Patologie Alcol-correlate

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No disclosures

Unità di misura del consumo di alcol (*drink*)

Drink **= bevanda alcolica che contiene circa 12-14 grammi di alcol etilico**

1 boccale di birra leggera 425 ml

1 boccale di birra 330 ml

1 bicchiere di vino 125 ml

1 bicchiere di vino liquoroso 60 ml

1 bicchierino di liquore 40 ml

Ethanol is a toxin

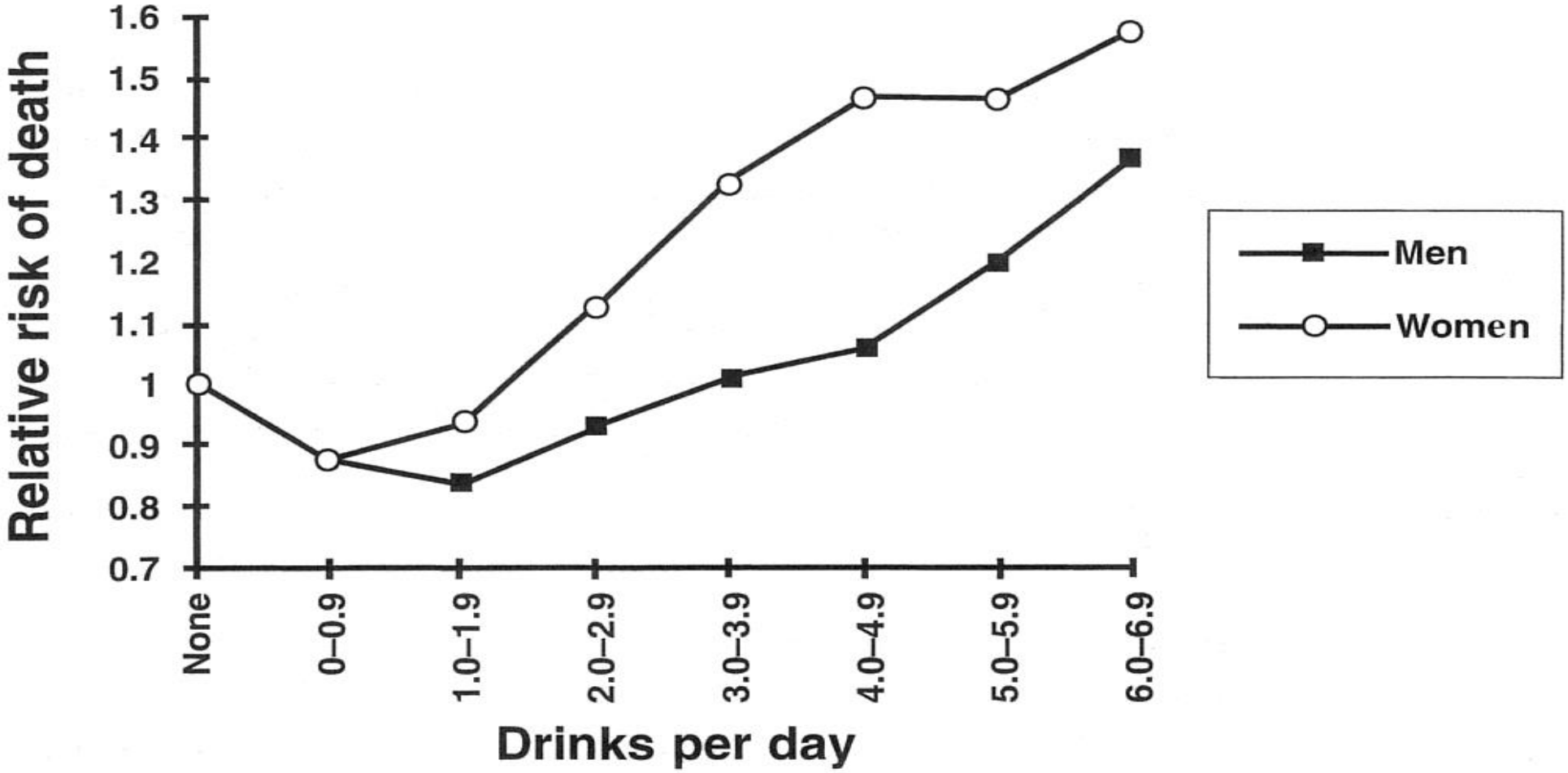
- **High doses of alcohol induce toxic effects**

  >30 g male >20 g female

  > 2 drinks >1 drinks

- **Free radicals and tissue peroxidation are involved in the pathogenesis of the damage**

Alcohol and RR of death



"French Paradox"

>40 prospective studies

show benefits from low dose ethanol on cardiovascular events

- **Primary prevention**

  Criqui, Lancet 1994 Rimm, BMJ 1996

  Sacco, JAMA 1999 Gronbaeck, Ann Int Med 2000

- **Secondary prevention**

  Muntwyler, Lancet 1998

Food and Nutrition Board, PNAS 1989

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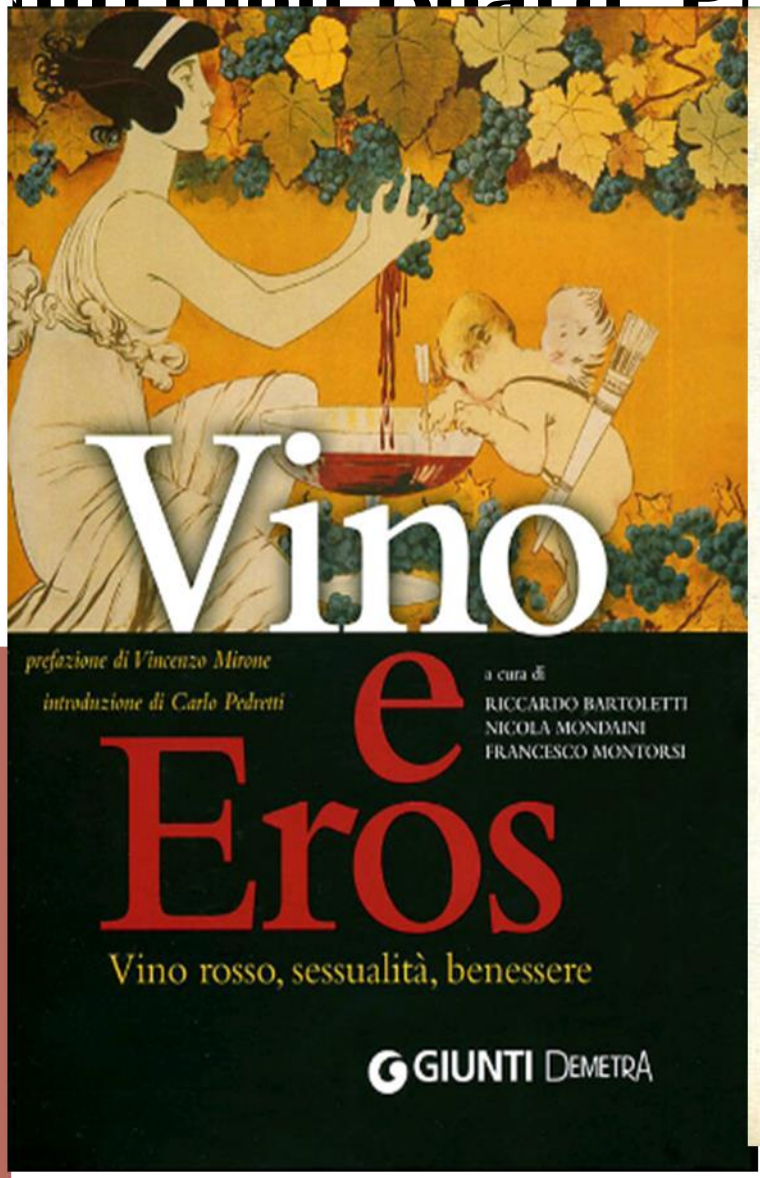
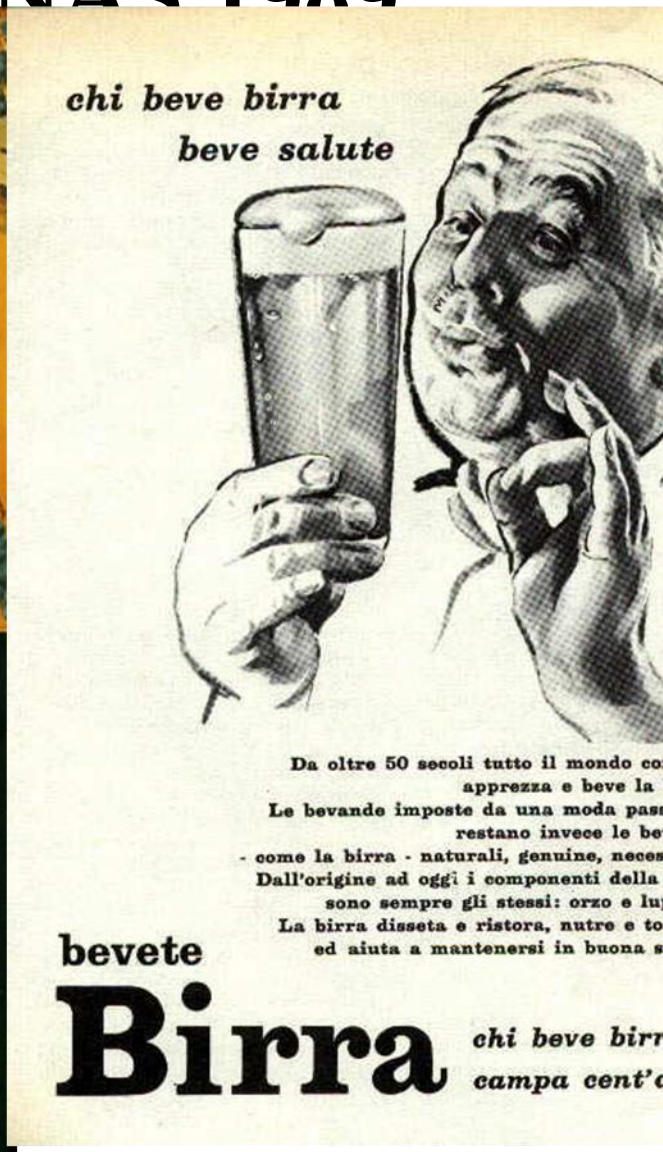




Lancet 2009; 373:

This is the first in a **Series** of three papers about alcohol and global health

Alcohol and Global Health 1

Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders

Jürgen Rehm, Colin Mathers, Svetlana Popova, Montarat Thavorncharoensap, Yot Teerawattananon, Jayadeep Patra

Alcohol consumption has been identified as an important risk factor for chronic disease and injury. In the first paper in this Series, we quantify the burden of mortality and disease attributable to alcohol, both globally and for ten large countries. We assess alcohol exposure and prevalence of alcohol-use disorders on the basis of reviews of published work. After identification of other major disease categories causally linked to alcohol, we estimate attributable fractions by sex, age, and WHO region. Additionally, we compare social costs of alcohol in selected countries. The net effect of alcohol consumption on health is detrimental, with an estimated 3·8% of all global deaths and 4·6% of global disability-adjusted life-years attributable to alcohol. Disease burden is closely related to average volume of alcohol consumption, and, for every unit of exposure, is strongest in poor people and in those who are marginalised from society. The costs associated with alcohol amount to more than 1% of the gross national product in high-income and middle-income countries, with the costs of social harm constituting a major proportion in addition to health costs. Overall, we conclude that alcohol consumption is one of the major avoidable risk factors, and actions to reduce burden and costs associated with alcohol should be urgently increased.

Public Health and Regulatory Policies, Centre for Addiction and Mental Health, Toronto, Canada (J Rehm PhD, S Popova MD, J Patra PhD); **Dalla Lana School of Public Health, University of Toronto, Toronto, Canada** (J Rehm, S Popova); **WHO Collaboration Centre for Substance Abuse, Zurich, Switzerland** (J Rehm); **Epidemiological Research Unit, Klinische Psychologie und Psychotherapie, Technische Universität Dresden, Dresden, Germany** (J Rehm); **WHO, Department of Health Statistics, Geneva, Switzerland** (C Mathers PhD); **Factor-Inwentash Faculty of Social Work, University of Toronto, Toronto, Canada** (S Popova); **Health Intervention and Technology Assessment Program (HITAP); Ministry of Public Health, Nonthaburi, Thailand** (M Thavorncharoensap PhD, Y Teerawattananon PhD); **and Department of Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand** (M Thavorncharoensap)

Correspondence to:
Jürgen Rehm, Centre for Addiction and Mental Health, 33 Russell Street, Room 2035B, Toronto ON M5S 2S1, Canada

	Men (%)*	Women (%)*	Total
Diseases for which alcohol has a detrimental effect			
Maternal and perinatal disorders (low birthweight)	2 (0·1%)	1 (0·3%)	3
Cancer	377 (18·5%)	111 (25·0%)	487
Diabetes mellitus	0 (0·0%)	0 (0·1%)	0
Neuropsychiatric disorders	109 (5·4%)	25 (5·7%)	135
Cardiovascular diseases	466 (22·8%)	80 (18·0%)	545
Cirrhosis of the liver	297(14·6%)	76 (17·1%)	373
Unintentional injuries	556 (27·3%)	110 (24·8%)	666
Intentional injuries	232 (11·4%)	40 (9·0%)	272
Total detrimental effects attributable to alcohol	2039 (100·0%)	443 (100·0%)	2482
Diseases for which alcohol has a beneficial effect			
Diabetes mellitus	–8 (8·3%)	–4 (3·2%)	–12
Cardiovascular diseases	–88 (91·7%)	–128 (96·8%)	–215
Total beneficial effects attributable to alcohol	–96 (100·0%)	–132 (100·0%)	–227
All alcohol-attributable net deaths	1944	311	2255
All deaths	31 063	27 674	58 738
Percentage of all net deaths attributable to alcohol	6·3%	1·1%	3·8%
CRA 2000 (for comparison)	5·6%	0·6%	3·2%

CRA=comparative risk assessment. *Numbers are rounded to the nearest thousand. Zero indicates fewer than 500 alcohol-attributable deaths in the disease category. Percentages refer to all deaths either caused or prevented by alcohol.

Table 1: **Alcohol-attributable deaths (in thousands) by sex and cause of death in 2004**

	Men (%)*	Women (%)*	Total
Diseases for which alcohol has a detrimental effect			
Maternal and perinatal disorders (low birthweight)	64 (0·1%)	55 (0·5%)	119
Cancer	4732 (7·6%)	1536 (13·5%)	6268
Diabetes mellitus	0 (0·0%)	28 (0·3%)	28
Neuropsychiatric disorders	23 265 (37·6%)	3417 (30·1%)	26 682
Cardiovascular diseases	5985 (9·7%)	939 (8·3%)	6924
Cirrhosis of the liver	5502 (8·9%)	1443 (12·7%)	6945
Unintentional injuries	15 694 (25·4%)	2910 (25·6%)	18 604
Intentional injuries	6639 (10·7%)	1021 (9·0%)	7660
Total detrimental effects attributable to alcohol	61 881 (100·0%)	11 349 (100·0%)	73 231
Diseases for which alcohol has a beneficial effect			
Diabetes mellitus	–238 (22·2%)	–101 (8·1%)	–340
Cardiovascular diseases	–837 (77·8%)	–1145 (91·9%)	–1981
Total beneficial effects attributable to alcohol	–1075 (100·0%)	–1246 (100·0%)	–2321
All alcohol-attributable net DALYs	60 806	10 104	70 910
All DALYs	799 536	730 631	1 530 168
Percentage of all net DALYs attributable to alcohol	7·6%	1·4%	4·6%
CRA 2000 (for comparison)	6·5%	1·3%	4·0%

CRA=comparative risk assessment. DALY=disability-adjusted life-year. *Numbers are rounded to the nearest thousand. Zero indicates fewer than 500 alcohol-attributable disability-adjusted life-years in the disease category. Percentages refer to all disability-adjusted life-years either caused or prevented by alcohol.

