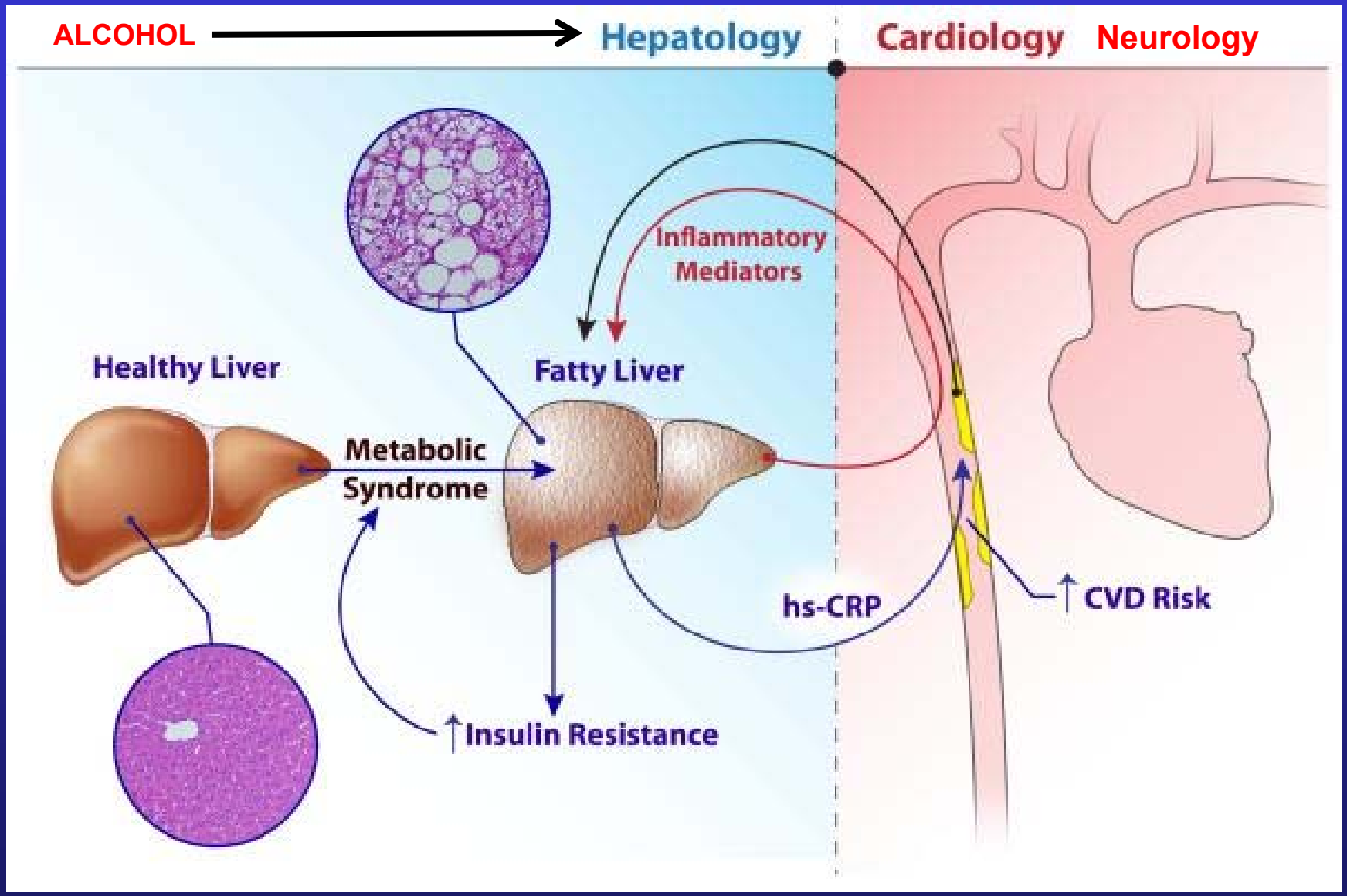


Figure 6: Causes of liver disease in patients on liver transplantation waiting list as of January, 2017

Williams et al, The Lancet, Vol 391 March 17, 2018



F. Bonino, Liver Day, Genova 2017

ALCOHOL AND ALZHEIMER'S DISEASE

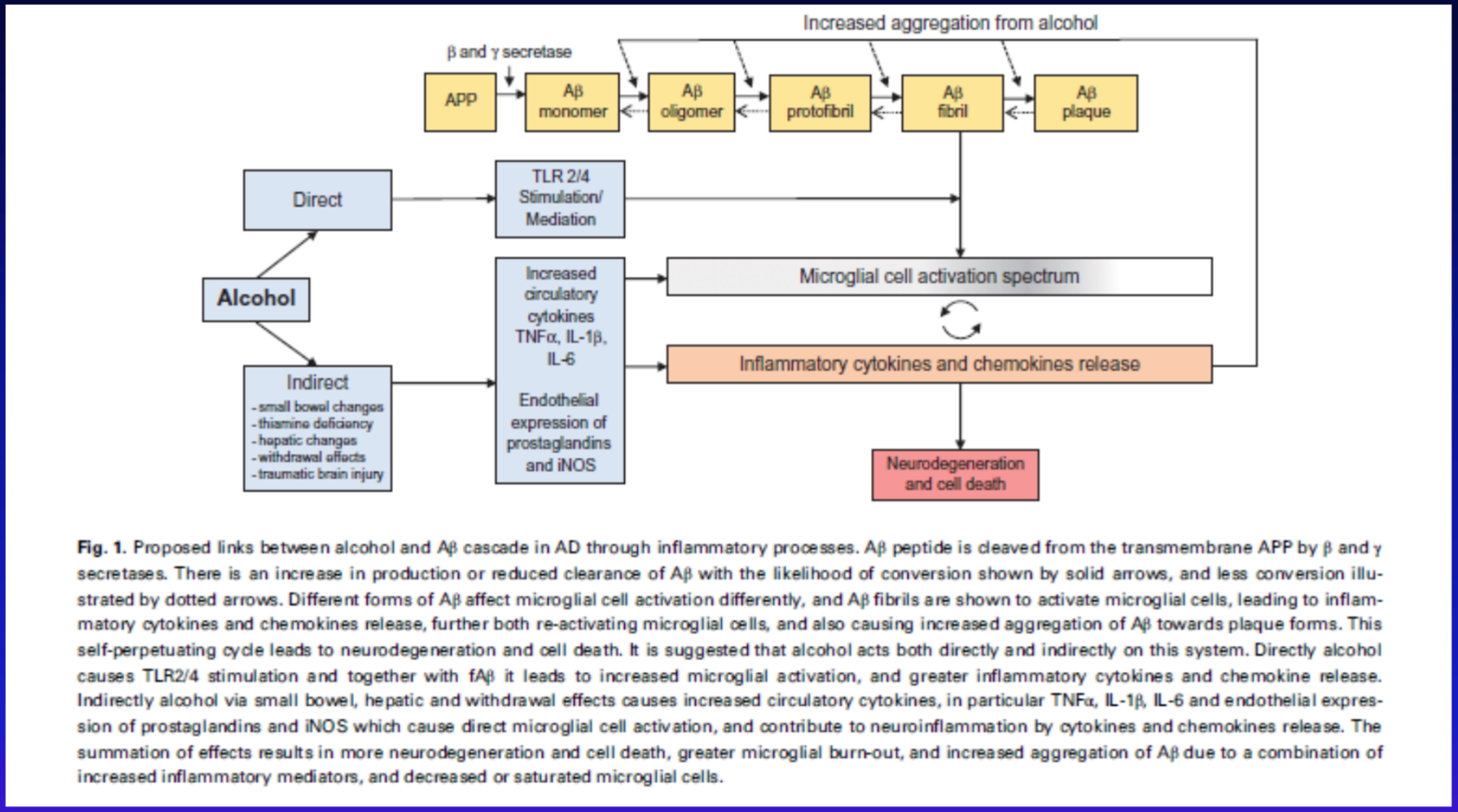


Fig. 1. Proposed links between alcohol and Aβ cascade in AD through inflammatory processes. Aβ peptide is cleaved from the transmembrane APP by β and γ secretases. There is an increase in production or reduced clearance of Aβ with the likelihood of conversion shown by solid arrows, and less conversion illustrated by dotted arrows. Different forms of Aβ affect microglial cell activation differently, and Aβ fibrils are shown to activate microglial cells, leading to inflammatory cytokines and chemokines release, further both re-activating microglial cells, and also causing increased aggregation of Aβ towards plaque forms. This self-perpetuating cycle leads to neurodegeneration and cell death. It is suggested that alcohol acts both directly and indirectly on this system. Directly alcohol causes TLR2/4 stimulation and together with fAβ it leads to increased microglial activation, and greater inflammatory cytokines and chemokine release. Indirectly alcohol via small bowel, hepatic and withdrawal effects causes increased circulatory cytokines, in particular TNFα, IL-1β, IL-6 and endothelial expression of prostaglandins and iNOS which cause direct microglial cell activation, and contribute to neuroinflammation by cytokines and chemokines release. The summation of effects results in more neurodegeneration and cell death, greater microglial burn-out, and increased aggregation of Aβ due to a combination of increased inflammatory mediators, and decreased or saturated microglial cells.