Table 2: **Alcohol-attributable burden of disease (in 1000 disability-adjusted life-years) by sex and cause in 2004**

Lancet 2018; 392: 1015–35

Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016

*GBD 2016 Alcohol Collaborators**

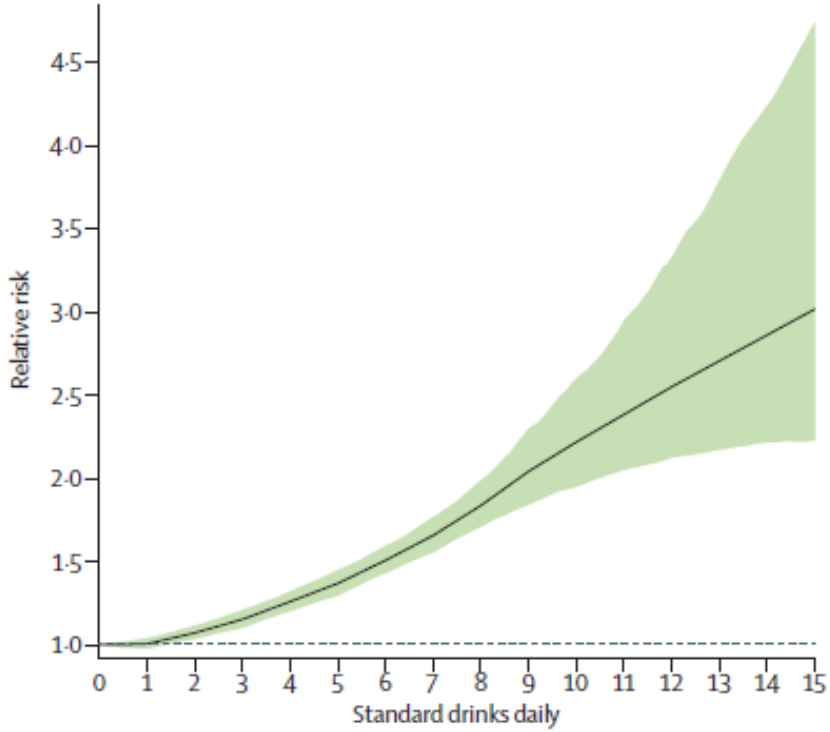
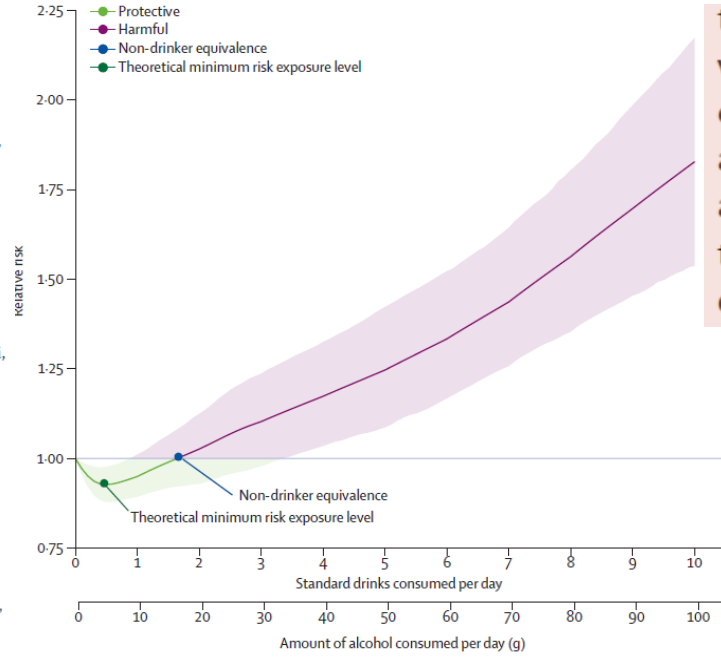


Figure 5: **Weighted relative risk of alcohol for all attributable causes, by standard drinks consumed per day**
Age-standardised weights determined by the DALY rate in 2016, for both sexes. The dotted line is a reference line for a relative risk of 1. DALY=disability-adjusted life-year.

Lancet 2022; 400: 185–235

Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020

Dana Bryazka, Marissa B Reitsma, Max G Griswold, Kalkidan Hassen Abate, Cristiana Abbafati, Mohsen Abbasi-Kangevari, Zeinab Abbasi-Kangevari, Amir Abdoli, Mohammad Abdollahi, Abu Yousuf Md Abdullah, E S Abhilash, Eman Abu-Gharbieh, Juan Manuel Acuna, Giovanni Addolorato, Oladimeji M Adebayo, Victor Adekanmbi, Kishor Adhikari, Sangeet Adhikari, Qorinah Estiningtyas Sakilah Adnani, Saira Afzal, Wubetu Yimam Agegnehu, Manik Aggarwal, Bright Opoku Ahinkorah, Araz Ramazan Ahmad, Sajjad Ahmad, Tauseef Ahmad, Ali Ahmadi, Sepideh Ahmadi, Haroon Ahmed, Tarik Ahmed Rashid, Chisom Joyqueenet Akunna, Hanadi Al Hamad, Md Zakiul Alam, Dejene Tsegaye Alem, Kefyalew Addis Alene, Yousef Alimohamadi, Atiyeh Alizadeh, Kasim Allel, Jordi Alonso, Saba Alvand, Nelson Alvis-Guzman, Firehiwot Amare, Edward Kwabena Ameyaw, Sohrab Amiri, Robert Ancuceanu, Jason A Anderson, Catalina Liliana Andrei, Tudorel Andrei, Jalal Arabloo, Muhammad Arshad, Anton A Artamonov, Zahra Aryan, Malke Asaad, Mulusew A Asemahagn, Thomas Astell-Burt, Seyyed Shamsadin Athari, Desta Debalkie Atnafu, Prince Atorkey, Alok Atreya, Floriane Ausloos, Marcel Ausloos, Getinet Ayano, Martin Amogre Ayanore, Olatunde O Ayinde, Jose L Ayuso-Mateos, Sina Azadnajafabad, Melkalem Mamuye Azanaw, Mohammadreza Azangou-Khyavy, Amirhossein Azari Jafari, Ahmed Y Azzam, Ashish D Badiye, Nasser Bagheri, Sara Bagherieh, Mohan Bairwa, Shankar M Bakkannavar, Ravleen Kaur Bakshi, Awraris Hailu Balchut/Bilchut, Tikrnighausen, Fabio Barra, Amadou Barrow, Pritish Baskaran, Luis Belo, Derrick A Bennett, Isabela M Bensenor, Akshaya Srikanth Bhagavathula, Neeraj Bhala, Ashish Bhalla, Nikha Bhardwaj, Pankaj Bhardwaj, Sonu Bhaskar, Krittika Bhattacharyya, Vijayalakshmi S Bhojaraja, Bagas Suryo Bintoro, Elena A Elena Blokhina, Belay Boda Abule Bodicha, Archith Boloor, Cristina Bosetti, Dejana Braithwaite, Hermann Brenner,



the level of alcohol consumption that minimises health loss varies significantly across populations and remains zero or very close to zero for several population groups, particularly young adults. At the same time, small amounts of alcohol consumption are associated with improved health outcomes in populations that predominantly face a high burden of cardiovascular diseases, particularly older adults in many world regions. Given

Figure 1: **Exemplifying a weighted all-attributable cause alcohol relative risk curve**
Points mark the theoretical minimum risk exposure level and non-drinker equivalence level. The shaded areas denote consumption levels with a lower risk (green) and greater risk (purple), compared to no consumption. The solid line indicates the mean aggregate relative risk estimate, whereas the shaded area reflects the 95% uncertainty interval of the aggregate relative risk estimate. One standard drink is equivalent to 10 g of pure ethanol.

Global patterns in alcohol-attributable deaths and disease burden

In **high SDI countries, cancers** were the predominant source of attributable burden among both sexes.

In **low SDI countries, tuberculosis** was the primary cause of burden for both sexes, followed by **cirrhosis and other chronic liver diseases.**

The profile of attributable burden in **high-to-middle SDI and middle SDI countries** for females and males was largely composed of **ischaemic stroke and haemorrhagic stroke**, followed by liver cancer for females.

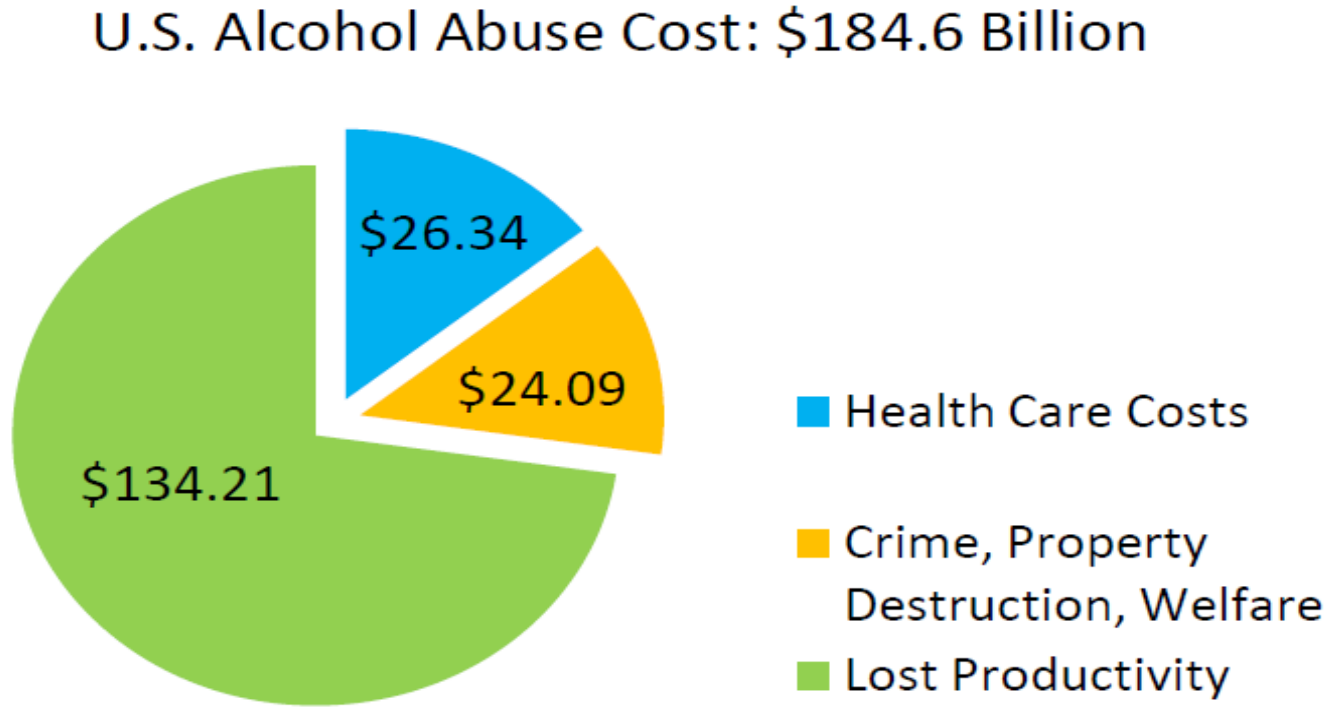
Health risks associated with alcohol consumption

- Statistically significant J-shaped curves for ischaemic heart disease.
- For all other outcomes, including all cancers, the relative risk monotonically increased with alcohol consumption
- The protective effects for ischaemic heart disease, were offset when overall health risks were considered (strong association between alcohol consumption and the risk of cancer, injuries, and communicable disease).

- In 2016, alcohol use led to **2·8 million deaths** and was the leading risk factor for premature death and disability among people aged 15–49 years, with nearly 9% of all attributable DALYs for men and more than 2% for women.
- Acohol use was associated with far **more health loss for males than for females**, with the attributable burden for men around three times higher than that for women in 2016.
- **Consuming zero standard drinks daily minimises the overall risk to health.**

Prevalence and Cost of Alcohol Abuse

- **Why is severe drinking a health concern?**
  - **High risk of alcohol-related problems**
  - **Morbidity**
  - **Mortality**



Alcohol and Preventable Deaths

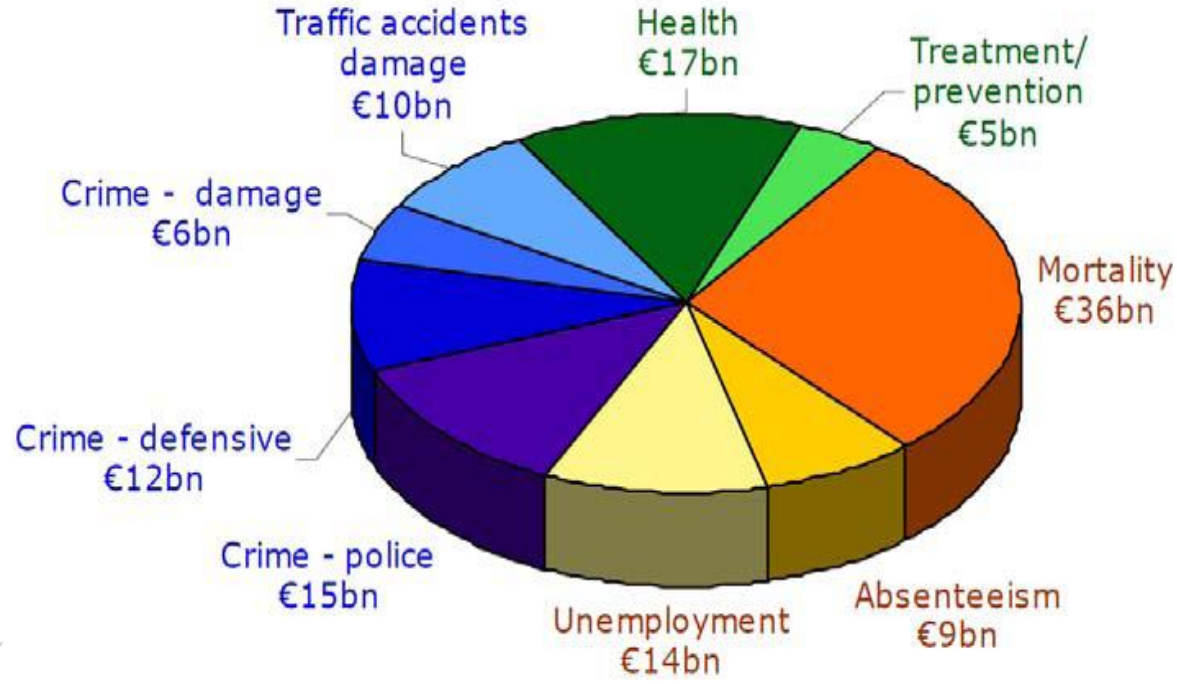
The Centers for Disease Control ranks alcohol as the source for the third leading cause of preventable deaths in the U.S.

Table 2. Actual Causes of Death in the United States in 1990 and 2000

Actual Cause	No. (%) in 1990*	No. (%) in 2000
Tobacco	400 000 (19)	435 000 (18.1)
Poor diet and physical inactivity	300 000 (14)	400 000 (16.6)
Alcohol consumption	100 000 (5)	85 000 (3.5)
Microbial agents	90 000 (4)	75 000 (3.1)
Toxic agents	60 000 (3)	55 000 (2.3)
Motor vehicle	25 000 (1)	43 000 (1.8)
Firearms	35 000 (2)	29 000 (1.2)
Sexual behavior	30 000 (1)	20 000 (0.8)
Illicit drug use	20 000 (<1)	17 000 (0.7)
Total	**1 060 000** (50)	**1 159 000** (48.2)

*Data are from McGinnis and Foege.[1] The percentages are for all deaths.

Mokdak et al, JAMA 2004



124 miliardi di € / anno → costi tangibili

270 miliardi di € / anno → costi intangibili

Ministero della Salute - "Relazione sullo Stato Sanitario del Paese 2007-2008", 2009
Anderson, P. & Baumberg, B. (2006) Alcohol in Europe: A Public Health Perpsective – Report to the European Commission. London: Institute of alcohol studies

3,5 % del PIL → 53 miliardi di €/anno

- mortalità
- morbilità
- perdita di produttività
- assenteismo
- ospedalizzazione
- ecc.