Venkataraman et al, Alcohol Alcohol 2017; doi: 10.1093/alcalc/agw092

Alcol, Ipertensione, Aritmie

Femmine

	0 gr	1-19 gr/die	20-39 gr/die
IPETENSIONE (RR)	1	**1.4**	**2**
ARITMIE (RR)*	**1**	**1.5**	**2.2**

***Sino al 30% delle FA da consumo sociale di alcol**

Scafato E., Istituto Superiore di Sanita', 2010

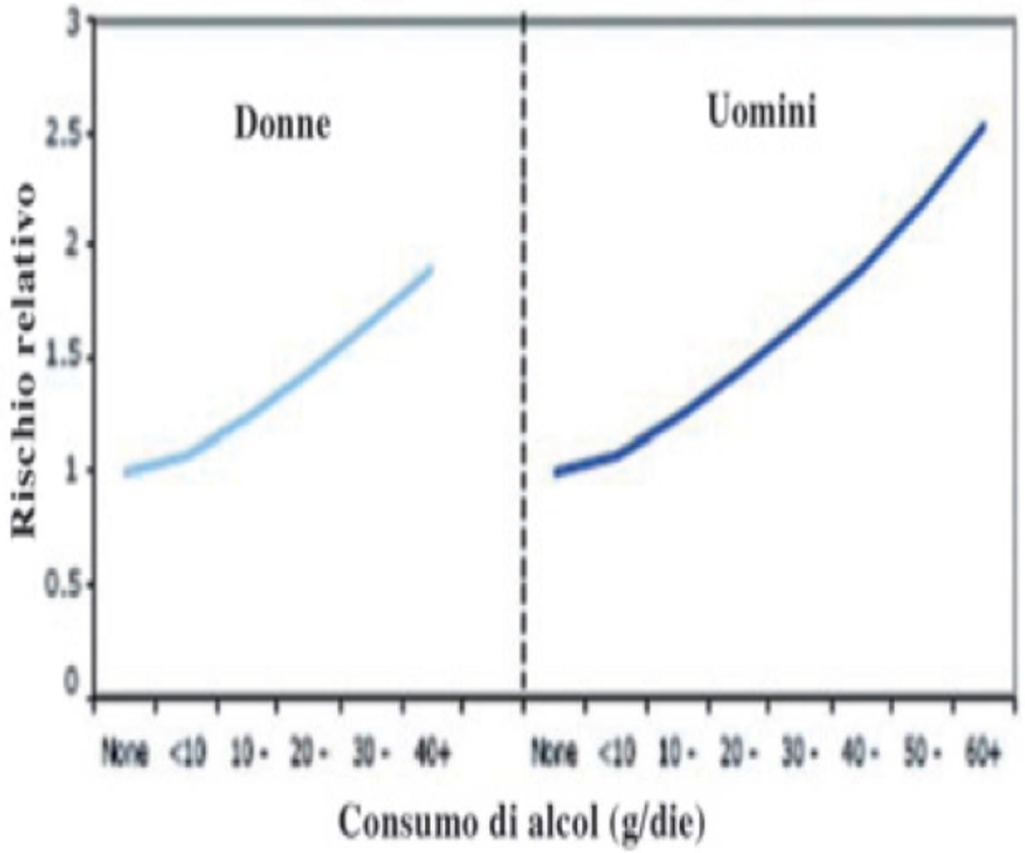


Figura 4.5. Rischio relativo di ipertensione per consumo alcolico.
Fonte: Strategy Unit (2003).

E. Scafato, ISS 2010

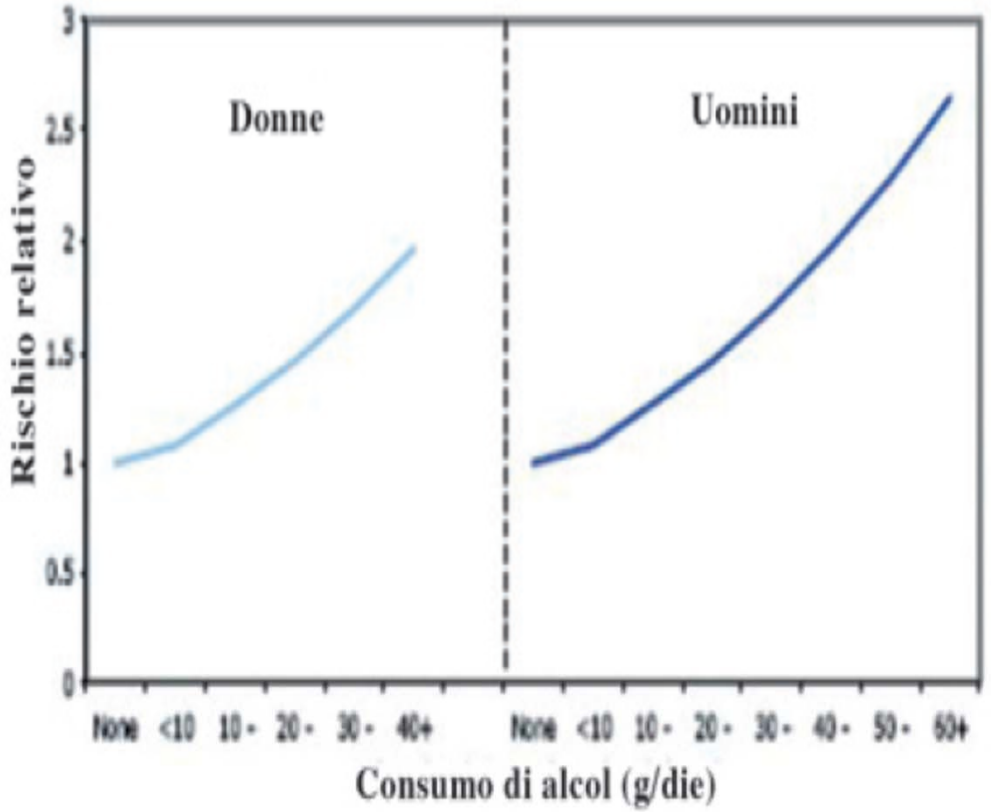


Figura 4.6. Rischio relativo di ictus emorragico per consumo alcolico. Fonte: Strategy Unit (2003).

E. Scafato, ISS 2010

Alcohol use disorders, cardiomyopathy and heart transplantation: a new management

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Alcohol use disorders (AUDs) are one of the main causes of cardiomyopathy (CM). CM is a major cause of cardiac disease responsible for around 400,000 global deaths per year (>15 years of age). This represents 0.7% of all adult deaths (0.7% women, 0.8% men) and 2.2% of all cardiovascular deaths.[1] The prevalence of alcoholic CM (ACM) varies according to the geographical area. In major European cities, prevalence ranging from 23 to 40% of all forms of dilated CM has been reported. It has been estimated that 30% of alcoholics have echocardiographic evidence of systolic dysfunction. For these reasons ACM represents one of the main causes of heart transplantation.[2]

hypertension, atrial fibrillation and ventricular arrhythmia, hemorrhagic and ischemic strokes, and acute myocardial infarction.[5]

The CM framework is characterized by ventricular dilatation, cardiac hypertrophy with a reduction in ventricular wall thickness, disturbed myofibrillar architecture, dampened myocardial contractility, interstitial fibrosis, and a greater prevalence of hypertension and strokes. Ethanol and acetaldehyde cause CM through direct toxic action, oxidative stress (mitochondrial reactive oxygen species ROS), neurohormonal overactivation (catecholamines and angiotensin II) and apoptosis.[6] An alteration in autophagic activity induced by ethanol/acetaldehyde is certainly a

Minerva Cardioangiologica; 66: 744-6, 2018

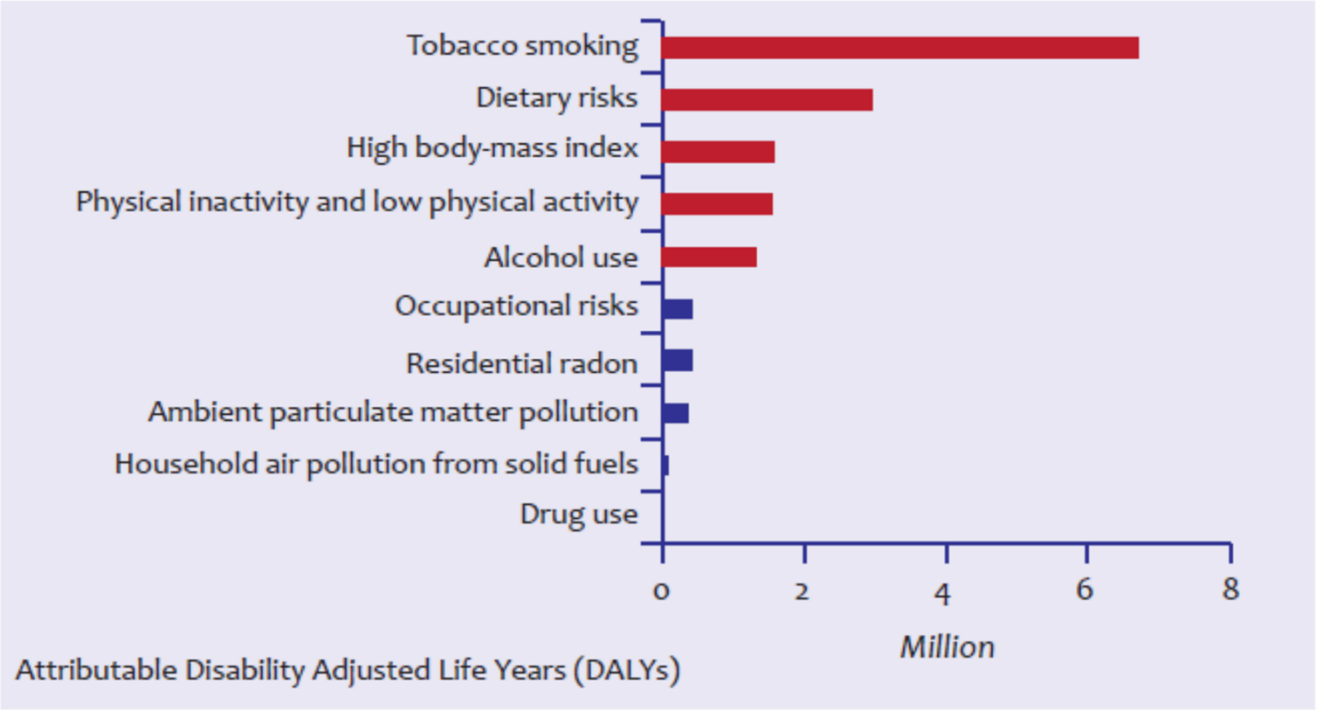
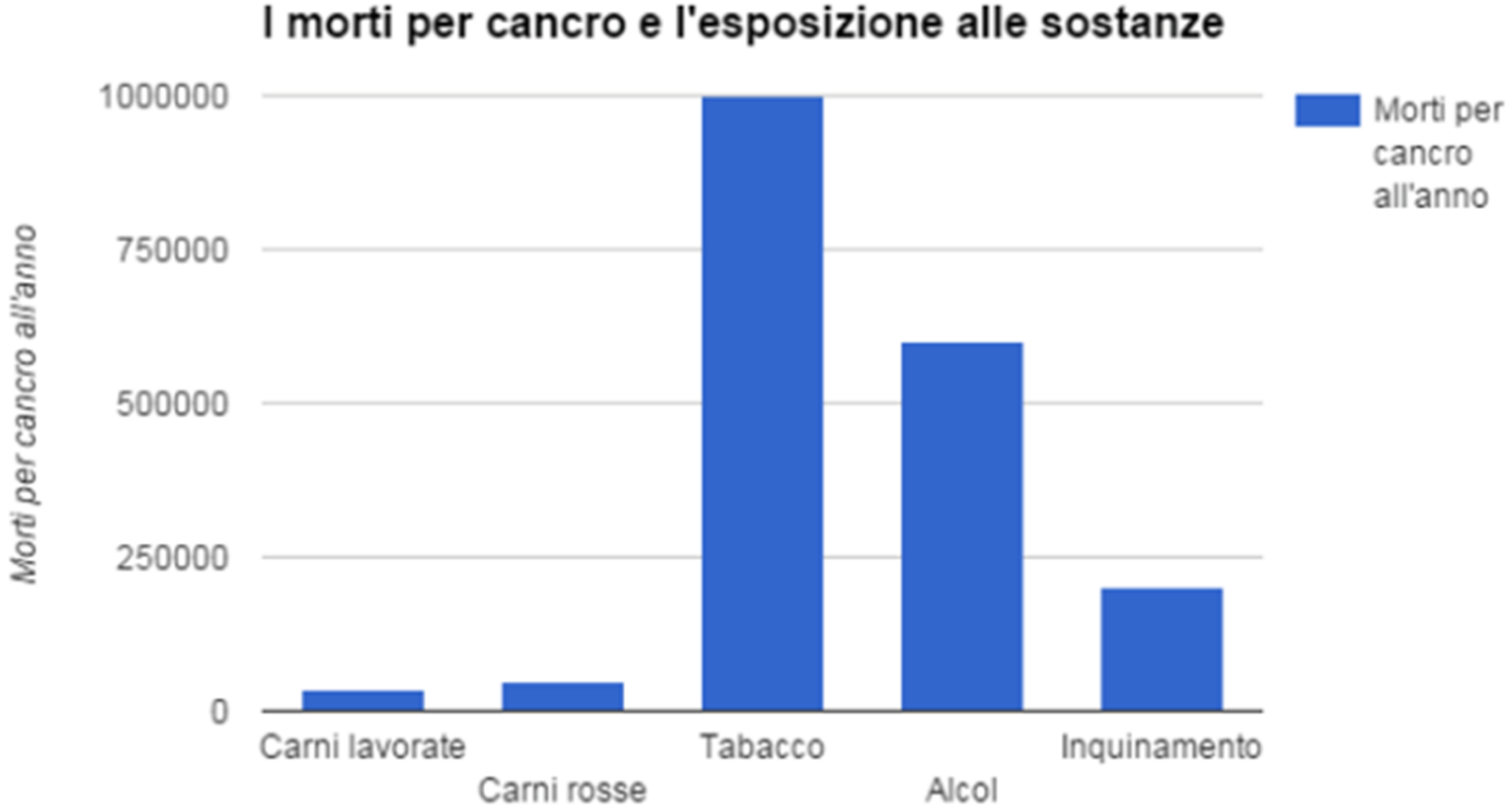


Figure 1 - Contribution of Lifestyle Risk Factors to thwe Burden of Cancer in Europe

Source: OECD elaboration of IHME Global Burden of Disease Data for EU and EFTA area, 2010

Salmaso et al; Istituto Superiore di Sanita', 2014



e stime del Global Burden of Disease Project sulla relazione tra casi di morte per cancro ed esposizione a certe ostanze o fattori ambientali

IARC; Lancet Oncology, November 2009

	Tumour sites for which there is sufficient evidence	Tumour sites for which there is limited evidence	Tumour sites for which there is evidence suggesting lack of carcinogenicity
Tobacco smoking	Oral cavity, oropharynx, nasopharynx, and hypopharynx, oesophagus (adenocarcinoma and squamous-cell carcinoma), stomach, colorectum,* liver, pancreas, nasal cavity and paranasal sinuses, larynx, lung, uterine cervix, ovary (mucinous)*, urinary bladder, kidney (body and pelvis), ureter, bone marrow (myeloid leukaemia)	Female breast*	Endometrium (postmenopausal*), thyroid*
Parental smoking (cancer in the offspring)	Hepatoblastoma*	Childhood leukaemia (in particular acute lymphocytic leukaemia)*	
Second-hand smoke	Lung	Larynx,* pharynx*	
Smokeless tobacco	Oral cavity, oesophagus,* pancreas		
Areca nut			
Betel quid with added tobacco	Oral cavity, pharynx, oesophagus		
Betel quid without added tobacco	Oral cavity, oesophagus*	Liver*	
Alcohol consumption	Oral cavity, pharynx, larynx, oesophagus, liver, colorectum, female breast	Pancreas*	Kidney, non-Hodgkin lymphoma
Acetaldehyde associated with alcohol consumption	Oesophagus,* head and neck*		
Chinese-style salted fish	Nasopharynx	Stomach*	
Indoor emissions from household combustion of coal	Lung		

*New sites.

Table: Evidence for carcinogenicity in humans of Group 1 agents assessed

IARC; Lancet Oncology, November 2009

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Acetaldehyde associated with alcohol consumption	Oesophagus,* head and neck*		
Chinese-style salted fish	Nasopharynx	Stomach*	
Indoor emissions from household combustion of coal	Lung		

*New sites.

Table: Evidence for carcinogenicity in humans of Group 1 agents assessed

There is *sufficient evidence* in humans for the carcinogenicity of alcohol consumption. Alcohol consumption causes cancers of the oral cavity, pharynx, larynx, oesophagus, colorectum, liver (hepatocellular carcinoma) and female breast. Also, an association has been observed between alcohol consumption and cancer of the pancreas.

For cancer of the kidney and non-Hodgkin lymphoma, there is *evidence suggesting lack of carcinogenicity.*

There is *sufficient evidence* in humans for the carcinogenicity of acetaldehyde associated with the consumption of alcoholic beverages. Acetaldehyde associated with the consumption of alcoholic beverages causes cancer of the oesophagus and of the upper aerodigestive tract combined.

There is *sufficient evidence* in experimental animals for the carcinogenicity of ethanol.

There is *sufficient evidence* in experimental animals for the carcinogenicity of acetaldehyde.

Alcohol consumption is *carcinogenic to humans (Group 1).*

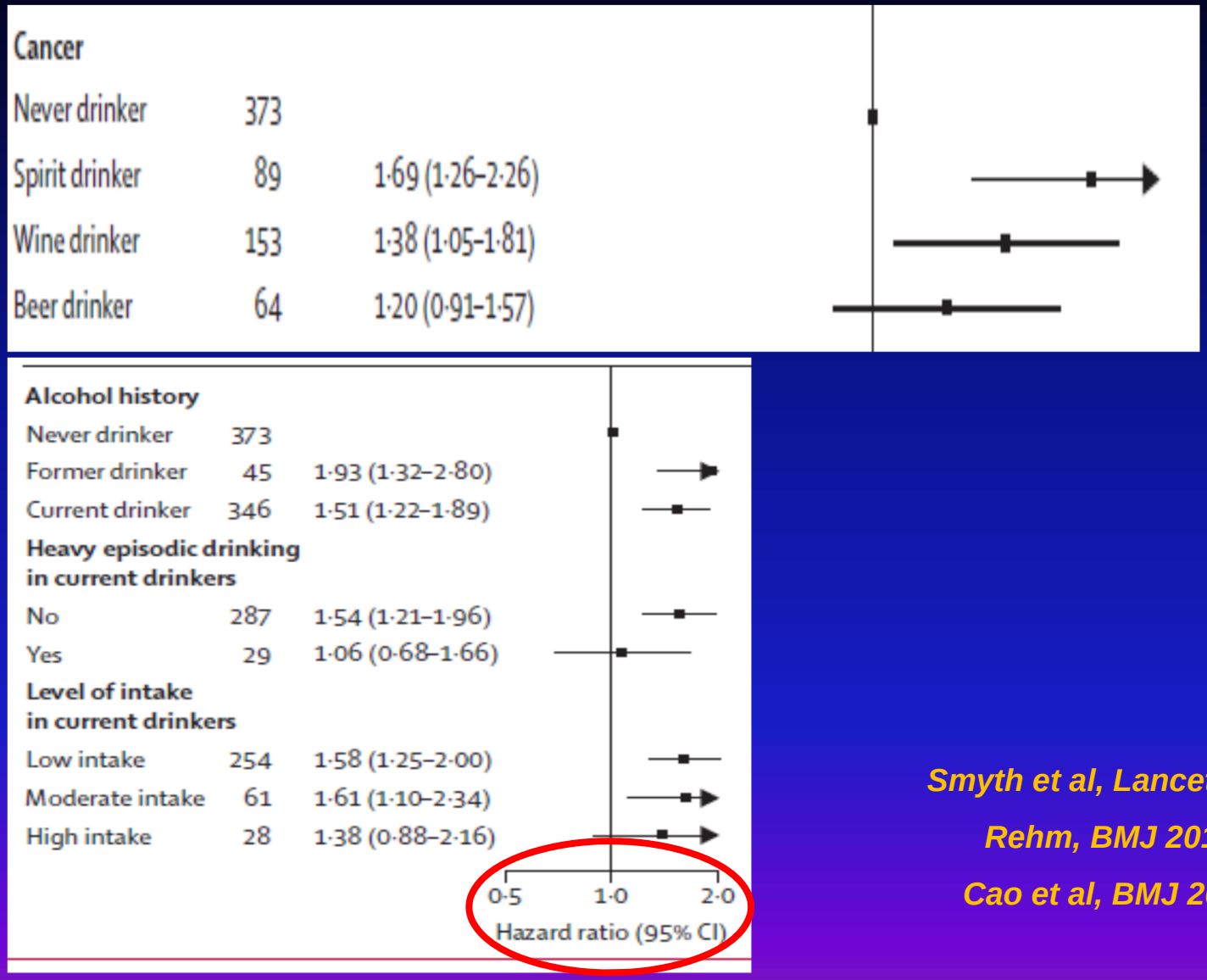
Ethanol in alcoholic beverages is *carcinogenic to humans (Group 1).*

Acetaldehyde associated with the consumption of alcoholic beverages is *carcinogenic to humans (Group 1).*