OMS

30.000 morti /anno

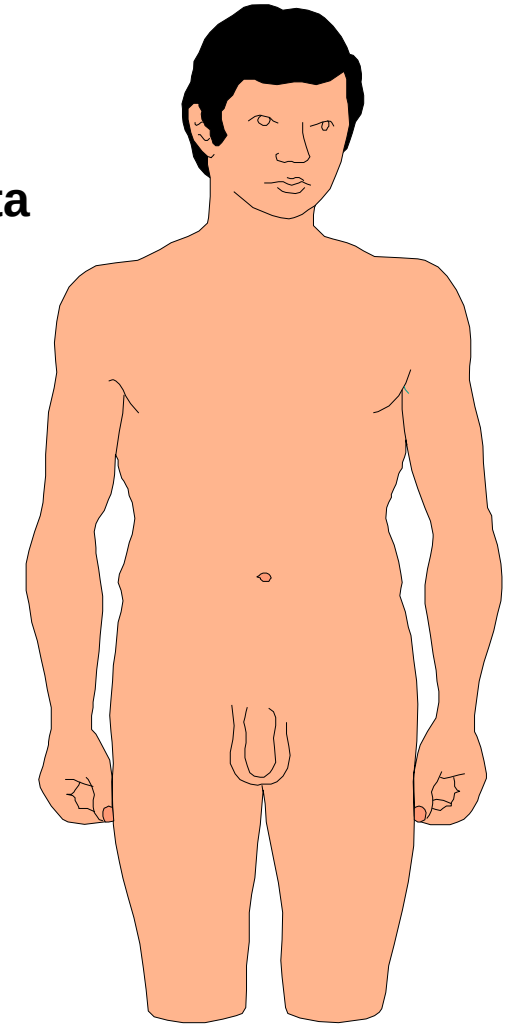
prima causa di morte fino a 24 anni

ISS

Patologie organiche

ACUTO

- Epatite acuta alcolica
- Pancreatite acuta
- Esofagite acuta
- Gastrite acuta emorragica
- Rabdomiolisi



CRONICO

- Esofagite cronica
- Sindrome di Mallory Weiss
- Alterazioni della motilità intestinale - Malassorbimento- Diarrea
- Dispepsia e gastrite cronica
- Pancreatite cronica
- Tubercolosi
- Polmonite e broncopneumopatie croniche
- Anemia macrocitica
- Miopatia cronica alcolica
- Alterazioni elettrolitiche
- Gotta
- Osteoporosi
- Alterazioni cutanee
- suscettibilità insogenza tumori
- Sindrome Fetale Alcolica

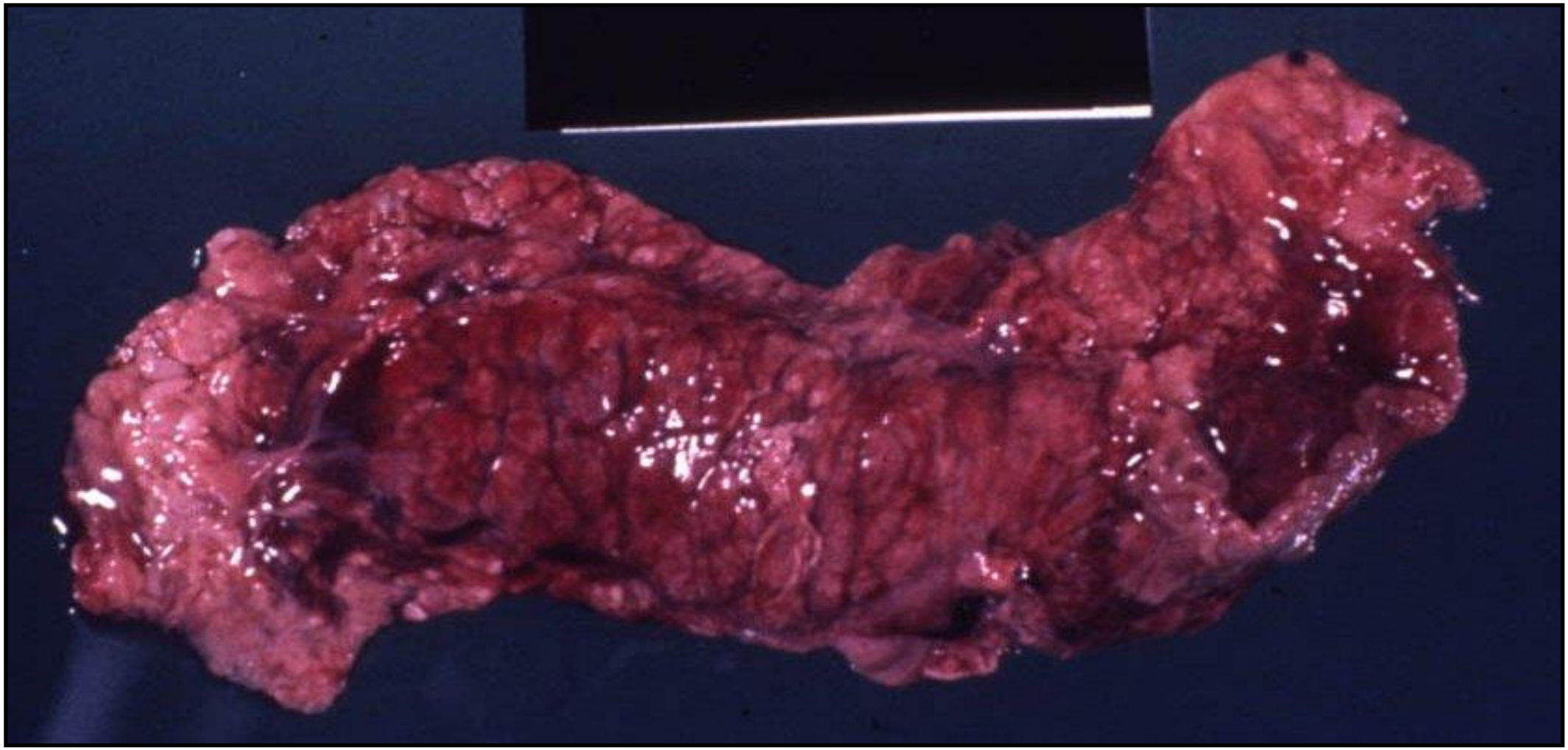
Sindrome feto-alcolica

openings
e folds

edizione di "A tutta birra", la manifesta-
icata a quel fenomeno 'commerciale e
bevanda, con lo scopo di promuoverne
a'. Per la parte culturale, il programma

Tutto ciò che avreste voluto sapere sulla birra e non avete mai osato chiedere

Pancreatite emorragica



Alcoholic cardiomyopathy

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

43 (2017) 1–5

Narrative Review

Alcoholic cardiomyopathy: What is known and what is not known

Antonio Mirijello [a,b,*], Claudia Tarli [a], Gabriele Angelo Vassallo [a], Luisa Sestito [a], Mariangela Antonelli [a], Cristina d'Angelo [a,c], Anna Ferrulli [a], Salvatore De Cosmo [b], Antonio Gasbarrini [a], Giovanni Addolorato [a]

[a] Department of Medical Sciences, Hepatology and Gastroenterology Unit, Catholic University of Rome, Italy
[b] Department of Medical Sciences, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy
[c] "Gli Angeli di Padre Pio", Padre Pio Rehabilitation Centres Foundation, San Giovanni Rotondo, Italy

- **Congestive cardiomyopathy characterized by an increase in myocardial mass, dilation of the ventricles, and wall thinning**

Controllo

AUD

- **Excessive alcohol consumption is associated with coronary heart disease**

Alcoholic cardiomyopathy

European Journal of Internal Medicine 101 (2022) 76–85

Contents lists available at ScienceDirect

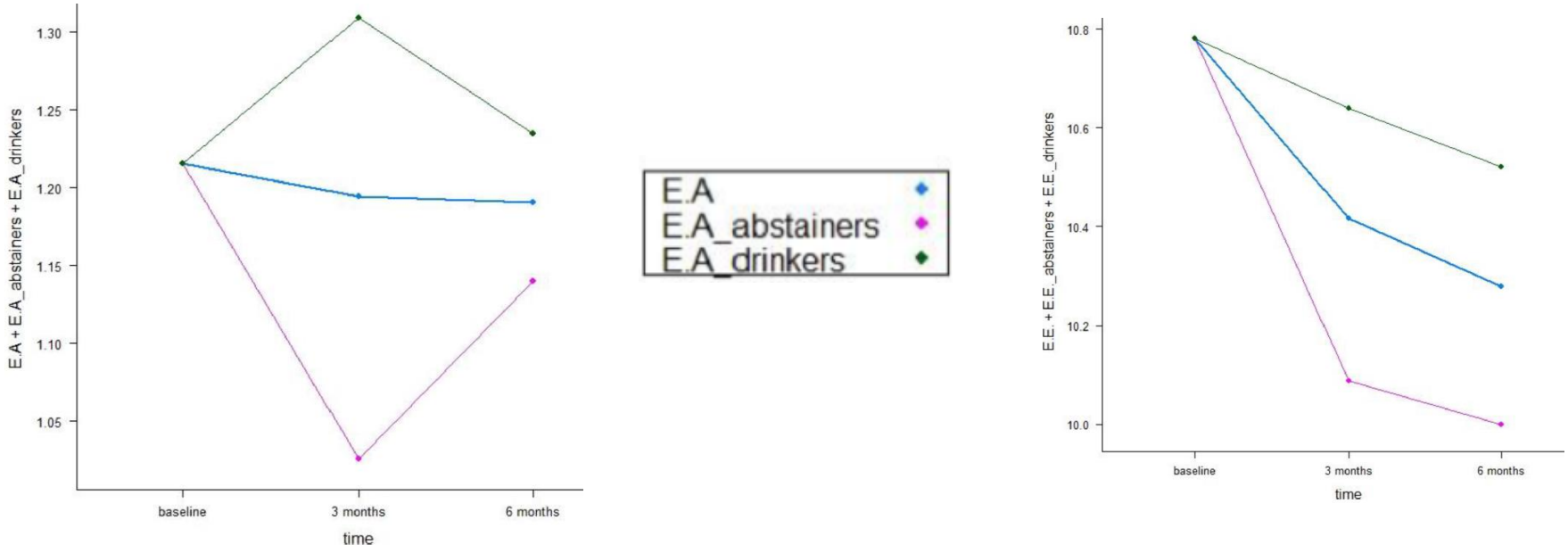
European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

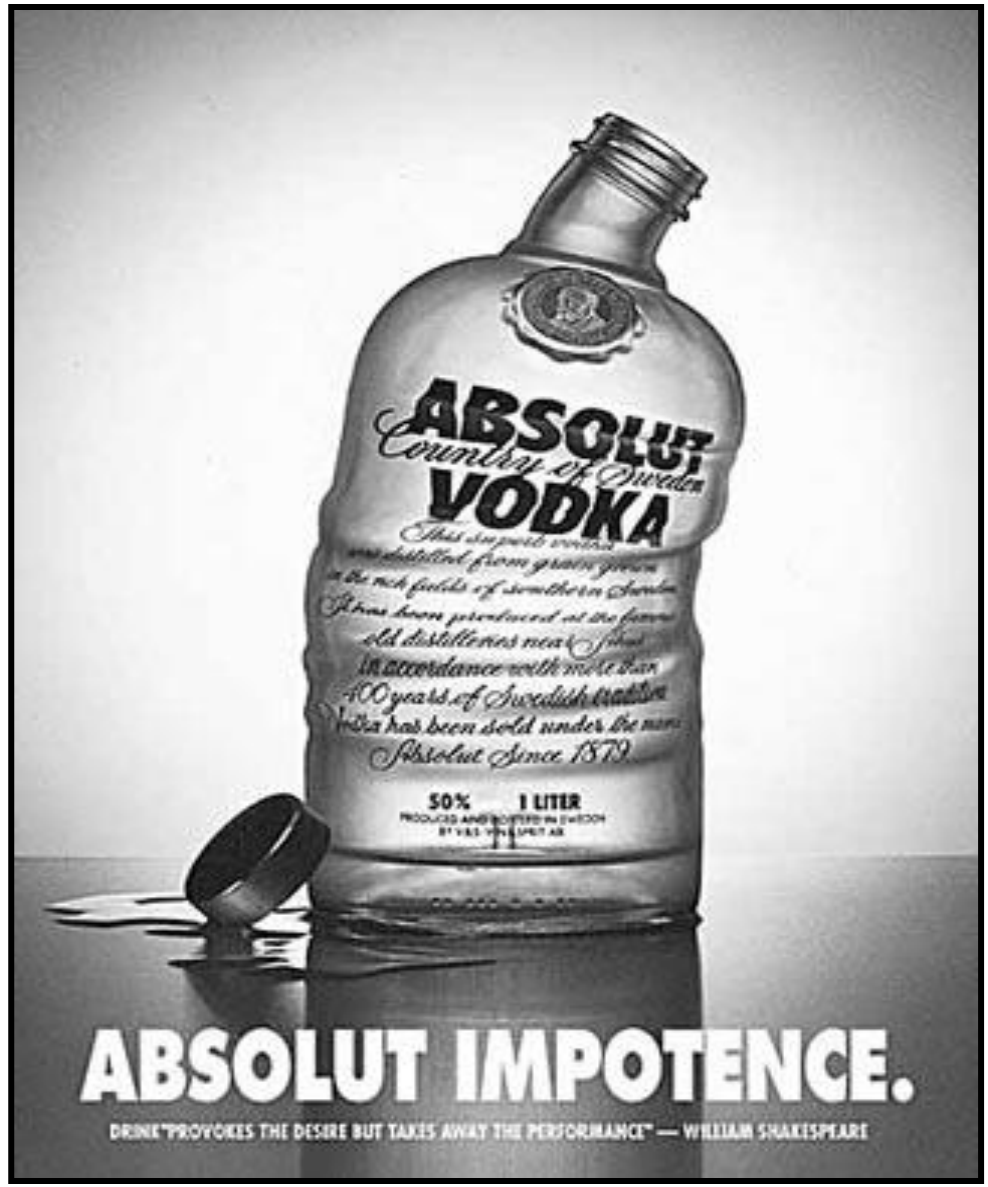
Original article

Echocardiographic markers of early alcoholic cardiomyopathy: Six-month longitudinal study in heavy drinking patients

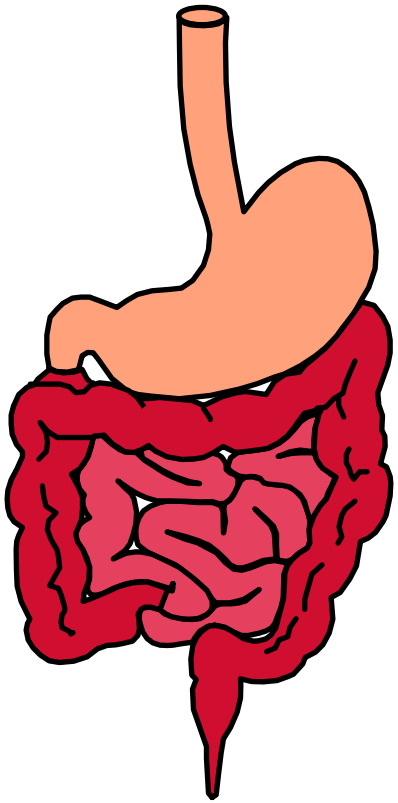
Antonio Mirijello [a,*], Luisa Sestito [b], Christian Lauria [c], Claudia Tarli [b], Gabriele Angelo Vassallo [d], Mariangela Antonelli [b], Cristina d'Angelo [e], Anna Ferrulli [f,g], Filippo Crea [c], Anthony Cossari [h], Lorenzo Leggio [i,j,k,l,m], Salvatore De Cosmo [a], Antonio Gasbarrini [b], Giovanni Addolorato [b,*]



Impotenza sessuale



Intestino



- **Altera il TTOC**
  - **in acuto (riduzione)**
  - **in cronico (allungamento)**

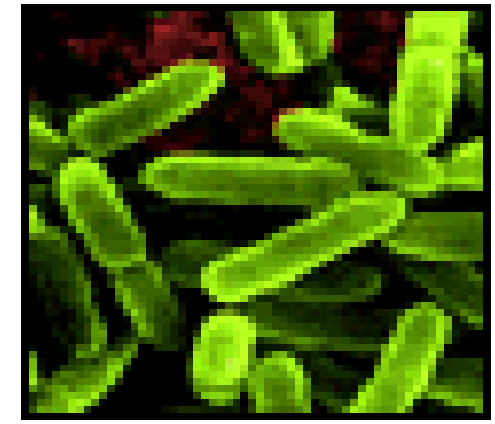
Addolorato et al, Gut 1997
Izbeki et al, Alcohol Alcohol 2001

- **Incrementa la permeabiltà intestinale**

Parlesak et al, J Hepatol 2000

Alcol e immunità

Aumentata suscettibilità e gravità delle infezioni



- ***Mycobacterium tuberculosis***
- ***Klebsiella***
- ***Streptococcus p.***
- ***Nippostrongylus***
- ***Salmonella***
- ***Listeria***

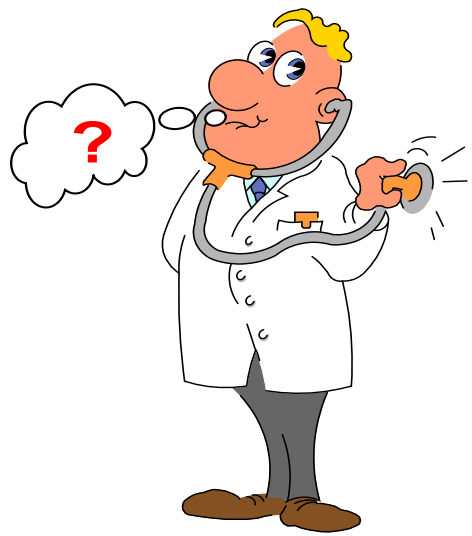
- Colturali dei liquidi biologici
- Rx torace
- Esami ematologici di screenig (frequente neutropenia)

Addolorato et al. Alcohol Clin Exp Res 1997

A L C O L

Fattore di rischio
per insorgenza di Cancro

- Bocca
- Laringe
- Esofago
- Fegato
- Pancreas
- Mammella



?