World Health Organization, International Agency for Cancer Research,

Volume 100 E, pag. 476 – Lyon, France 2012

ALCOHOL AND CANCER



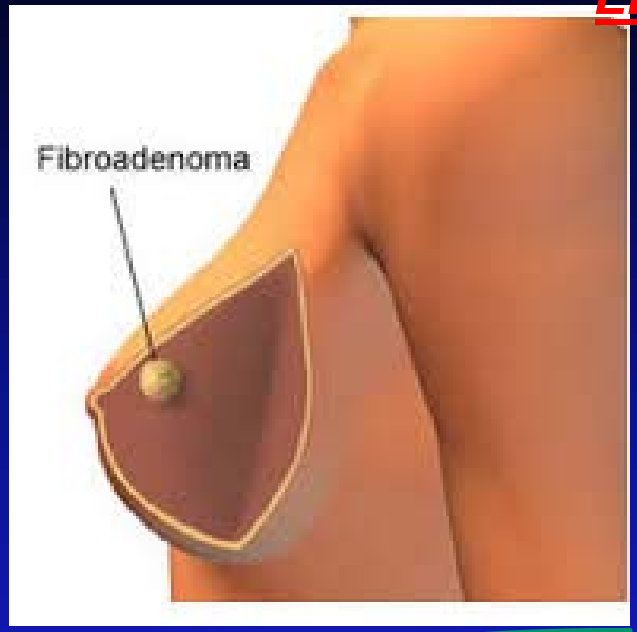
Smyth et al, Lancet 2015

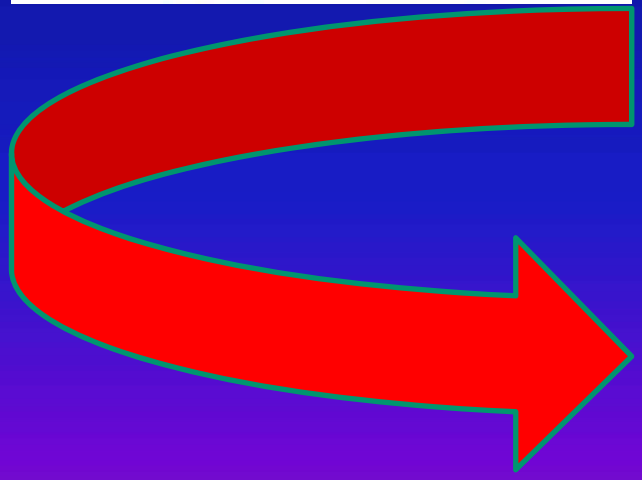
Rehm, BMJ 2015

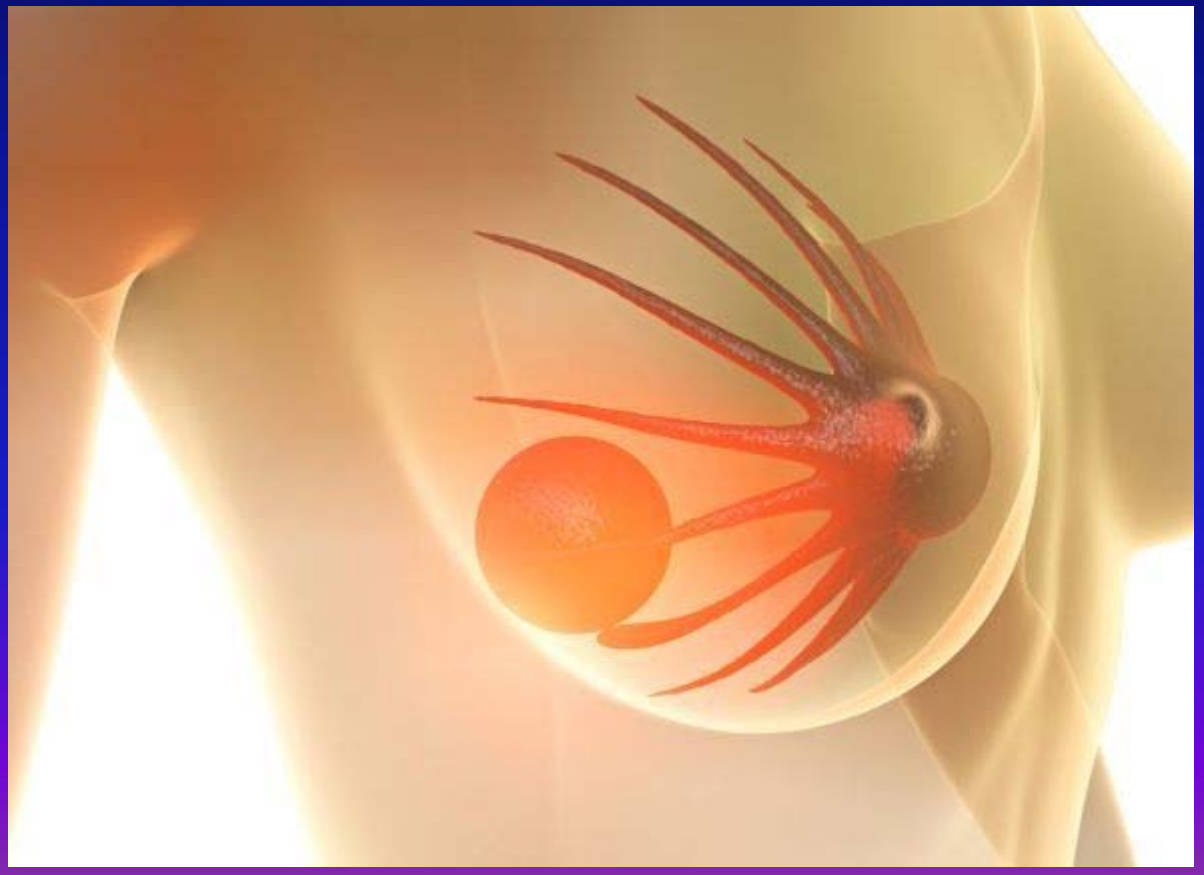
Cao et al, BMJ 2015

ALCOL

LESIONI ALLA MAMMELLA IN ACCRESCIMENTO





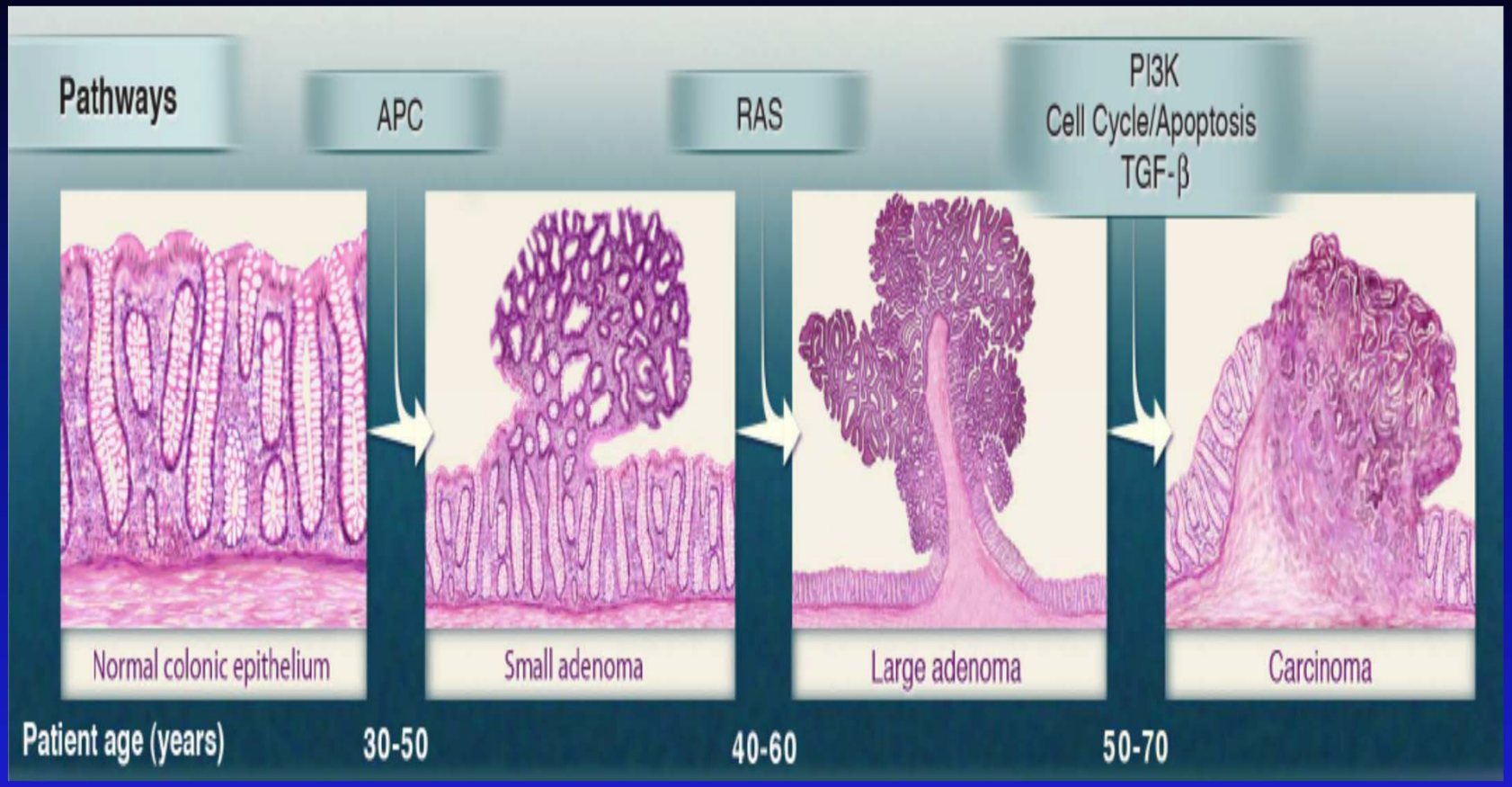


Prospective Study of Adolescent Alcohol Consumption and Risk of Benign Breast Disease in Young Women

Drinking Frequency	OR
Never to less than weekly	1.00 (referent)
1-2 U/ wk	1.72
3-5 U/ wk	3.34
6-7 U/ wk	5.94

Berkey CS et al, Pediatrics 2010

Printz C, Cancer 2010



Social Consumption

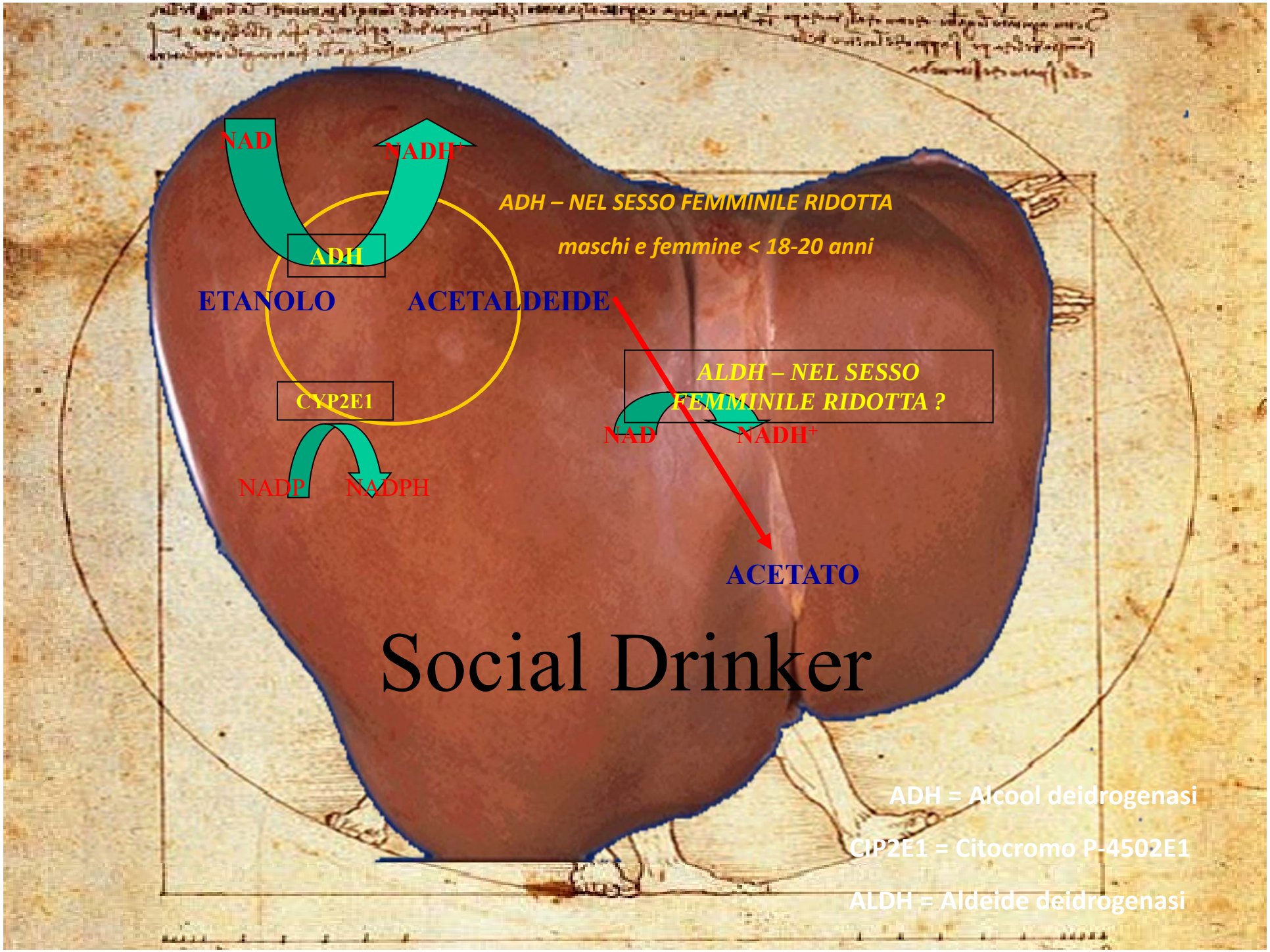
Testino, 2011

Volgelstein et al, Science 2013

IMPACT OF ALDH2-DEFICIENCY GENES ON THE RISK FOR OESOPHAGEAL CANCER

Genes/polymorphisms	Alcohol 1-30 g/day	Alcohol > 30/ g/day
ALDH2-active	OR <7.2	
ALDH2-deficiency	OR 14.5	OR 102.5
Slow ADH1B + ALDH2-deficiency	OR 37.5	OR 382.3

Salaspuro M, Scand J Gastroenterol 2009


NAD
NADH+
ADH
ETANOLO
ACETALDEIDE
ADH – NEL SESSO FEMMINILE RIDOTTA
maschi e femmine < 18-20 anni
CYP2E1
NADP
NADPH
ALDH – NEL SESSO FEMMINILE RIDOTTA ?
NAD
NADH+
ACETATO
Social Drinker
ADH = Alcool deidrogenasi
CIP2E1 = Citocromo P-4502E1
ALDH = Aldeide deidrogenasi

GENDER DIFFERENCES IN ALCOHOL METABOLISM

Smaller volume of distribution of ethanol

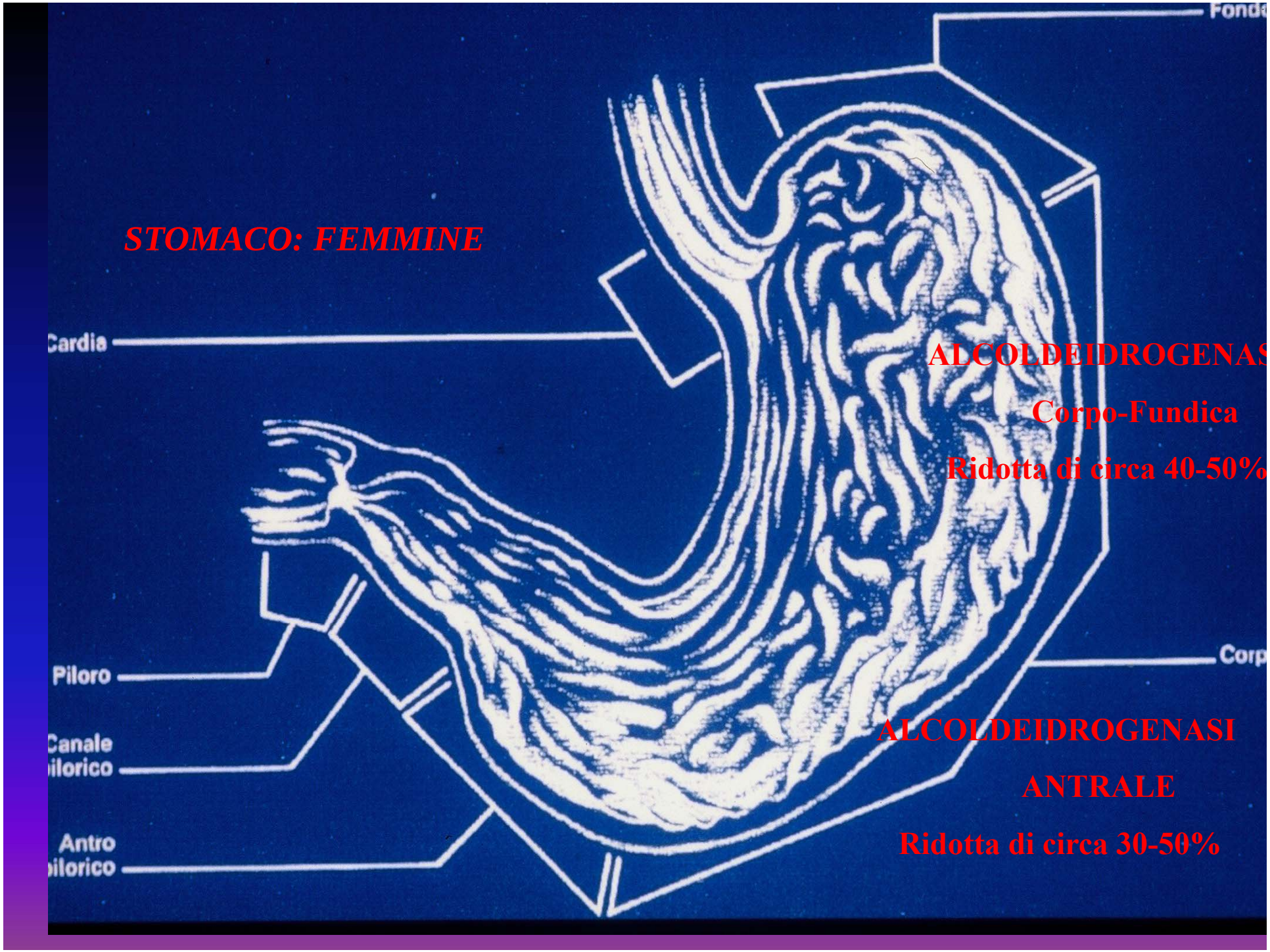
Sex hormones

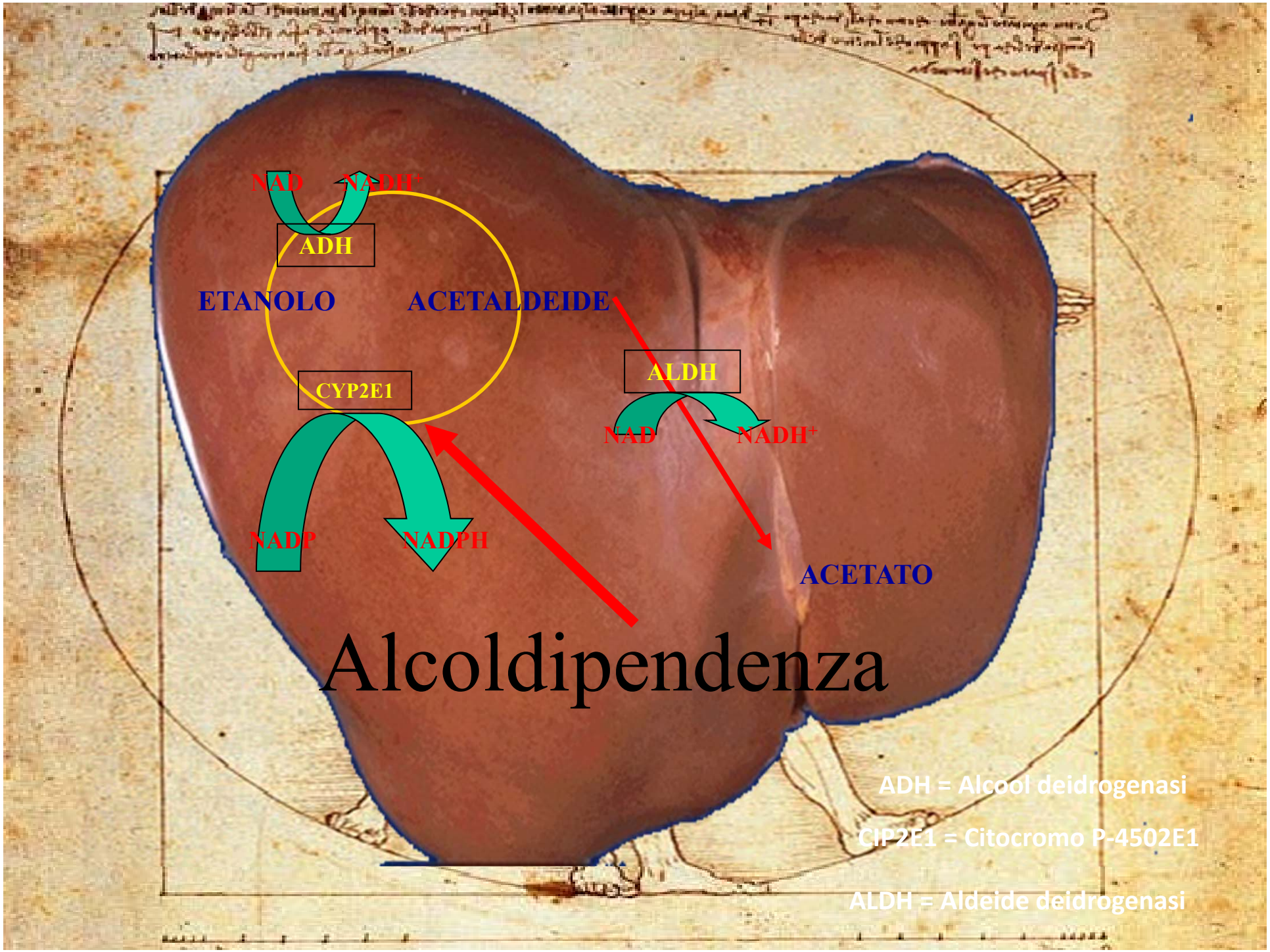
Decreased first-pass metabolism or more rapid absorption

Hepatic ADH activity reduced

Liver volume

Hepatic P450IIE1 (?)