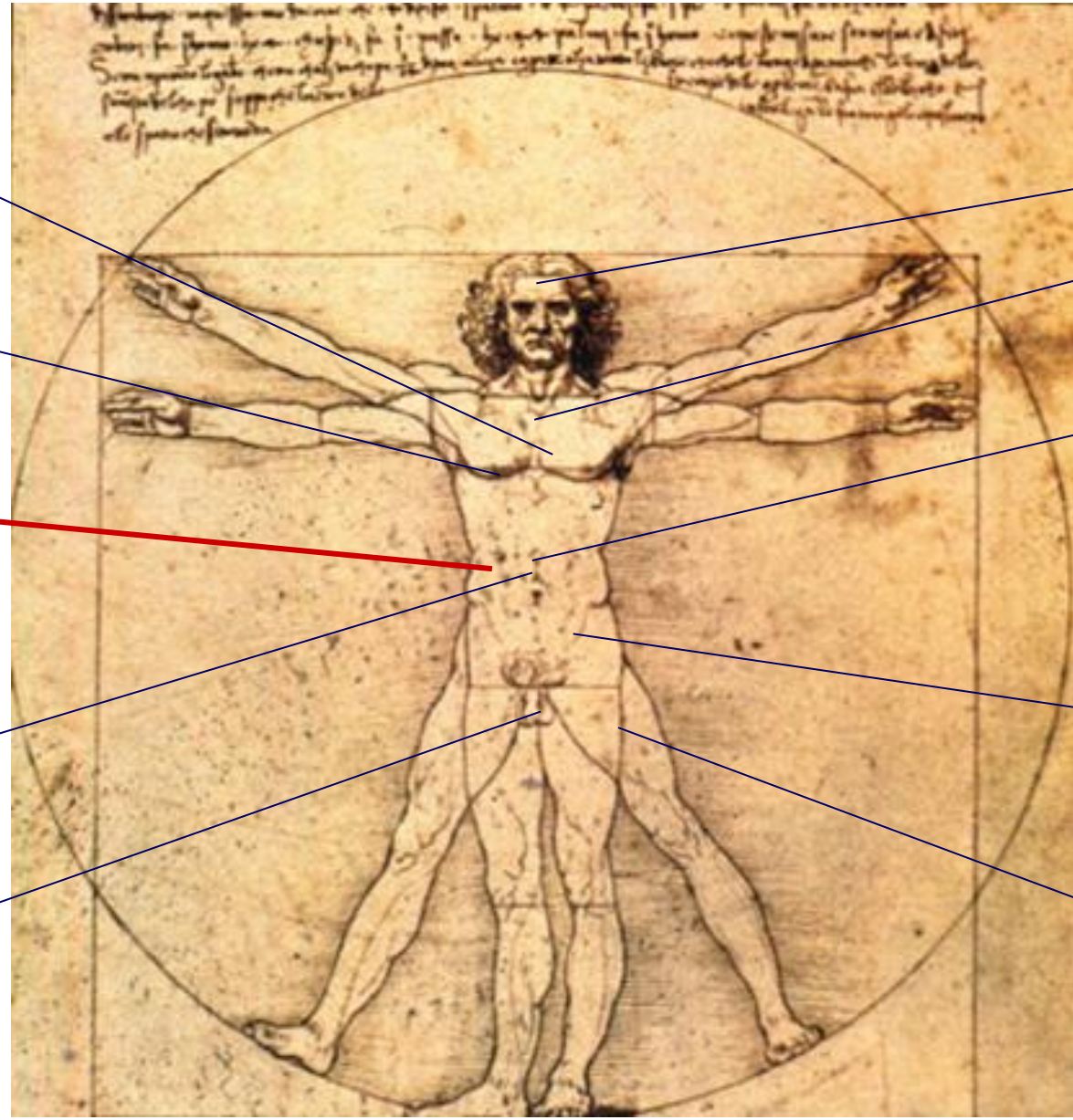
- Colon
- Stomaco
- Prostata

Bisogna Pensarci

EPIC Study **Il 10% dei casi registrati di cancro negli uomini e il 3% nelle donne in 8 paesi EU, è attribuibile al consumo di alcol**

Schutze et al, BMJ 2011

PATOLOGIE ALCOL - RELATE



CARDIOPATIA

INFEZIONI

EPATOPATIA

PANCREATITE

IMPOTENZA

ENCEFALOPATIA

MIELOPATIA

ULCERA GASTRICA
E DUODENALE

NEOPLASIE
TUBO DIGERENTE

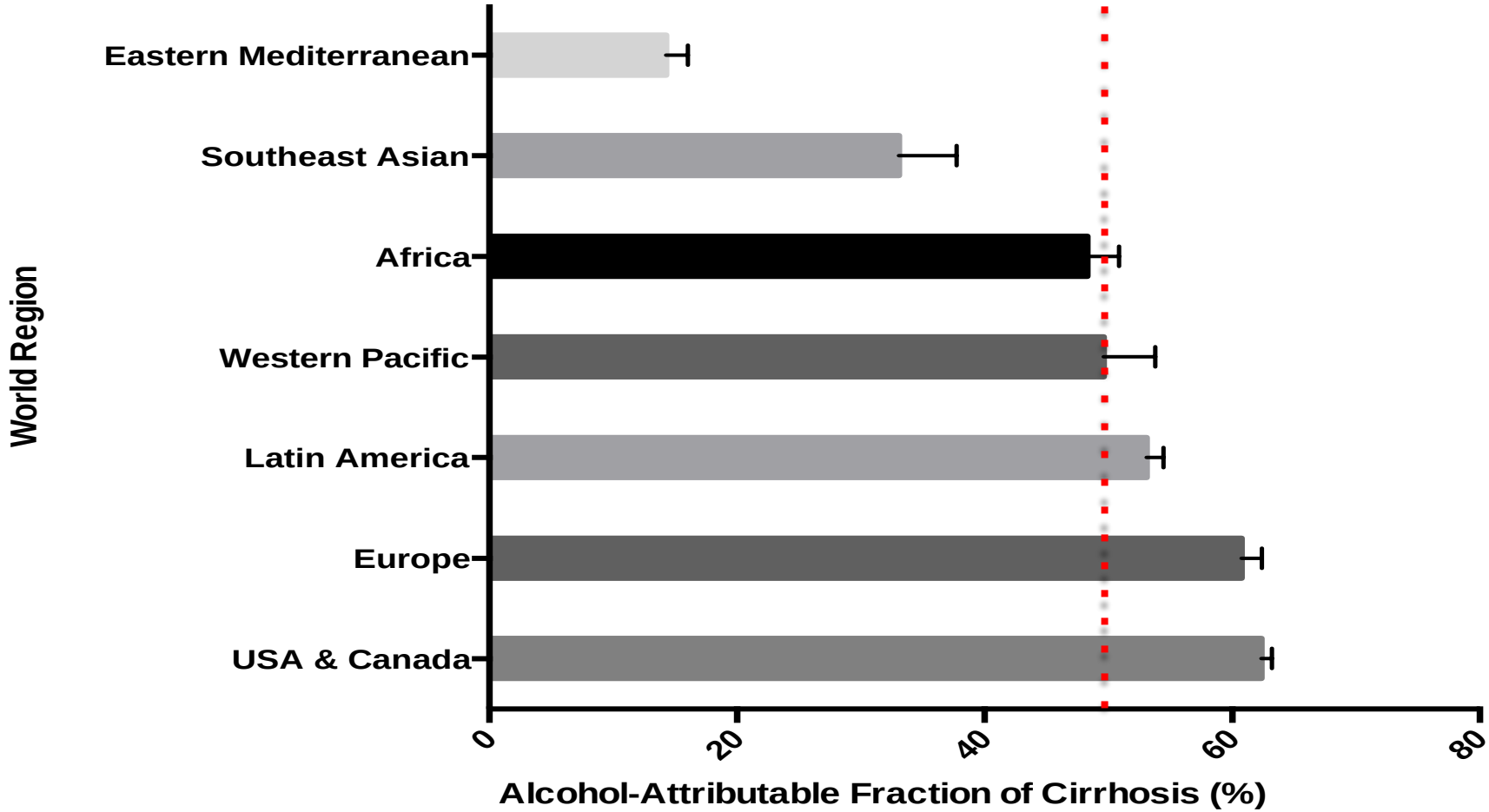
MIOPATIA E
MALNUTRIZIONE

Alcoholic Liver Disease

ALD is the most common cause of liver cirrhosis in the Western World

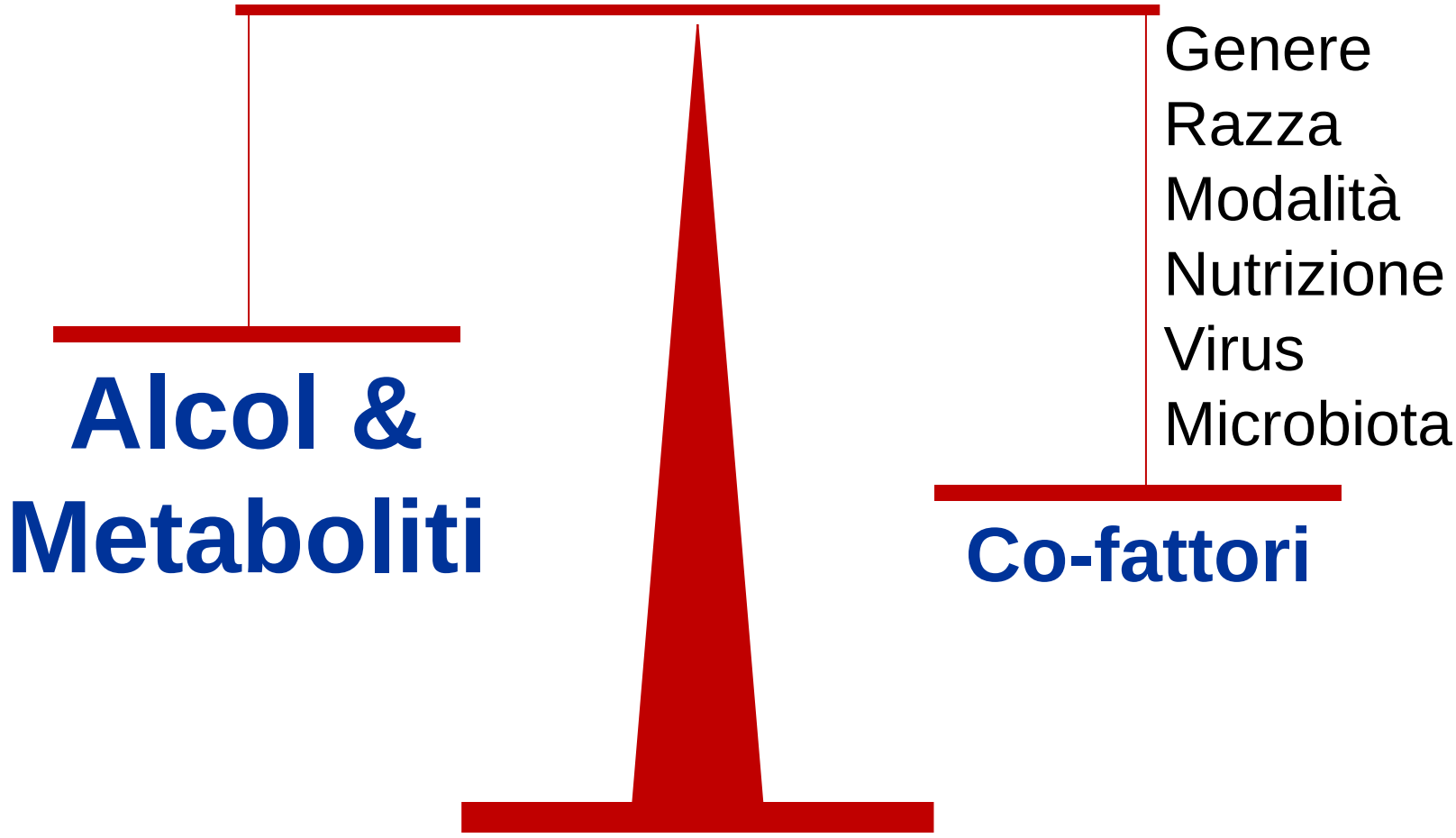
Tilg & Day, Nat Clin Pract Gastroenterol Hepatol 2007

ALCOHOL AS A CAUSE OF CIRRHOSIS: 2014 ALCOHOL REPORT BY WHO

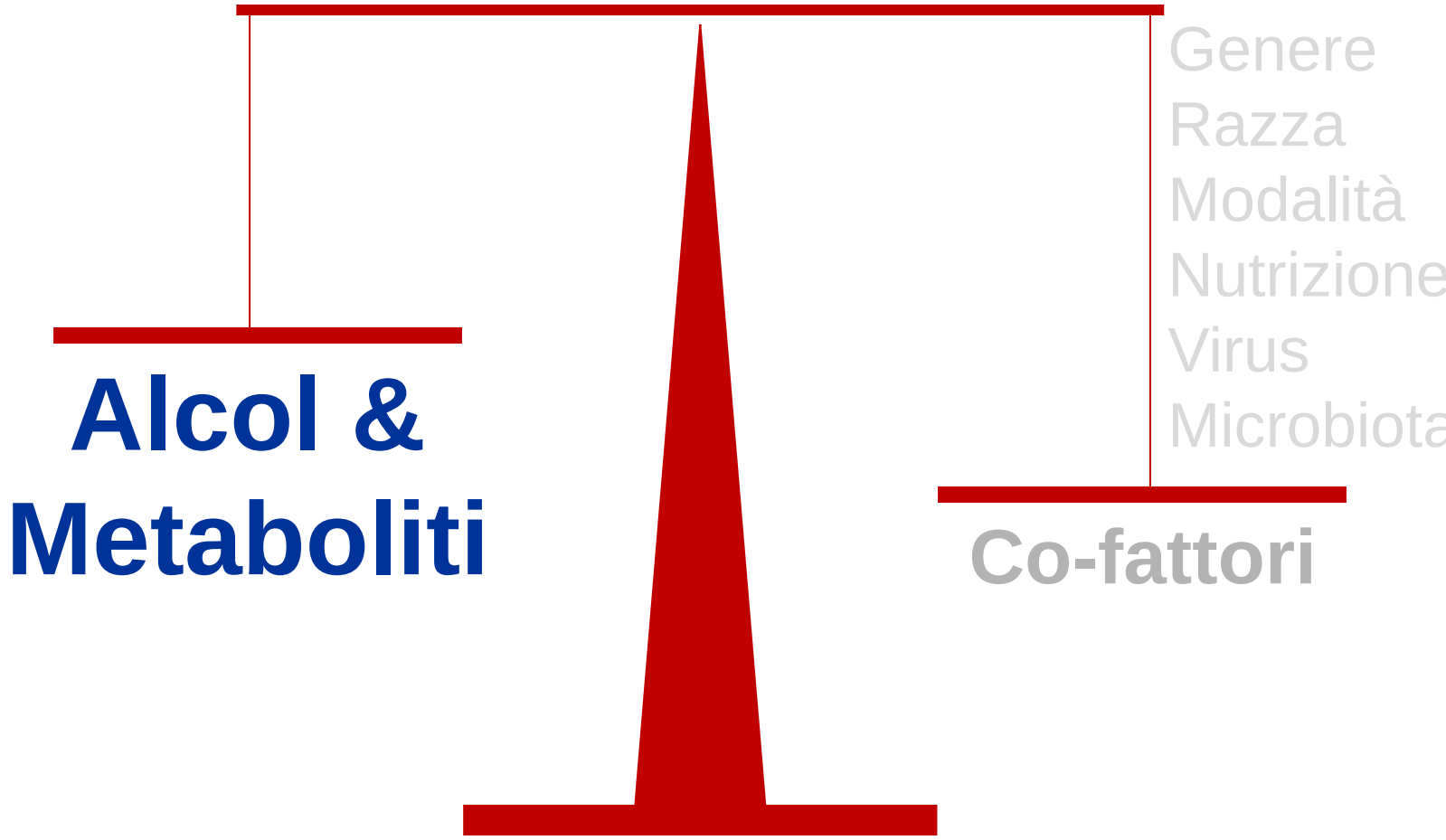


Stein E, et al. EASL 2015

Danno Alcol-relato



Danno Alcol-relato



METABOLISMO ALCOL
(danno diretto)

- **↑acetaldeide e addotti dell'acetaldeide tossica per membrane e citoscheletro → lipoperossidazione → *stress ossidativo***

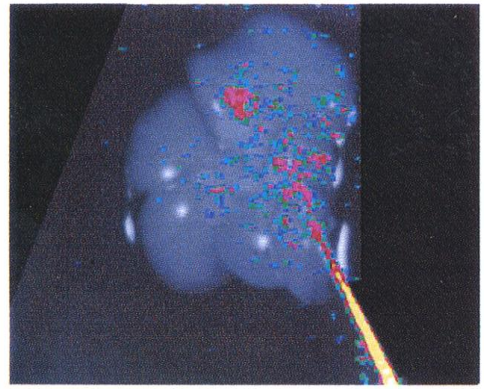
- **Attivazione MEOS produzione RLO_2 → lipoperossidazione → *stress ossidativo***

↓ NAD/NADH; ↓ NADP/NADPH; GSH/GSSG

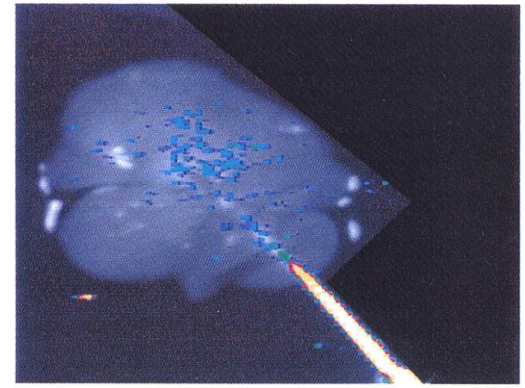
(↓ anti-ossidanti, ↑ pro-ossidanti → *stress ossidativo)*