STOMACO: FEMMINE
Cardia
Piloro
Canale
ilorico
Antro
ilorico
ALCOLDEIDROGENAS
Corpo-Fundica
Ridotta di circa 40-50%
Corp
ALCOLDEIDROGENASI
ANTRALE
Ridotta di circa 30-50%


NAD
NADH+
ADH
ETANOLO
ACETALDEIDE
CYP2E1
ALDH
NAD
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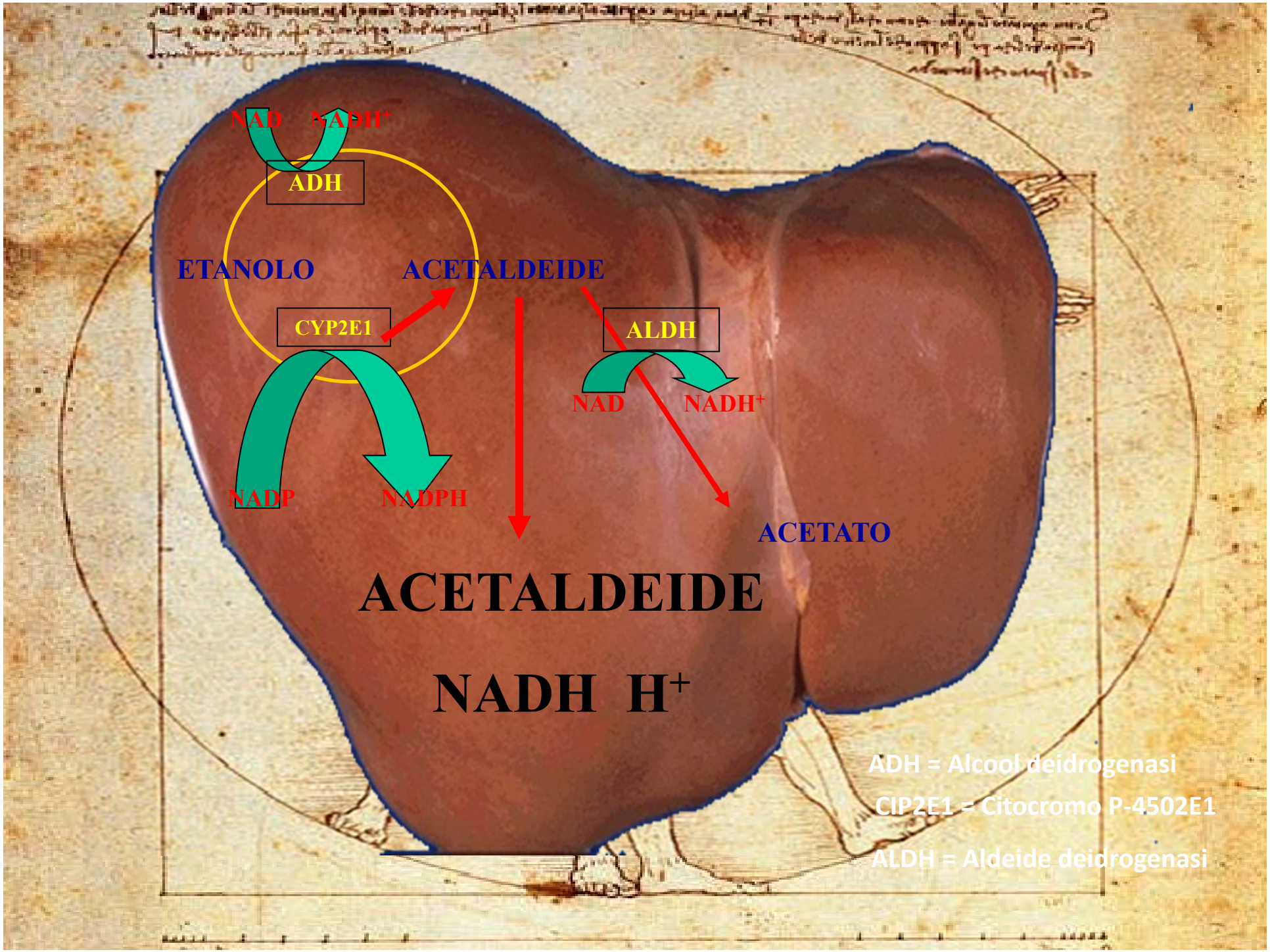
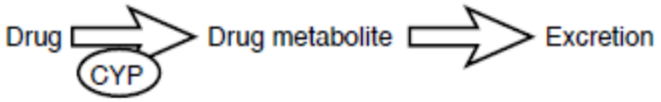
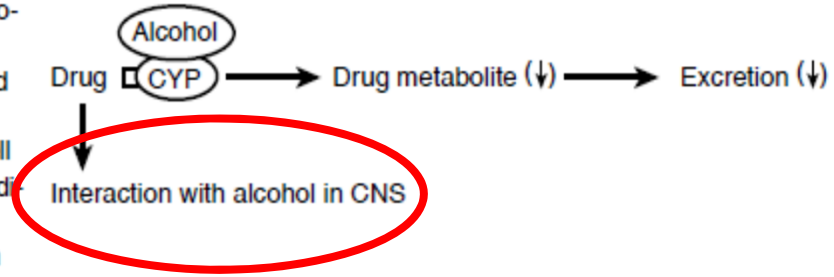
ADH = Alcool deidrogenasi
CIP2E1 = Citocromo P-4502E1
ALDH = Aldeide deidrogenasi


NAD
NADH+
ADH
ETANOLO
ACETALDEIDE
CYP2E1
ALDH
NAD
NADH+
NADP
NADPH
ACETATO
ACETALDEIDE
NADH H+
ADH = Alcool deidrogenasi
CIP2E1 = Citocromo P-4502E1
ALDH = Aldeide deidrogenasi

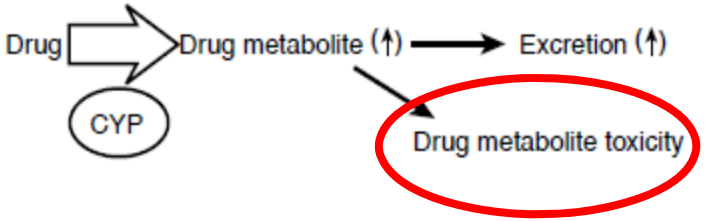
(A) In the absence of alcohol, CYP activity is relatively low. CYP breaks down the medication, and the resulting products (i.e., metabolites) are excreted.



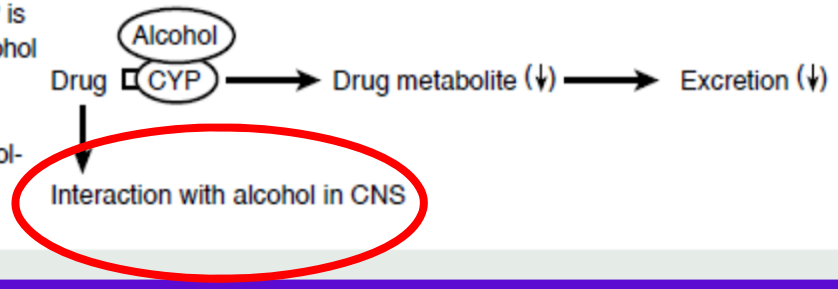
(B) After moderate alcohol consumption, CYP metabolizes alcohol in addition to the medication. As a result of competition for CYP between alcohol and the medication, the medication's metabolism is reduced, and the production of metabolites as well as their excretion declines, resulting in higher medication levels in the body. In addition, interactions between alcohol and the medication may occur in the central nervous system (CNS).



(C) In chronic heavy drinkers who are sober, CYP activity is enhanced. As a result, the breakdown of medications metabolized by CYP increases, and metabolite levels as well as their excretion are elevated, possibly resulting in insufficient medication levels in the body. Furthermore, toxic metabolites may accumulate.



(D) In chronic heavy drinkers who are intoxicated, CYP is activated, but most of the enzyme is involved in alcohol metabolism. Consequently, the CYP-dependent metabolism of other medications is reduced, and metabolite levels and their excretion decline. Alcohol-medication interactions also can occur in the CNS.



Weathermon and Crabb, Alcohol Res Health 1999

Potential for Alcohol and Prescription Drug Interactions in Older People

Kristine E. Pringle, PhD, Frank M. Ahern, PhD,† Debra A. Heller, PhD,*† Carol H. Gold, PhD,† and Theresa V. Brown, MPA‡*

OBJECTIVES: To examine the patterns and prevalence of concomitant alcohol and alcohol-interactive (AI) drug use in older people.

DESIGN: Cross-sectional analysis of survey and prescription claims data.

SETTING: The Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PA-PACE) program, a state-funded program providing prescription benefits to older people with low to moderate incomes.

PARTICIPANTS: A total of 83,321 PA-PACE cardholders (age range 65–106) who were using any prescription medications at the time of survey completion.

MEASUREMENTS: All AI drugs were identified using a database of medication warning labels obtained from First DataBank. Prescription drug claims were used to characterize AI drug exposure according to therapeutic class of prescription drug use. A mail survey of PA-PACE cardholders was used to examine alcohol use, as well as sociodemographic and health factors associated with concomitant use of alcohol and AI drugs.

RESULTS: Seventy-seven percent of all prescription drug users were exposed to AI medications, with significant variation in exposure and concomitant alcohol use according to therapeutic class. Overall, 19% of AI drug users reported concomitant alcohol use, compared with 26% of non-AI drug users ($P < .001$). Multinomial logistic regression analyses showed that certain groups of older people, including younger older people, men, and those with higher educational levels, were at greater risk for concomitant exposure to alcohol and AI drugs.

CONCLUSION: Many older people use alcohol in combination with AI prescription drugs. Clinicians should warn every patient who is prescribed an AI drug about alcohol–drug interactions, especially those at high risk for concomitant exposure. **J Am Geriatr Soc 53:1930–1936, 2005.**

Key words: elderly; alcohol; prescription drug use; alcohol–drug interactions; concomitant use of alcohol and prescription drugs

Significant problems can result from the concomitant use of prescription drugs and alcohol.[1] For example, alcohol enhances the sedative effects of antidepressants, antihistamines, barbiturates, muscle relaxants, benzodiazepines, and opioids,[1] creating the potential for serious consequences, such as falls, automobile accidents, or even death.[2,3] When alcohol is used in combination with nonsteroidal antiinflammatory drugs (NSAIDs), stomach bleeding, gastric inflammation, and liver damage can result.[1–3] Alcohol-related adverse drug reactions (ADRs) are an important health concern for individuals of all ages, but the concern is especially salient for older people, because they are more likely to use multiple alcohol-interactive (AI) drugs.[1,4] Although older people typically have low rates of heavy drinking,[5,6] many older adults engage in patterns of alcohol consumption that exceed current guidelines.[6] In addition, even small amounts of alcohol consumed by an older person who is taking multiple medications can have serious consequences.[7,8]

Prior research suggests that older people are at risk for adverse effects due to concomitant use of alcohol and AI medications. One study[9] found that 25% of community-dwelling older people were at risk for alcohol–drug interactions. Another study[10] showed that nearly 38% of older people in three retirement communities were drinkers who used AI drugs. A third study found that more than 60% of older people referred for prescription drug abuse showed evidence of alcohol abuse.[7] Other research has suggested that—considering individuals of all ages—alcohol–drug interactions are a factor in at least 25% of emergency department admissions.[11] Despite the likelihood of severe adverse effects of alcohol–drug interactions, most studies of ADRs in older people have focused on concomitant use of

From the *First Health Services Corporation/Pennsylvania Pharmaceutical Assistance Contract for the Elderly, Harrisburg, Pennsylvania; †Department of Biobehavioral Health, Pennsylvania State University, University Park, Pennsylvania; and ‡Pennsylvania Department of Aging, Harrisburg, Pennsylvania.