Lieber, N Eng J Med, 1995

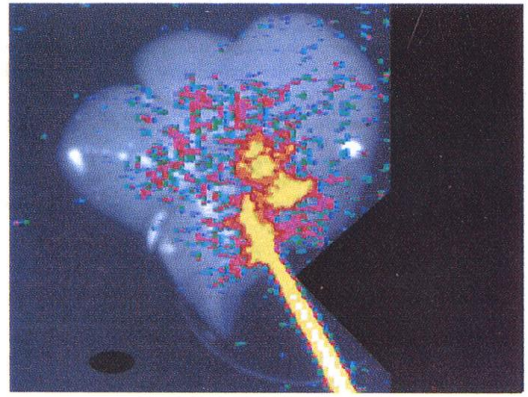
Oxidative damage and alcohol intake caused by free radical intermediates



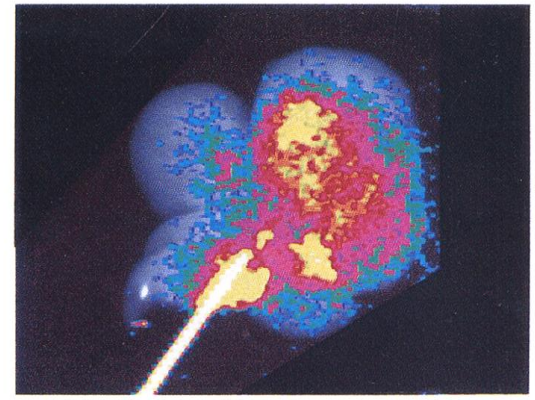
Group S



Group B



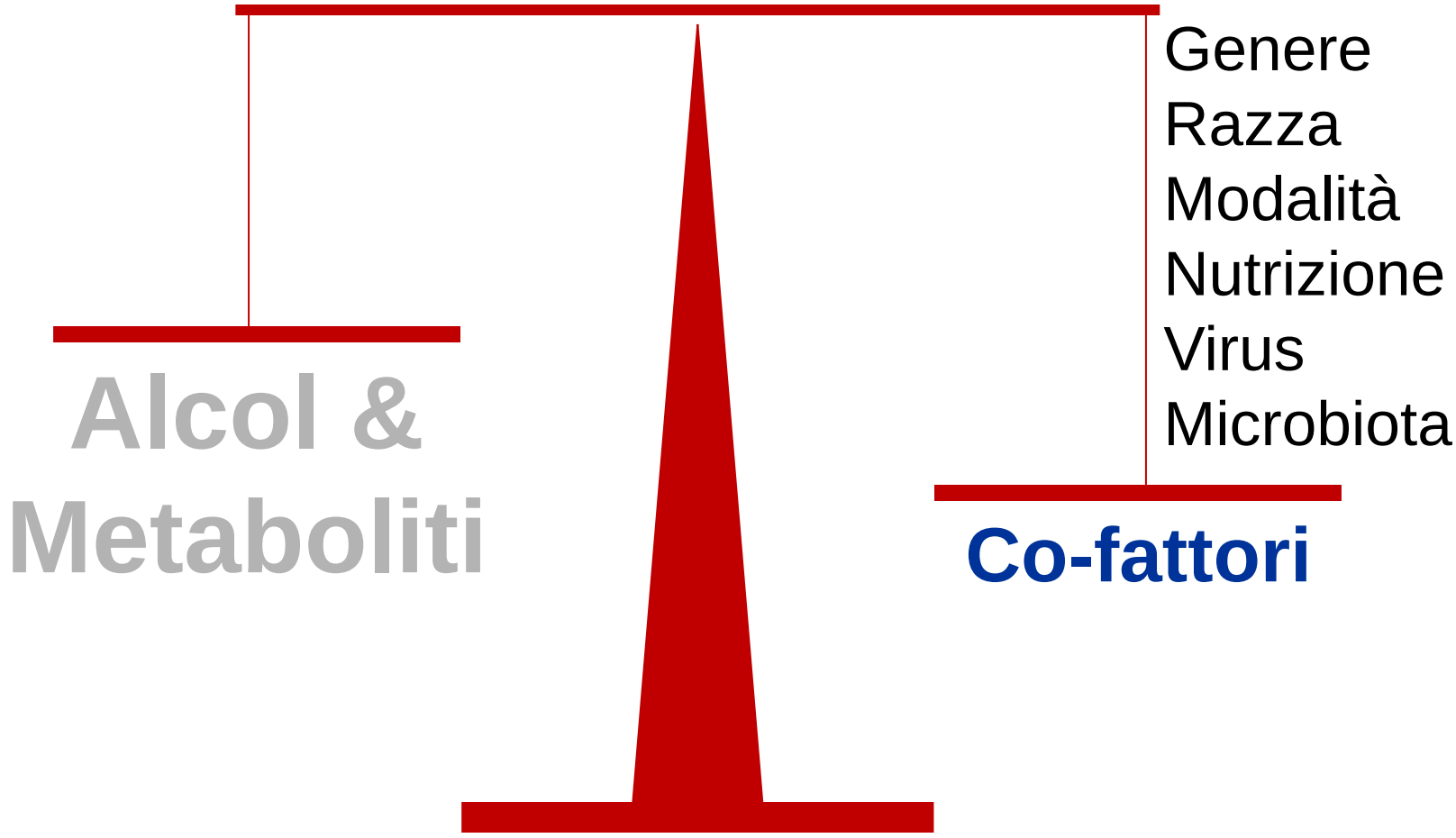
Group C



Group D

Addolorato et al. Dig Dis Sci, 2001

Danno Alcol-relato



- GENERE
- RAZZA
- MODALITA’ DI ASSUNZIONE

<

↓ volume di distribuzione

↓ ADH gastrica

estrogeni

↑ risposta immunitaria

- GENERE
- RAZZA
- MODALITA’ DI ASSUNZIONE

<

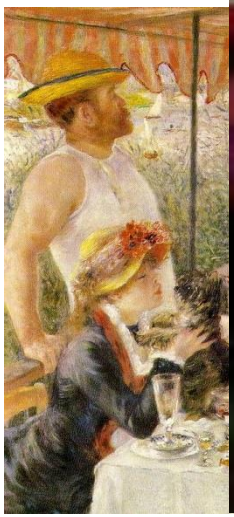
<

MODALITÀ DI ASSUNZIONE

prev

prev

prevale



…il Binge Drinking

• **Fenomeno in drammatico incremento con uso-abuso di bevande alcoliche nel fine settimana con modalità del binge drinking*, in particolare negli adolescenti nella fascia a rischio 14-19 anni e nel sesso femminile**

*** Binge Drinking: intake di più di 4-5 drinks in unica occasione e in breve tempo**

SCIENTIFIC REPORTS

Correction: Author Correction

nature SCIENTIFIC REPORTS

Binge Drinking among adolescents is related to the development of Alcohol Use Disorders: results from a Cross-Sectional Study

Received: 11 August 2017
Accepted: 9 July 2018
Published online: 22 August 2018

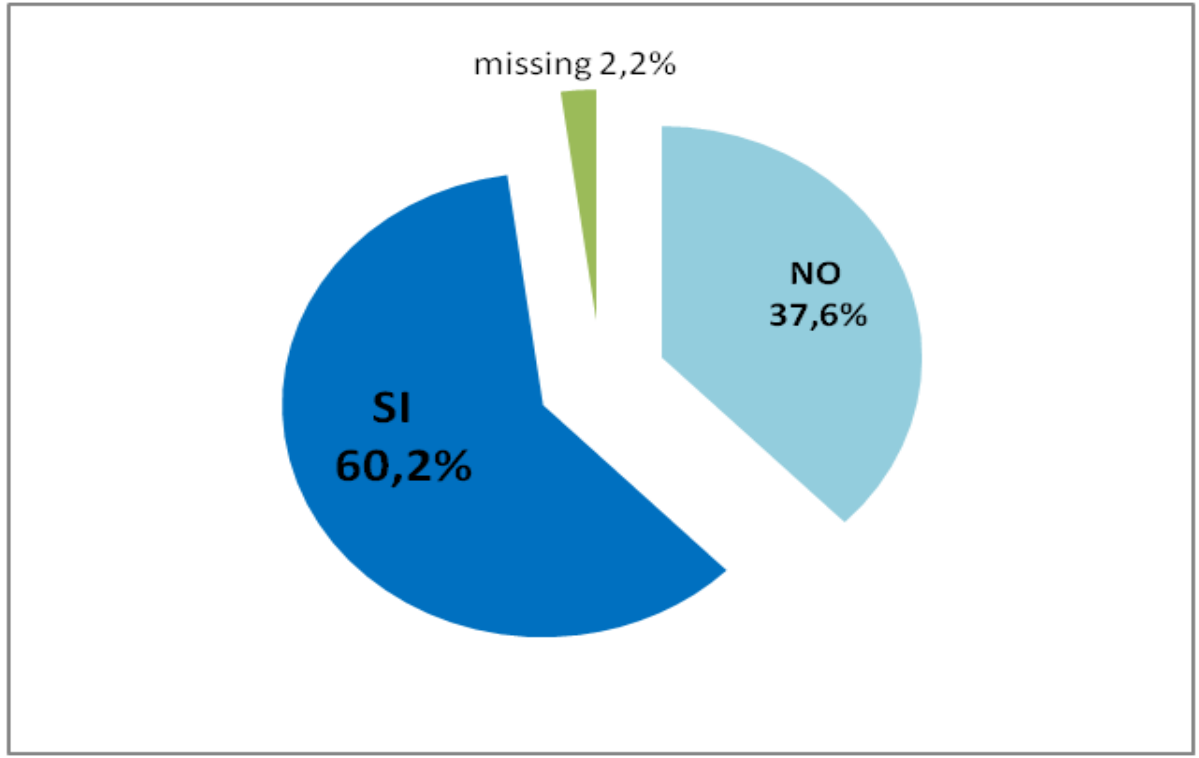
Giovanni Addolorato[1,2], Gabriele A. Vassallo[1,2], Giulio Antonelli[3], Mariangela Antonelli[1,2], Claudia Tarli[1,2], Antonio Mirijello[4], Adwoa Agyei-Nkansah[5], Maria C. Mentella[1], Daniele Ferrarese[1], Vincenzina Mora[1], Marco Barbàra[6], Marcello Maida[6], Calogero Cammà[6], Antonio Gasbarrini[1] & Alcohol Related Disease Consortium*

Binge drinking (BD) is a common pattern of alcohol consumption among adolescents. At present few data are available on the possible relationship between BD and alcohol use disorders (AUD) in adolescents. The aim of this study was to assess the prevalence of BD and relationship between BD behavior and AUD among adolescents. A total of 2704 students attending 10 purposively selected high schools from three Italian provinces were surveyed. Questionnaires regarding socio-demographic data, pattern and amount of alcohol intake, smoking habits, use of illicit drugs, and physical activity were administered. AUD and affective disorders were also evaluated. Alcohol intake was reported by 2126 participants; 1278 reported at least one episode BD in the last year and 715 in the last month. A diagnosis of AUD was made in 165 adolescents. The prevalence of AUD was higher in adolescents that reported BD behavior than in those that did not report BD (11.6% vs 0.9%, respectively; $p < 0.0001$). Logistic regression showed a positive relationship between a diagnosis of AUD and BD behavior (OR 9.6; 95% CI 4.7–22·9; $p < 0.0001$). In conclusion alcohol consumption with the pattern of BD among adolescents is highly related to development of AUD.

Risultati

Binge Drinking:

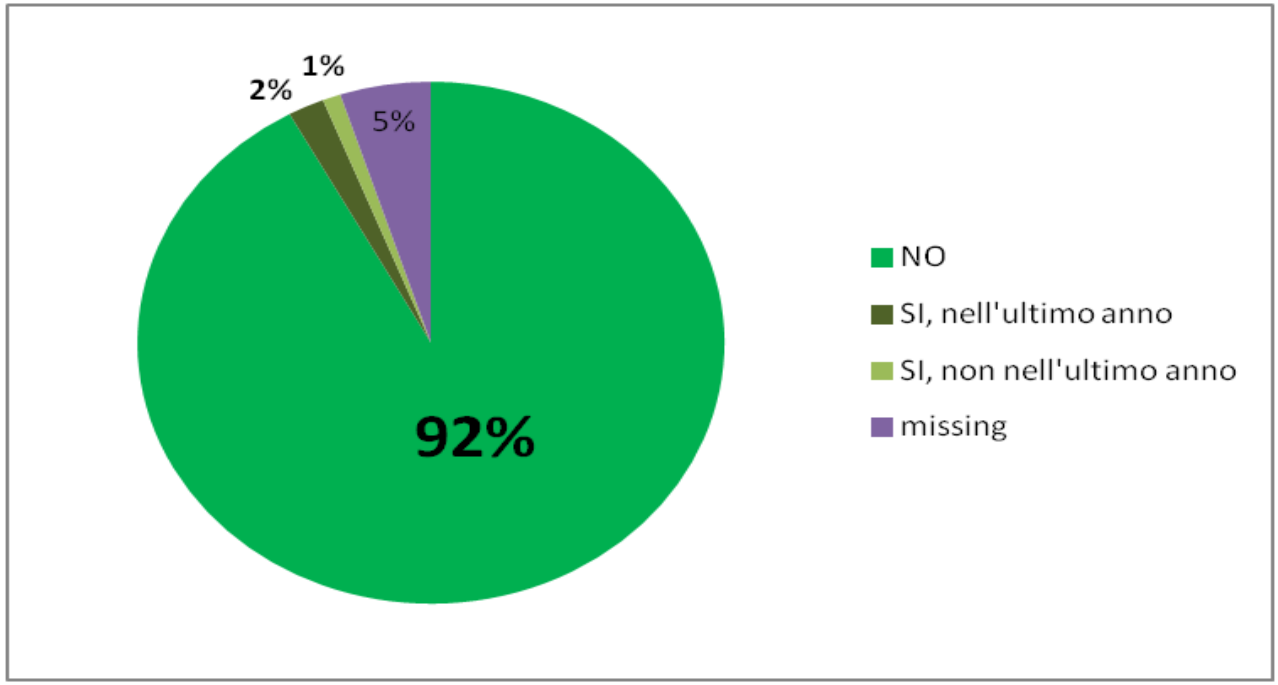
Negli ultimi 12 mesi ti è capitato di consumare ***5 bicchieri o più in un'unica occasione...***



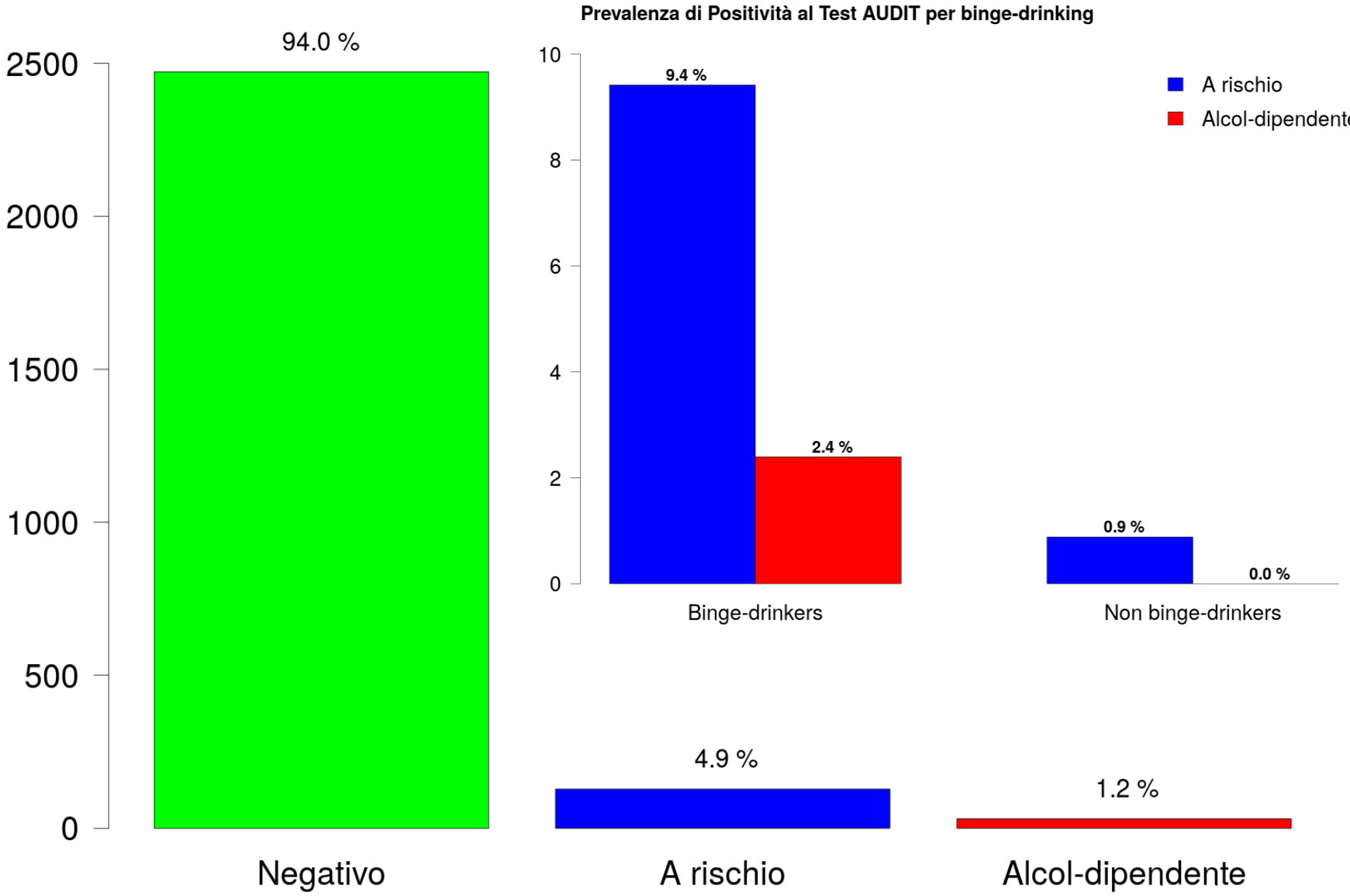
ciononostante…

Risultati

Un parente, un amico, un medico o altro operatore sanitario si sono occupati del tuo bere o ti hanno suggerito di non farlo e/o di smettere?

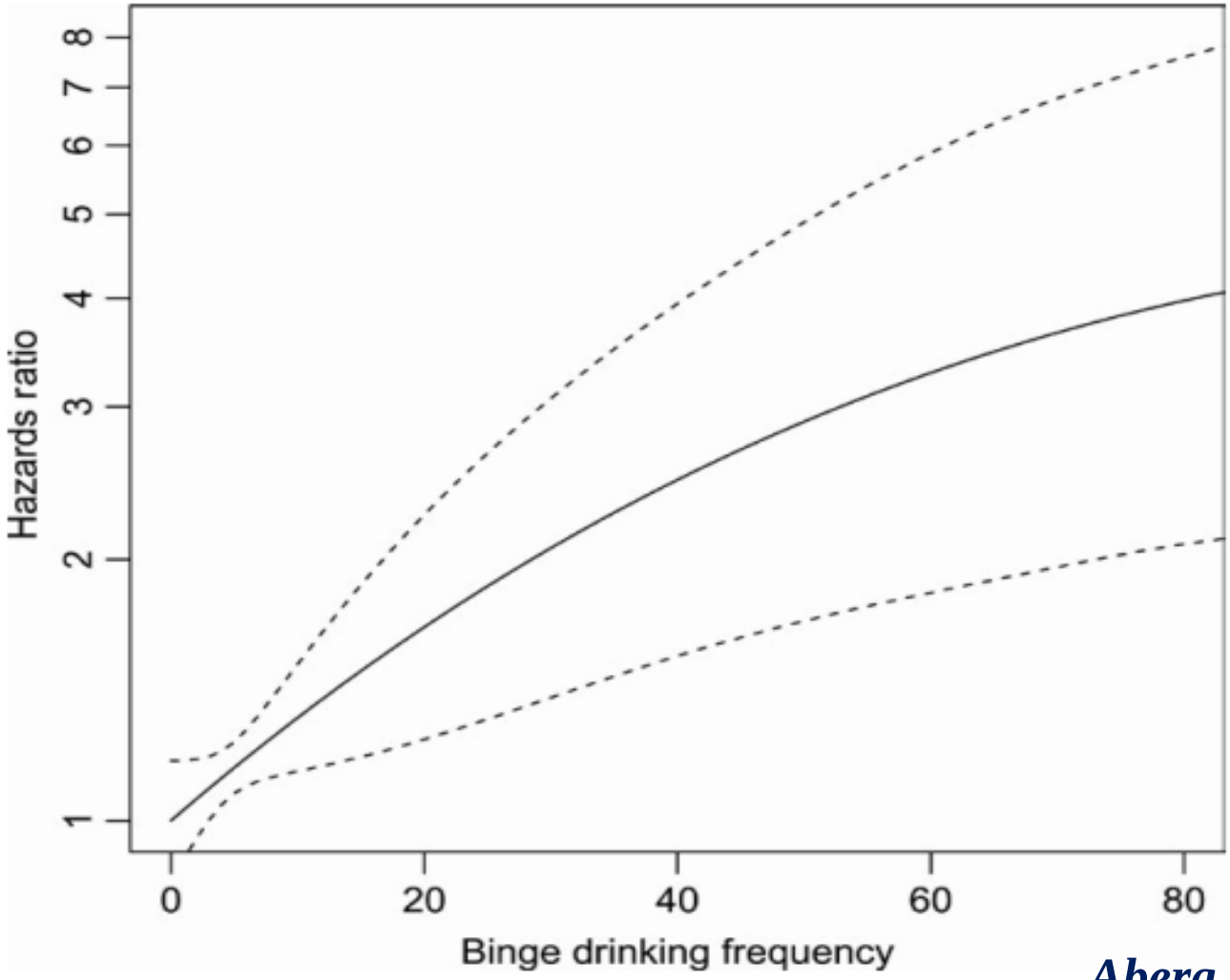


AUDIT Test Score



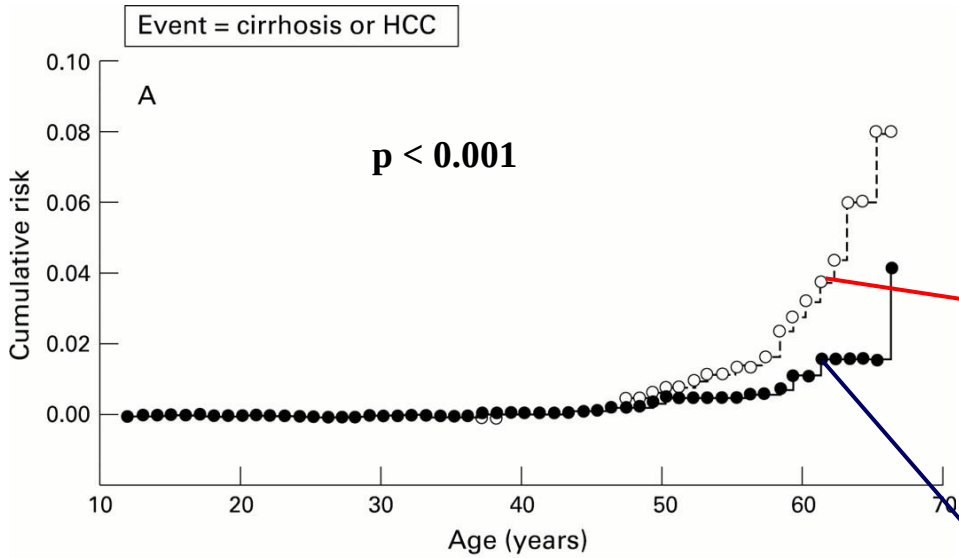
Binge drinking and liver disease

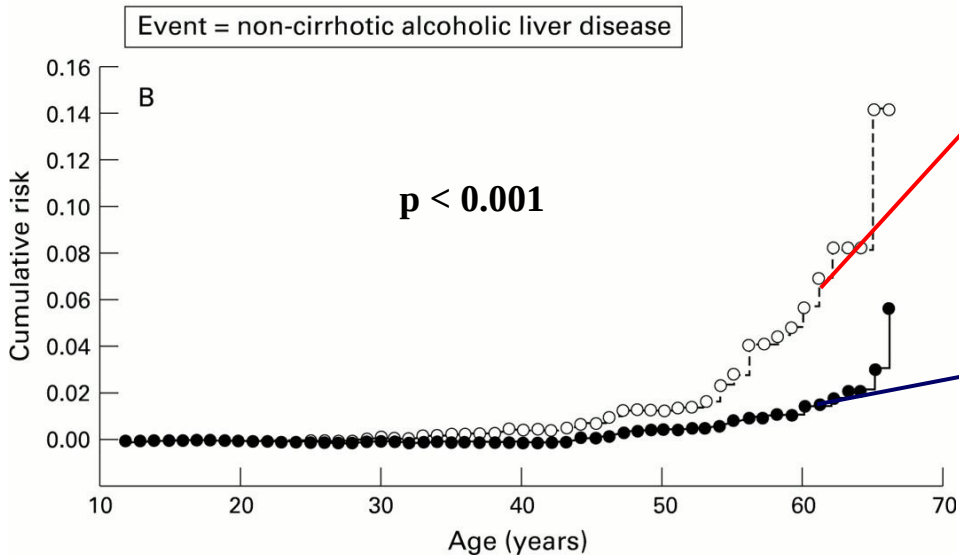
Association between number of binge drinking episodes/year and risk for decompensated liver disease



Aberg et al. Liver Int. 2017

ALCOL E FEGATO
MODALITÀ DI ASSUNZIONE





Assunzione prolungata di bevande alcoliche
> 30 g/die

FUORI DEI PASTI

SOLO AI PASTI

Bellentani et al, Gut 1997

FUORI PASTO: IN AUMENTO

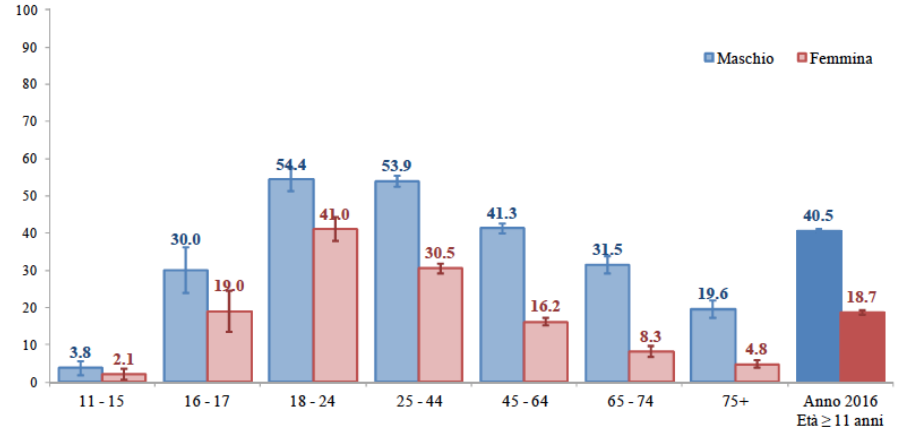


Figura I.6 Prevalenza (%) di consumatori di vino o alcolici fuori pasto per genere ed età (2016)

Fonte: Elaborazioni ONA-ISS e WHO CC Research on Alcohol su dati dell'Indagine ISTAT Multiscopo sulle famiglie

L'analisi del trend dei consumatori di vino o alcolici fuori pasto mostra che, per entrambi i generi, è aumentata la prevalenza dei consumatori, sia rispetto all'anno 2007 (M=+2,9 p.p.; F=4,2 p.p.) che rispetto alla precedente rilevazione (M=+1,6 p.p.; F=+0,9 p.p.). (**Figura I.7**).

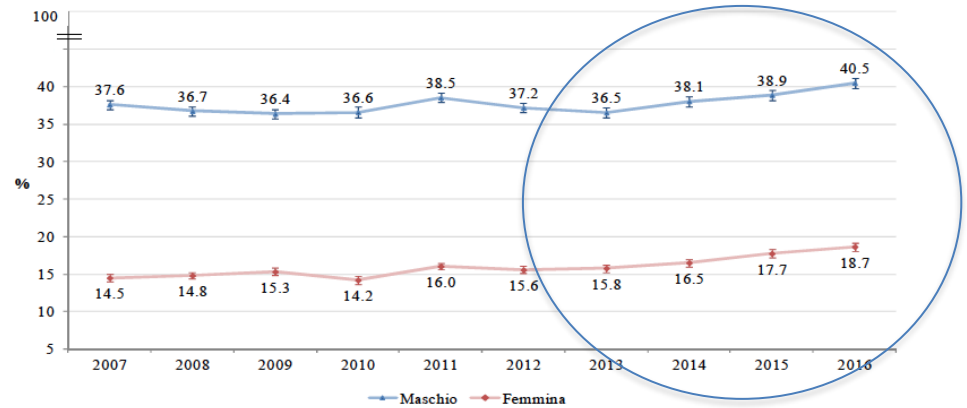
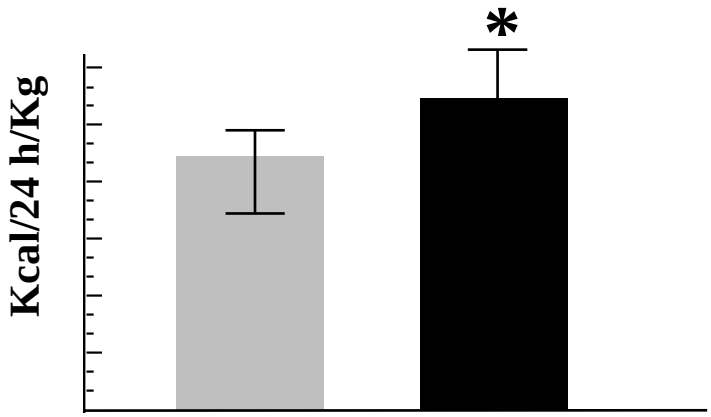


Figura I.7 Prevalenza (%) di consumatori di vino o alcolici fuori pasto (2007-2016)

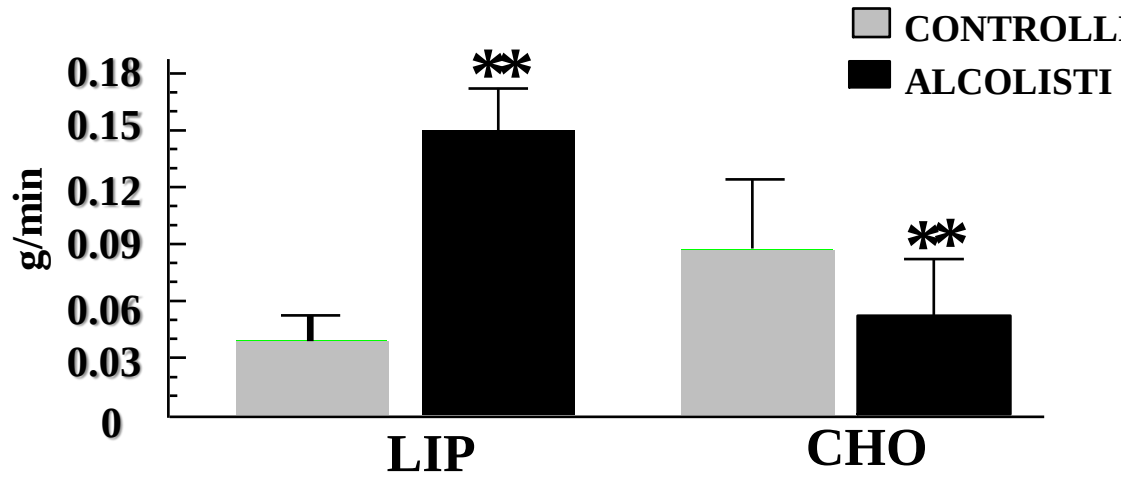
Fonte: Elaborazioni ONA-ISS e WHO CC Research on Alcohol su dati dell'Indagine ISTAT Multiscopo sulle famiglie