This paper was presented at the 132nd annual meeting of the American Public Health Association, November 2004.

Address correspondence to Kristine E. Pringle, PhD, First Health Services Corporation/PA-PACE, 4000 Crums Mill Road, Suite 301, Harrisburg, PA 17112. E-mail: pringlkr@fhsc.com

DOI: 10.1111/j.1532-5415.2005.00474.x

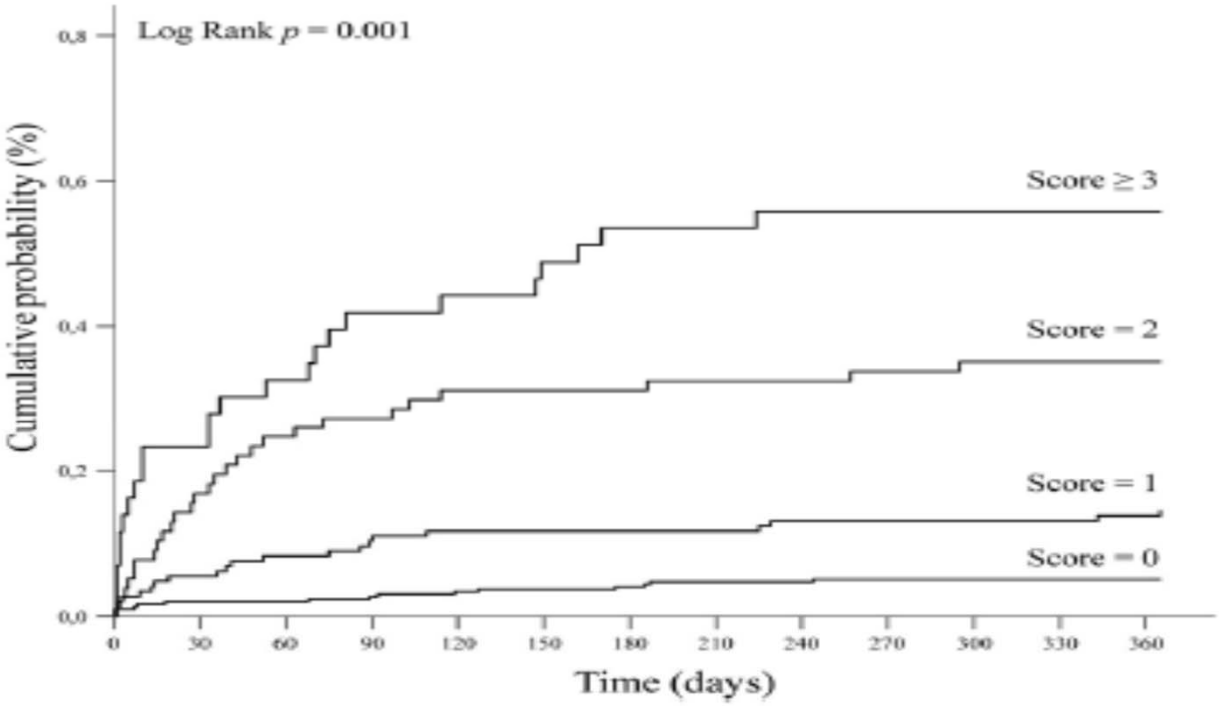


Fig. 2. Cumulative probability of readmission to the Emergency Department (ED) for Acute Alcohol Intoxication (AAI) within one year in patients presenting 0, 1, 2 or ≥ 3 risk factors at the first admission to the ED in the year 2014.

Past episodes of alcohol abuse

Social discomfort

Previous traumas

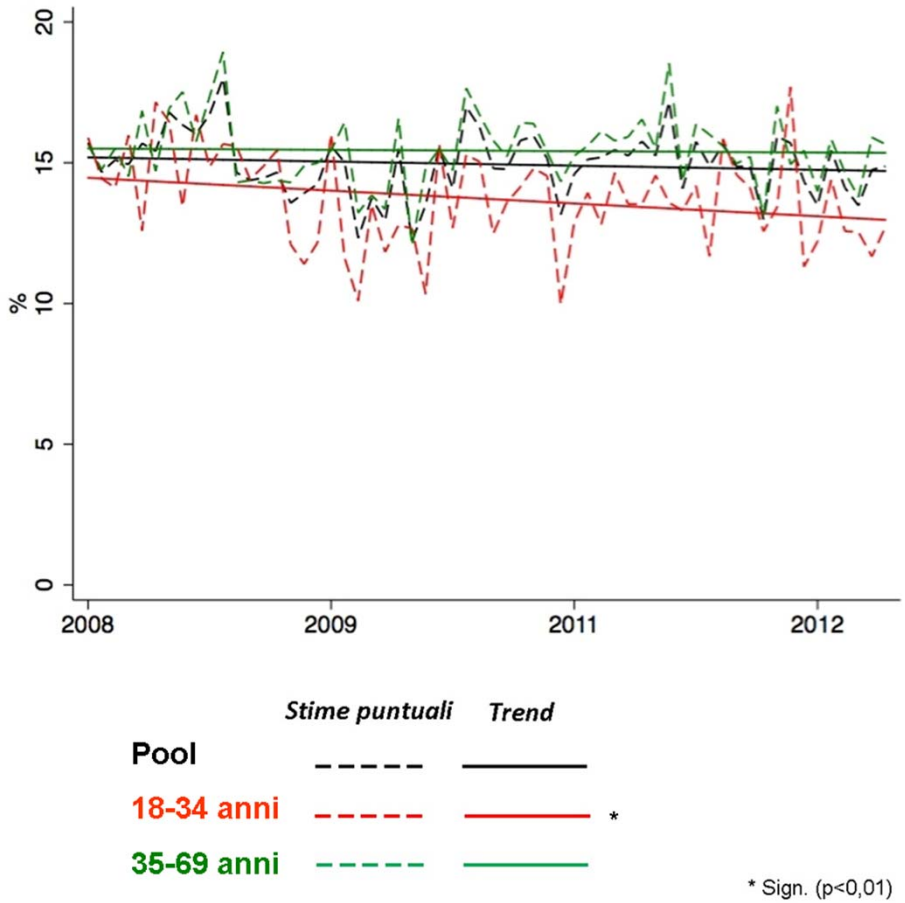
Psychiatric disorders

Baldassarre et al, Addictive Behaviors 2018

Sistema di sorveglianza PASSI 2012 (pop. 18-69 aa)
Pool di Asl di 21 Regioni e P.A. (n=32.208)

Trend del consumo di alcol chiesto dal medico

Prevalenze mensili - Pool di Asl - Passi **2008-12**



Attenzione degli operatori sanitari al consumo di alcol*

15%

- Significative differenze regionali: dal 7% della Basilicata al 25 del Friuli Venezia-Giulia

- Significativo trend in diminuzione nella classe di età più giovane (18-34 anni)

* Persone, che sono state dal medico o da un operatore sanitario negli ultimi 12 mesi, a cui è stato chiesto se bevono

ALCOL SCREENING SCORES
(CAGE e AUDIT)

RISCHIO DI COMPLICANZE GASTROINTESTINALI

Pazienti al di sotto di 50 anni
con CAGE > 2 o **AUDIT > 4**

hanno un rischio aumentato sino a 7 volte,
dopo un periodo di osservazione di 4/5 anni,
di sviluppare complicanze come:

- Cirrosi epatica scompensata
- Sanguinamento da varici gastro-esofagee
- Pancreatite

Au DH et Al,Alcoholism: Clinical and Experimental Research 2007; 31:443

ALCOHOL SCREENING AND BRIEF INTERVENTION FOR YOUTH

A PRACTITIONER'S GUIDE

National Institute on Alcohol Abuse and Alcoholism

2015

C: Have you ever ridden in a **CAR** driven by someone (including yourself) who was "high" or had been using alcohol or drugs?

R: Do you ever use alcohol or drugs to **RELAX**, feel better about yourself, or fit in?

A: Do you ever use alcohol or drugs while you are by yourself, **ALONE**?

F: Do you ever **FORGET** things you did while using alcohol or drugs?