ALCOL, DANNO METABOLICO E NUTRIZIONE

Spesa energetica/kg peso corporeo

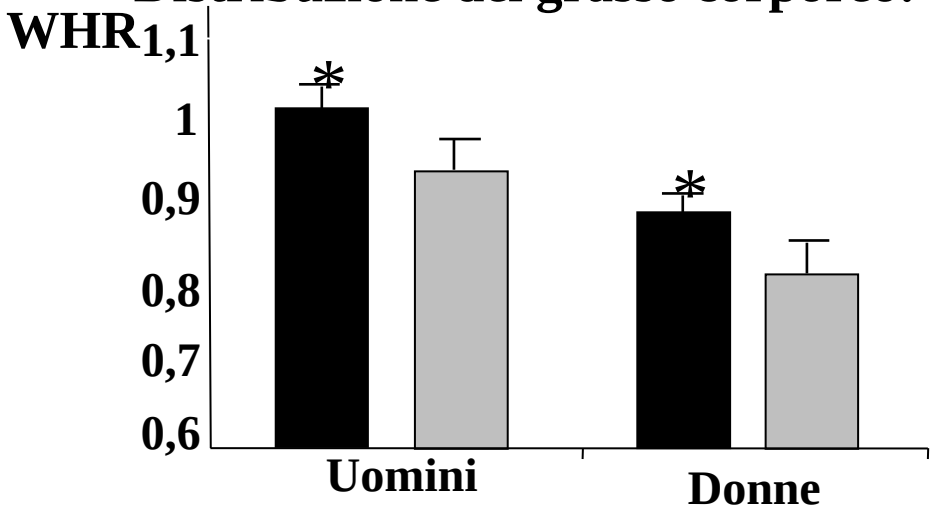


Velocità di ossidazione dei substrati



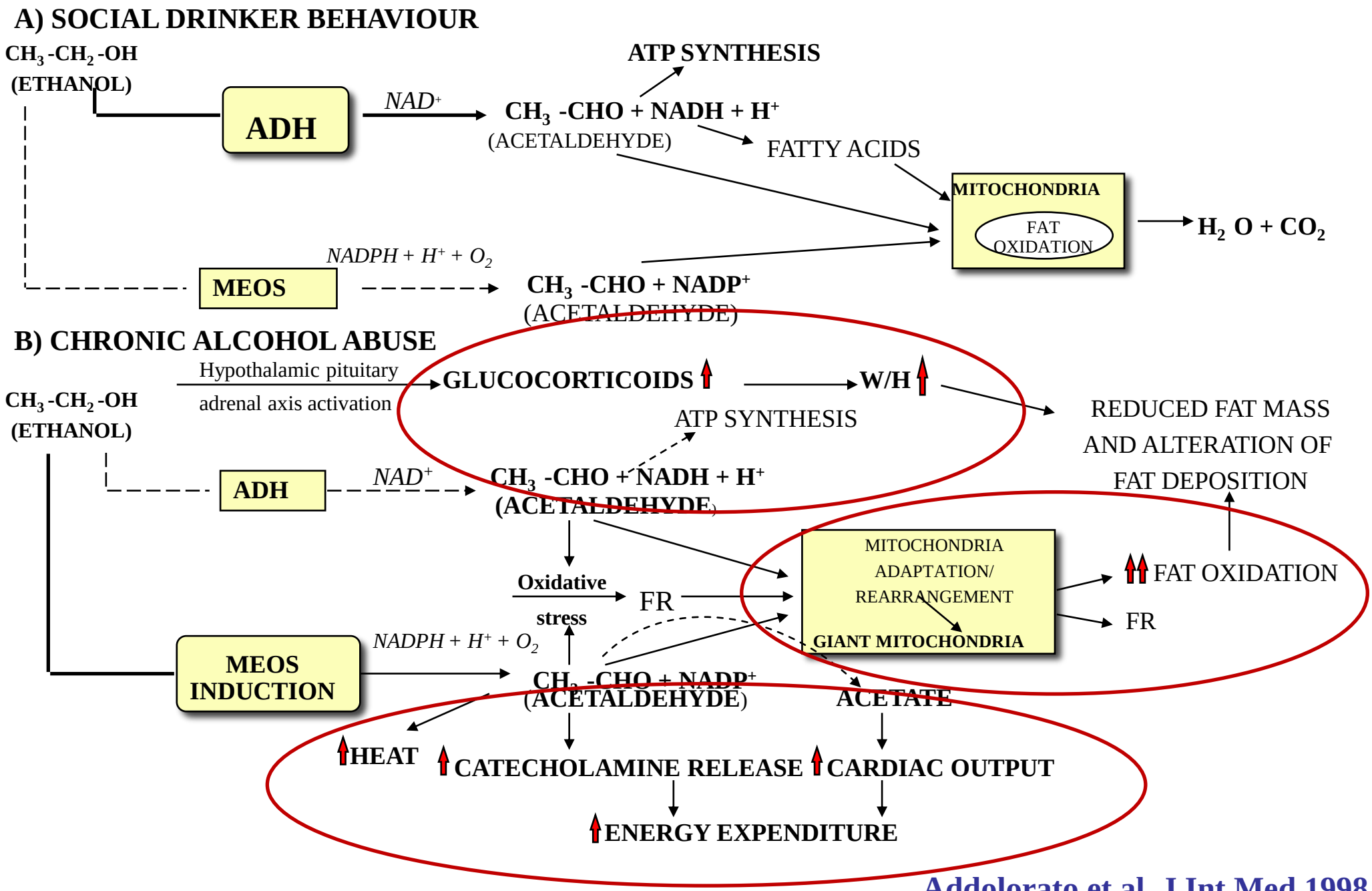
Addolorato et al, Am J Gastroenterol 2000

Distribuzione del grasso corporeo: WHR



* P < 0.01
** P < 0.001

Addolorato et al, J Internal Med 1998



Addolorato et al. J Int Med 1998

Alcoholic Steatohepatitis (ASH)

Predisposition

↓ 1st hit

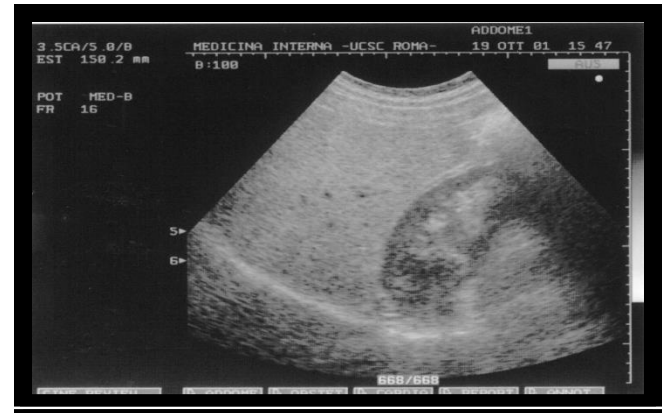
Fatty Liver

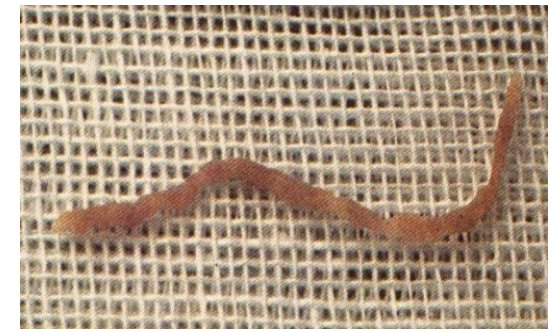
↓ 2nd hit

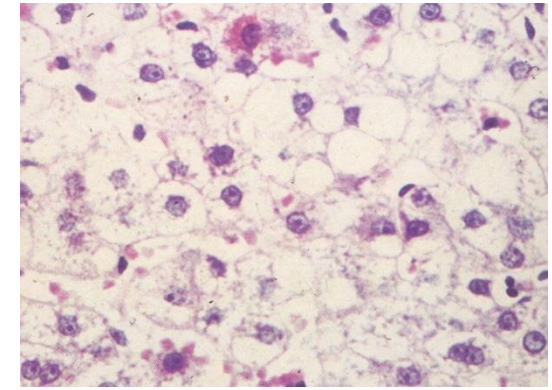
ASH

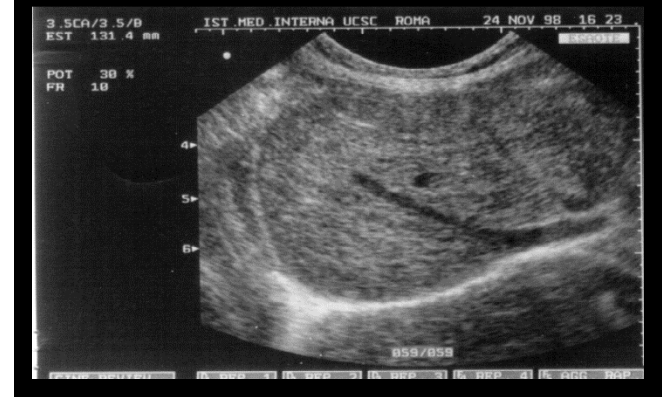
↓ ↑ Fibrosis

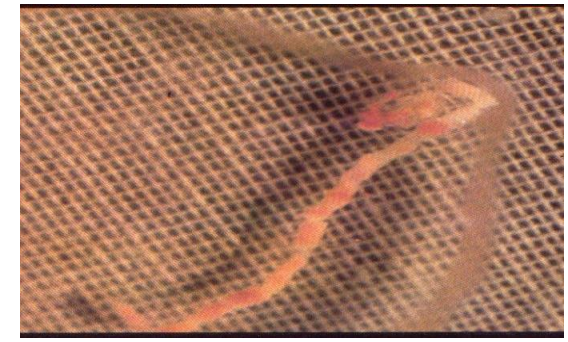
CIRRHOSIS





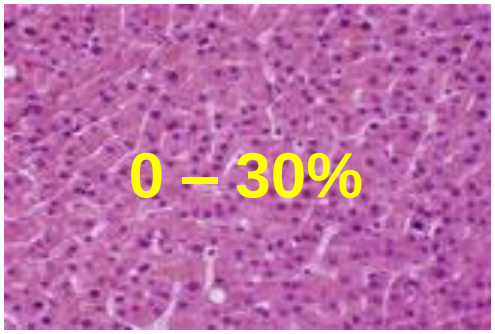




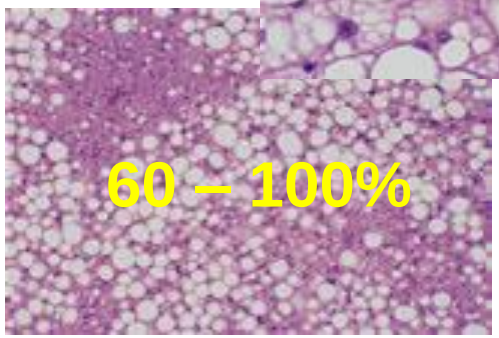


ALCOL E FEGATO

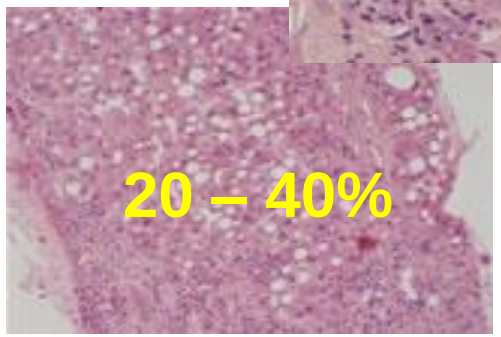
DANNO EPATICO



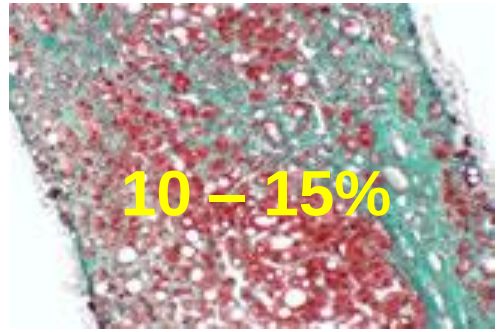
Fegato normale



Steatosi epatica



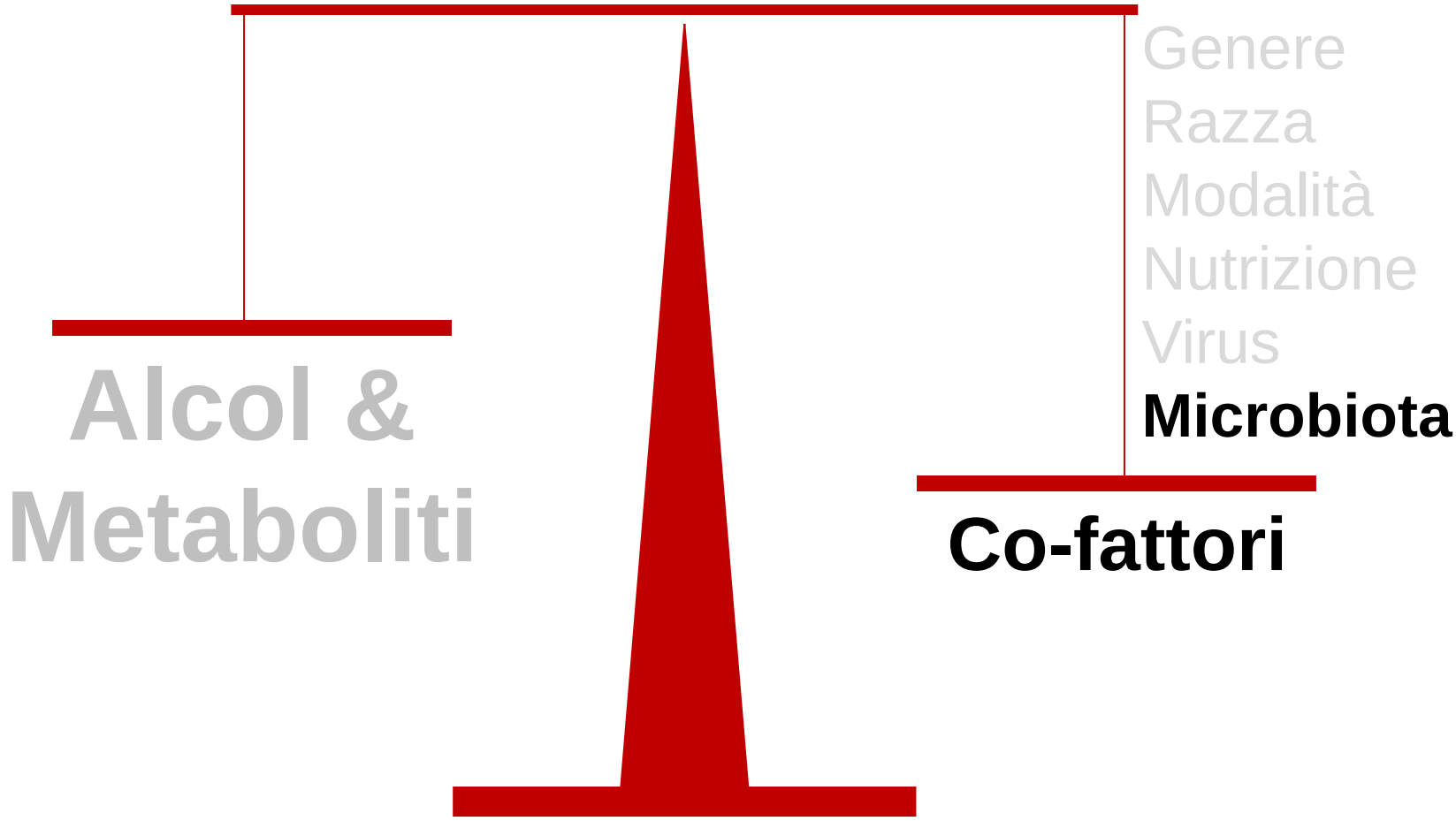
Steatoepatite



Fibrosi/Cirrosi

ALCOL E FEGATO

PATOGENESI DEL DANNO



DIET & LIFESTYLE

AGE

ALCOHOL

ORIGIN

Microbiota

AP&T Alimentary Pharmacology and Therapeutics

Review article: alcohol and gut microbiota - the possible role of gut microbiota modulation in the treatment of alcoholic liver disease

G. Vassallo[a], A. Mirijello[a], A. Ferrulli, M. Antonelli, R. Landolfi, A. Gasbarrini & G. Addolorato

Methods

Articles were identified using the PubMed database with the search terms 'Alcohol', 'Gut Microbiota', 'Alcoholic liver disease', 'Probiotic', 'Prebiotic', 'Symbiotic' and 'Antibiotic'. English-language articles were screened for relevance. Full review of publications for the relevant studies was conducted, including additional publications that were identified from individual article reference lists.

Results

Alcohol abuse induces changes in the composition of gut microbiota, although the exact mechanism for this alteration is not well known. The translocation of bacterial products into the portal blood appears to play a key role in alcohol-induced liver damage. Several studies show that the modulation of gut microbiota seem to be a promising strategy to reduce alcohol-induced liver injury.