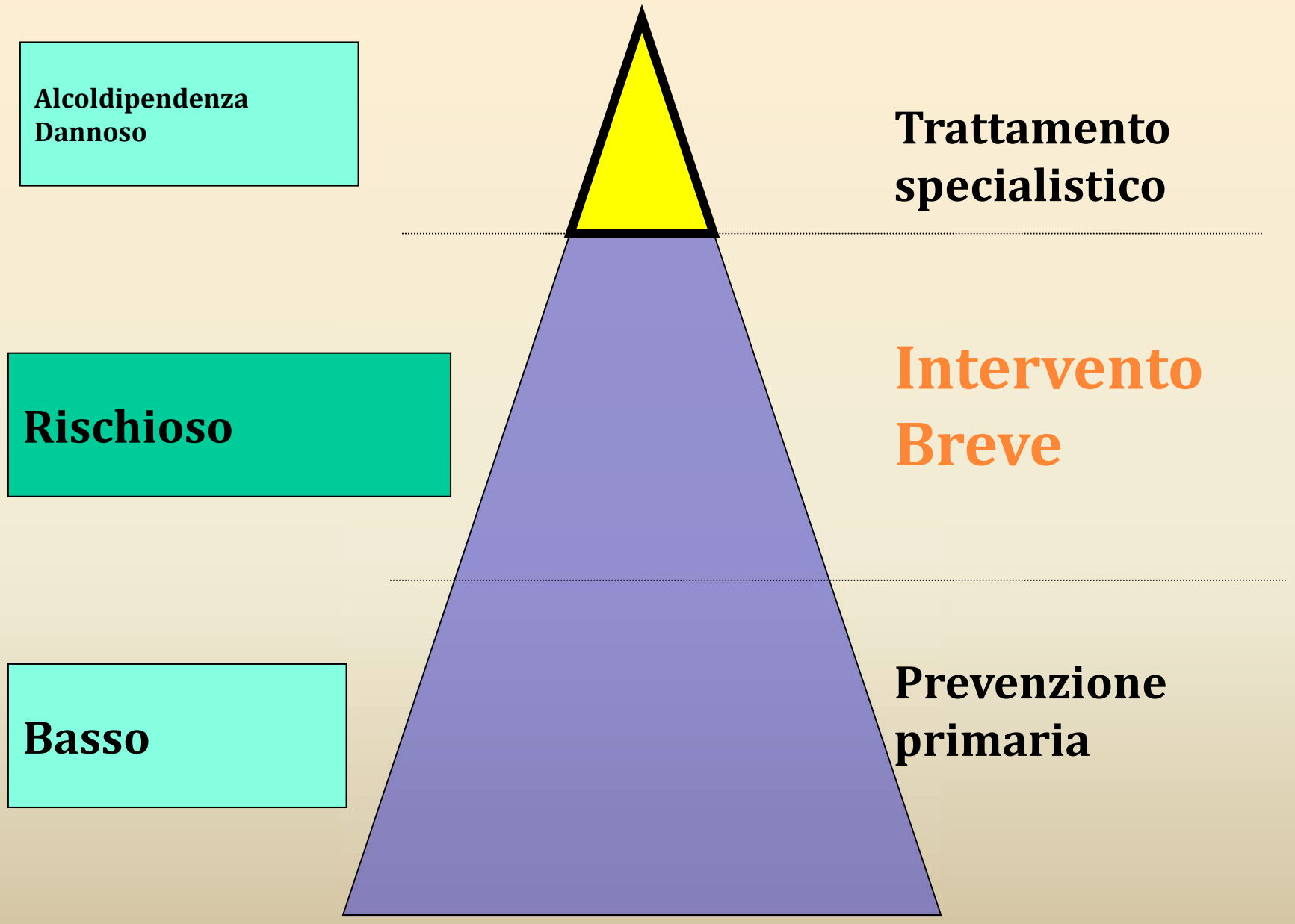
F: Do your family or **FRIENDS** ever tell you that you should cut down on your drinking or drug use?

T: Have you ever gotten into **TROUBLE** while you were using alcohol or drugs?

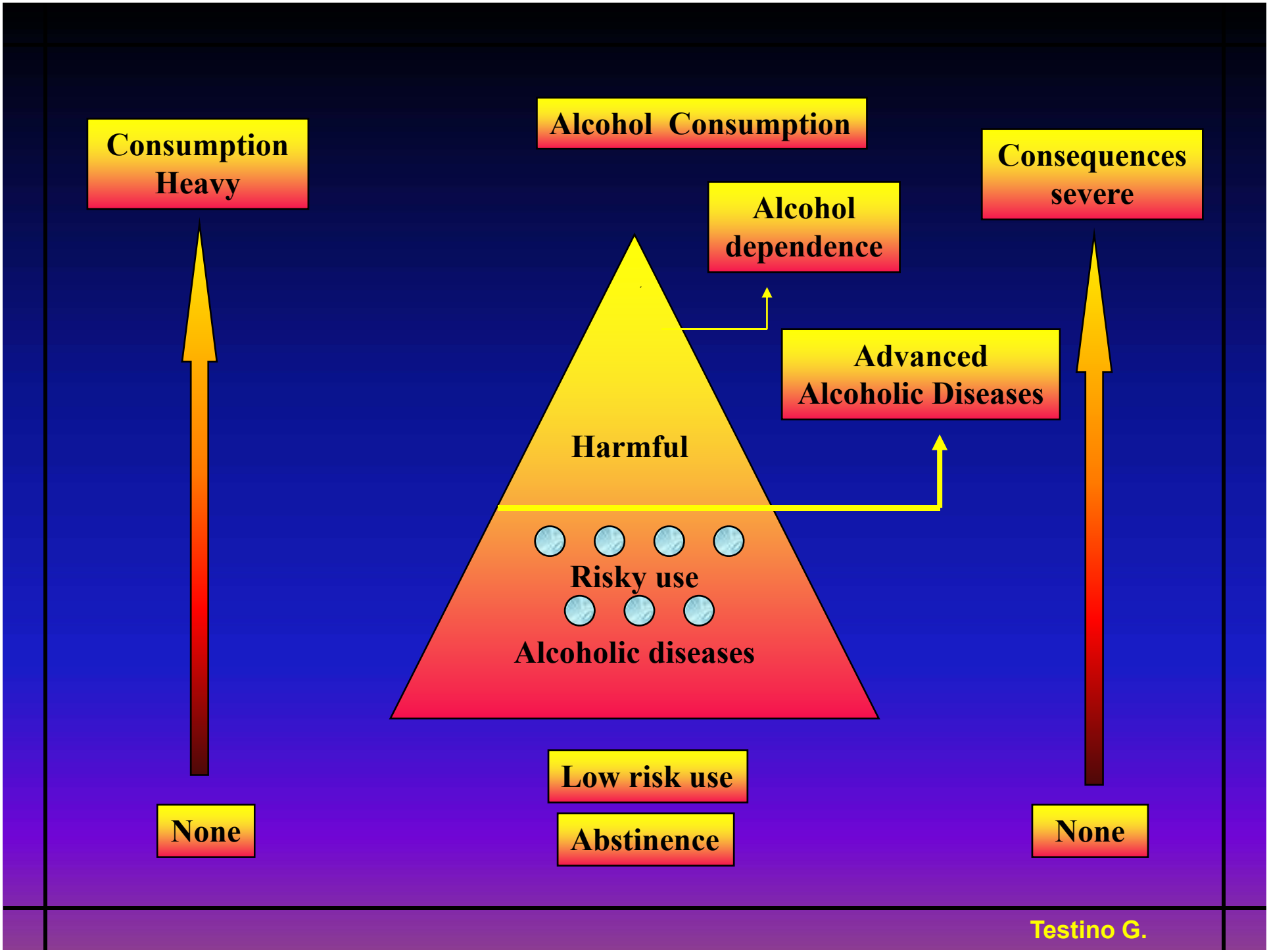
Johnston, L. D., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2011). *Monitoring the Future national survey results on adolescent drug use: Overview of key findings, 2010.* Ann Arbor: Institute for Social Research, The University of Michigan, 77 pp.

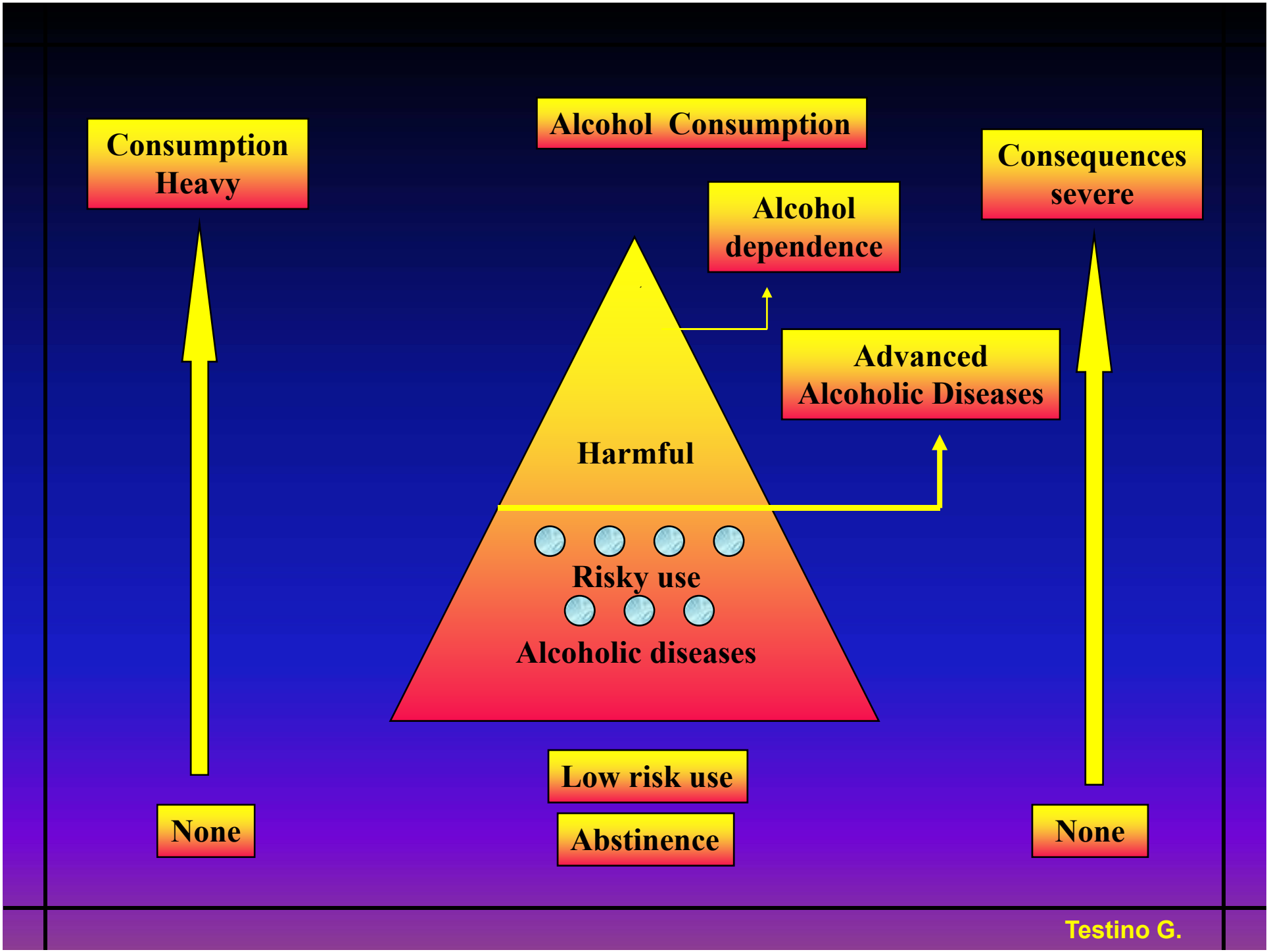
2-3 risposte approfondimento/ 4 risposte probabile dipendenza

GRAVITÀ CONSUMO/PPAC e TIPO DI INTERVENTO



V. Patussi; Centro Alcologico Toscano


Consumption
Heavy
Alcohol Consumption
Alcohol
dependence
Consequences
severe
Advanced
Alcoholic Diseases
Harmful
Risky use
Alcoholic diseases
Low risk use
Abstinence
None
None
Testino G.


Consumption
Heavy
Alcohol Consumption
Alcohol
dependence
Consequences
severe
Advanced
Alcoholic Diseases
Harmful
Risky use
Alcoholic diseases
None
Low risk use
Abstinence
None
Testino G.


Grazie