Aliment Pharmacol Ther 2015; 41: 917–927

Colonic microbiome is altered in patients with AUD

Authors	Number of patients enrolled	Type of sample	Method	Results
Hauge *et al.*[29]	22 alcoholic patients 12 control patients	Gastric and duodenal biopsies	Gastric and duodenal biopsies were taken for tissue pathology, quantitative and qualitative anaerobic and aerobic bacteriological culture and for culture of *Helicobacter pylori* (antral biopsies)	There were signs of gastritis by endoscopy in 64% of alcoholic patients and in 58% of the controls Significantly more bacteria, dominated by Gram-positive aerobic cocci, were present in the gastric biopsies of alcoholic patients than in those of controls There were 2.6 times more bacteria in the duodenal biopsies of alcoholic patients than in those of the controls Bacterial overgrowth was found in the stomach in 90% of alcoholic patients and in 50% of controls
Buzás[31]	73 alcoholic patients 40 control patients	Gastric biopsies	Samples were collected using upper gastrointestinal endoscopy. Histological examination, microbial culture and direct miscoscopy were used to detect *Helicobacter pylori*	There was no correlation between severity of drinking and *Helicobater pylori* infection
Bhonchal *et al.*[37]	Not available	Duodenal biopsies	Duodenal (D2) biopsies were obtained by upper gastrointestinal endoscopy and processed immediately for microbiological analysis	Marked qualitative and quantitative alterations of small intestinal microflora was documented in alcoholic patients There was increased bacterial growth of both Gram-positive cocci and Gram-negative bacilli in the patients with alcoholic liver disease
Chen *et al.*[35]	12 alcoholic patients with alcoholic cirrhosis 24 healthy subjects	Faecal samples	The faecal microbial communities was analysed by way of 454 pyrosequencing of the 16S ribosomal RNA V3 region followed by real-time quantitative polymerase chain reaction	Community-wide changes of faecal microbiota in alcoholic patients with liver cirrhosis were observed compared with healthy controls The proportion of phylum Bacteroidetes was significantly reduced, whereas Proteobacteria and Fusobacteria were highly enriched in the cirrhosis group. Enterobacteriaceae, Veillonellaceae and Streptococcaceae were prevalent in patients with liver cirrhosis at the family level A positive correlation was observed between Child–Turcotte–Pugh score and Streptococcaceae. Lachnospiraceae decreased significantly in patients with liver cirrhosis and correlated negatively with Child–Turcotte–Pugh score
Mutlu *et al.*[34]	48 alcoholic patients 18 healthy subjects	Colonic biopsies	Colonic biopsy samples from subjects were analysed for microbiota composition using length heterogeneity PCR fingerprinting and multitag pyrosequencing	Altered colonic microbiome (dysbiosis) in alcoholic patients Alcoholic patients with dysbiosis had lower median abundances of Bacteroidetes and higher ones of Proteobacteria Correlation with high levels of serum endotoxin
Gabbard *et al.*[33]	196 patients	Expired air	Patients were underwent to lactulose breath test	Higher prevalence of bacterial overgrowth in alcohol consumers than in teetotalers Significantly lower rates of a positive lactulose breath in patients with a history of cholecystectomy Neither proton pump inhibitor use nor tobacco use was associated with a positive lactulose breath test
Bode *et al.*[27]	27 alcoholic patients 13 control patients	Jejunal juice	Samples of jejunal juice were aspirated in the fasting state and were analysed using conventional culture techniques	The mean number of aerobic and anaerobic microorganisms was higher in alcoholic patients Significant counts of bacteria obtained during anaerobic incubation were more frequent in the alcoholics than in the controls Coliform microorganisms were cultured much more frequently from the jejunal fluid of alcoholic patients The incidence of Gram-negative anaerobic bacteria and endospore-forming rods was higher in the aspirates from alcoholic patients In both groups, the number of microorganisms in jejunal fluid correlated closely with the pH found in the gastric juice No correlation was found between the numbers or types of microorganisms in the jejunum and the type or degree of liver disease in alcoholic patients
Bode *et al.*[28]	45 alcoholic patients 60 control patients	Expired air	The hydrogen breath test has been used to investigate the incidence of small-bowel bacterial overgrowth	The percentage of cases with bacterial overgrowth in the group of patients with alcoholic liver disease was almost three times that of controls not abusing alcohol No significant difference in the incidence of bacterial overgrowth among alcoholic patients with cirrhosis and alcoholic patients without cirrhosis Among patients with alcoholic liver disease, the mouth-to-caecum transit time was prolonged by 21.5% in comparison with controls not abusing alcohol
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Casafont Morencos *et al.*[32]	89 alcoholic patients with alcoholic cirrhosis 40 control patients	Expired air	Bacterial overgrowth was measured by breath test after ingestion of glucose	Intestinal bacterial overgrowth was documented in the 30.3% of patients with alcoholic cirrhosis and in none of healthy subjects The prevalence of intestinal bacterial overgrowth was significantly higher in cirrhotic patients with ascites than in those with no evidence of ascites and among patients with Child–Pugh class C than in patients with a class A or B The prevalence of spontaneous bacterial peritonitis was significantly higher in patients who had intestinal bacterial overgrowth than in patients who did not

Vassallo et al, AP&T 2015

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Mutlu *et al.*[34]	48 alcoholic patients 18 healthy subjects	Colonic biopsies	Colonic biopsy samples from subjects were analysed for microbiota composition using length heterogeneity PCR fingerprinting and multitag pyrosequencing	Altered colonic microbiome (dysbiosis) in alcoholic patients Alcoholic patients with dysbiosis had lower median abundances of Bacteroidetes and higher ones of Proteobacteria Correlation with high levels of serum endotoxin
Gabbard *et al.*[33]	196 patients	Expired air	Patients were underwent to lactulose breath test	Higher prevalence of bacterial overgrowth in alcohol consumers than in teetotalers Significantly lower rates of a positive lactulose breath in patients with a history of cholecystectomy Neither proton pump inhibitor use nor tobacco use was associated with a positive lactulose breath test
Bode *et al.*[27]	27 alcoholic patients 13 control patients	Jejunal juice	Samples of jejunal juice were aspirated in the fasting state and were analysed using conventional culture techniques	The mean number of aerobic and anaerobic microorganisms was higher in alcoholic patients Significant counts of bacteria obtained during anaerobic incubation were more frequent in the alcoholics than in the controls Coliform microorganisms were cultured much more frequently from the jejunal fluid of alcoholic patients The incidence of Gram-negative anaerobic bacteria and endospore-forming rods was higher in the aspirates from alcoholic patients In both groups, the number of microorganisms in jejunal fluid correlated closely with the pH found in the gastric juice No correlation was found between the numbers or types of microorganisms in the jejunum and the type or degree of liver disease in alcoholic patients
Bode *et al.*[28]	45 alcoholic patients 60 control patients	Expired air	The hydrogen breath test has been used to investigate the incidence of small-bowel bacterial overgrowth	The percentage of cases with bacterial overgrowth in the group of patients with alcoholic liver disease was almost three times that of controls not abusing alcohol No significant difference in the incidence of bacterial overgrowth among alcoholic patients with cirrhosis and alcoholic patients without cirrhosis Among patients with alcoholic liver disease, the mouth-to-caecum transit time was prolonged by 21.5% in comparison with controls not abusing alcohol
Hauge *et al.*[30]	24 alcoholic patients 12 control patients	Gastric biopsies	Samples were collected using upper gastrointestinal endoscopy. Histological examination, microbial culture and direct microscopy were used to detect *Helicobacter pylori*	*Helicobater pylori* infection was not more frequent in alcoholic patients than in controls
Casafont Morencos *et al.*[32]	89 alcoholic patients with alcoholic cirrhosis 40 control patients	Expired air	Bacterial overgrowth was measured by breath test after ingestion of glucose	Intestinal bacterial overgrowth was documented in the 30.3% of patients with alcoholic cirrhosis and in none of healthy subjects The prevalence of intestinal bacterial overgrowth was significantly higher in cirrhotic patients with ascites than in those with no evidence of ascites and among patients with Child–Pugh class C than in patients with a class A or B The prevalence of spontaneous bacterial peritonitis was significantly higher in patients who had intestinal bacterial overgrowth than in patients who did not

Vassallo et al, AP&T 2015

Colonic microbiome is altered in patients with AUD

Authors	Number of patients enrolled	Type of sample	Method	Results
Hauge *et al.*[29]	22 alcoholic patients 12 control patients	Gastric and duodenal biopsies	Gastric and duodenal biopsies were taken for tissue pathology, quantitative and qualitative anaerobic and aerobic bacteriological culture and for culture of *Helicobacter pylori* (antral biopsies)	There were signs of gastritis by endoscopy in 64% of alcoholic patients and in 58% of the controls Significantly more bacteria, dominated by Gram-positive aerobic cocci, were present in the gastric biopsies of alcoholic patients than in those of controls There were 2.6 times more bacteria in the duodenal biopsies of alcoholic patients than in those of the controls Bacterial overgrowth was found in the stomach in 90% of alcoholic patients and in 50% of controls
Buzás[31]	73 alcoholic patients 40 control patients	Gastric biopsies	Samples were collected using upper gastrointestinal endoscopy. Histological examination, microbial culture and direct miscoscopy were used to detect *Helicobacter pylori*	There was no correlation between severity of drinking and *Helicobater pylori* infection
Bhonchal *et al.*[37]	Not available	Duodenal biopsies	Duodenal (D2) biopsies were obtained by upper gastrointestinal endoscopy and processed immediately for microbiological analysis	Marked qualitative and quantitative alterations of small intestinal microflora was documented in alcoholic patients There was increased bacterial growth of both Gram-positive cocci and Gram-negative bacilli in the patients with alcoholic liver disease
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Vassallo et al, AP&T 2015

ORIGINAL ARTICLE

Liver INTERNATIONAL WILEY

Gut microbiota compositional and functional fingerprint in patients with alcohol use disorder and alcohol-associated liver disease

Giovanni Addolorato[1,2] | Francesca R. Ponziani[3] | Tommaso Dionisi[2] | Carolina Mosoni[2] | Gabriele A. Vassallo[4] | Luisa Sestito[2] | Valentina Petito[3] | Anna Picca[5] | Emanuele Marzetti[5] | Claudia Tarli[2] | Antonio Mirijello[6] | Maria Assunta Zocco[3] | Loris R. Lopetuso[3] | Mariangela Antonelli[2] | Maria M. Rando[2] | Francesco Paroni Sterbini[7] | Brunella Posteraro[3,8] | Maurizio Sanguinetti[7,8] | Antonio Gasbarrini[1,3]

Methods: This study included 36 AUD patients (14 with cirrhosis) who were active drinkers and an equal number of matched controls. Stool microbial composition, serum levels of lipopolysaccharide, cytokines/chemokines and gut microbiota functional profile were assessed.

Conclusions: AUD patients present a specific gut microbial fingerprint, associated with increased endotoxaemia, systemic inflammatory status and functional alterations that may be involved in the progression of the AALD and in the pathogenesis of AUD.

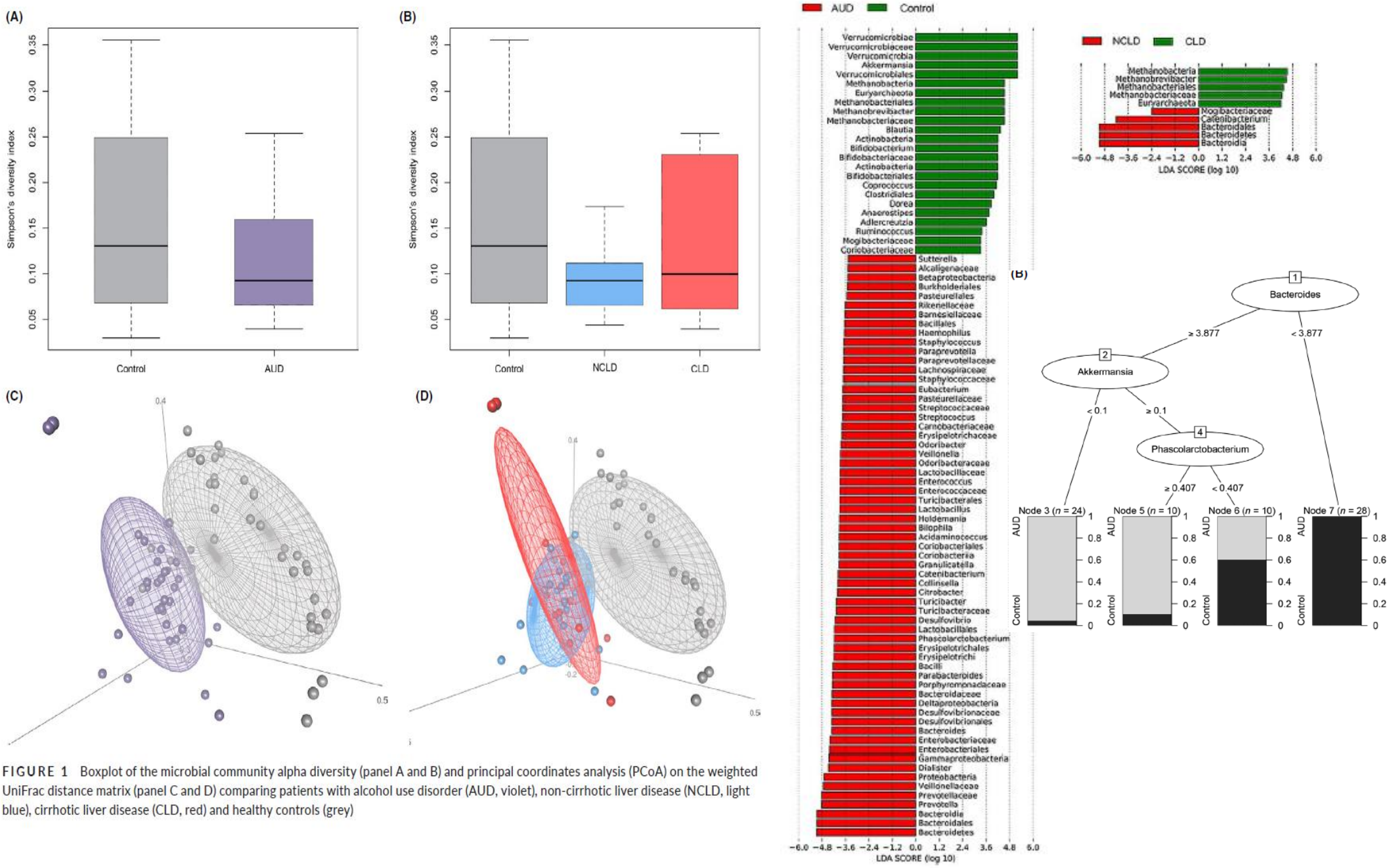
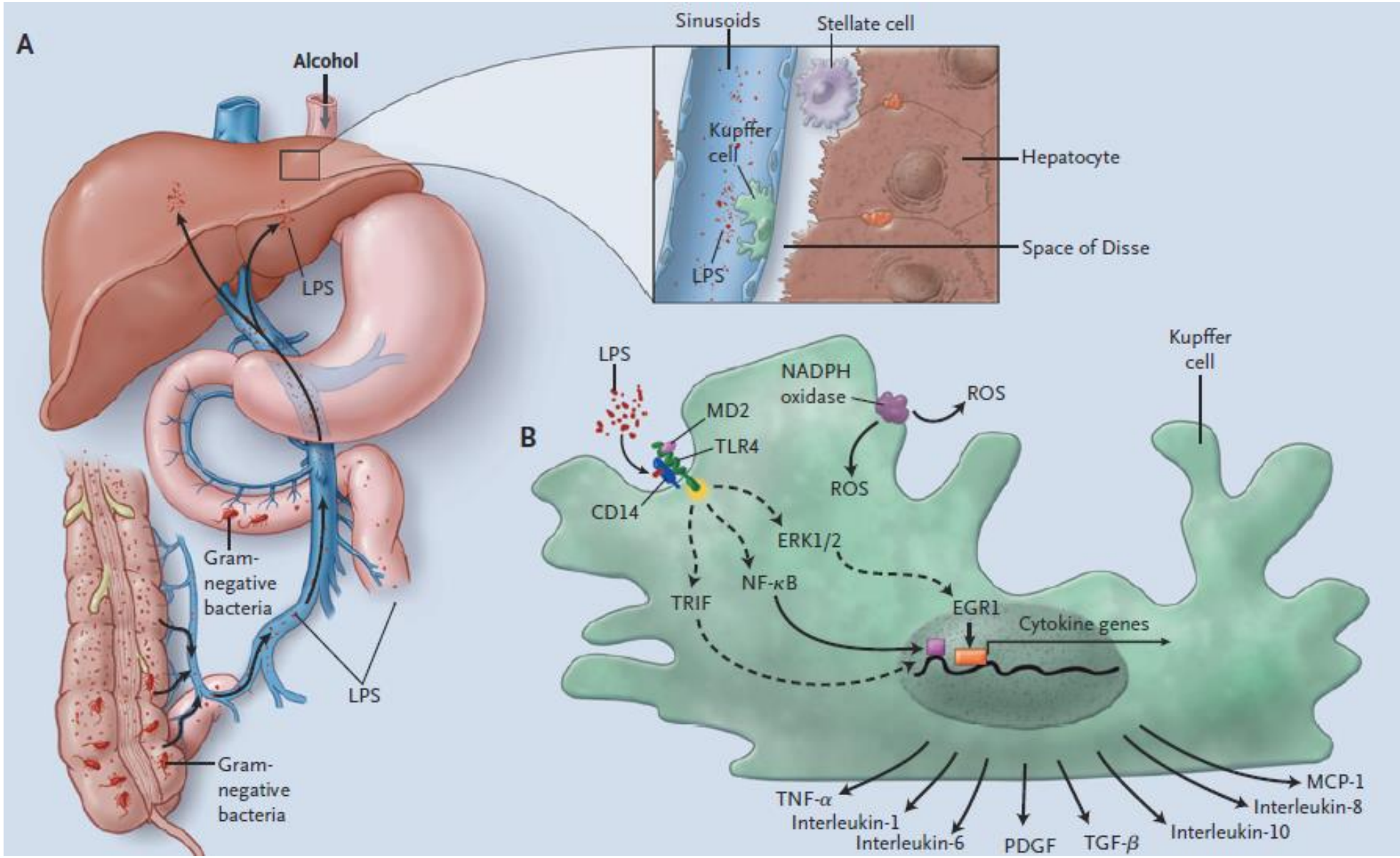


FIGURE 1 Boxplot of the microbial community alpha diversity (panel A and B) and principal coordinates analysis (PCoA) on the weighted UniFrac distance matrix (panel C and D) comparing patients with alcohol use disorder (AUD, violet), non-cirrhotic liver disease (NCLD, light blue), cirrhotic liver disease (CLD, red) and healthy controls (grey)

Interaction between gut microbiota and liver damage



Lucey MR et al, N Engl J Med 2009

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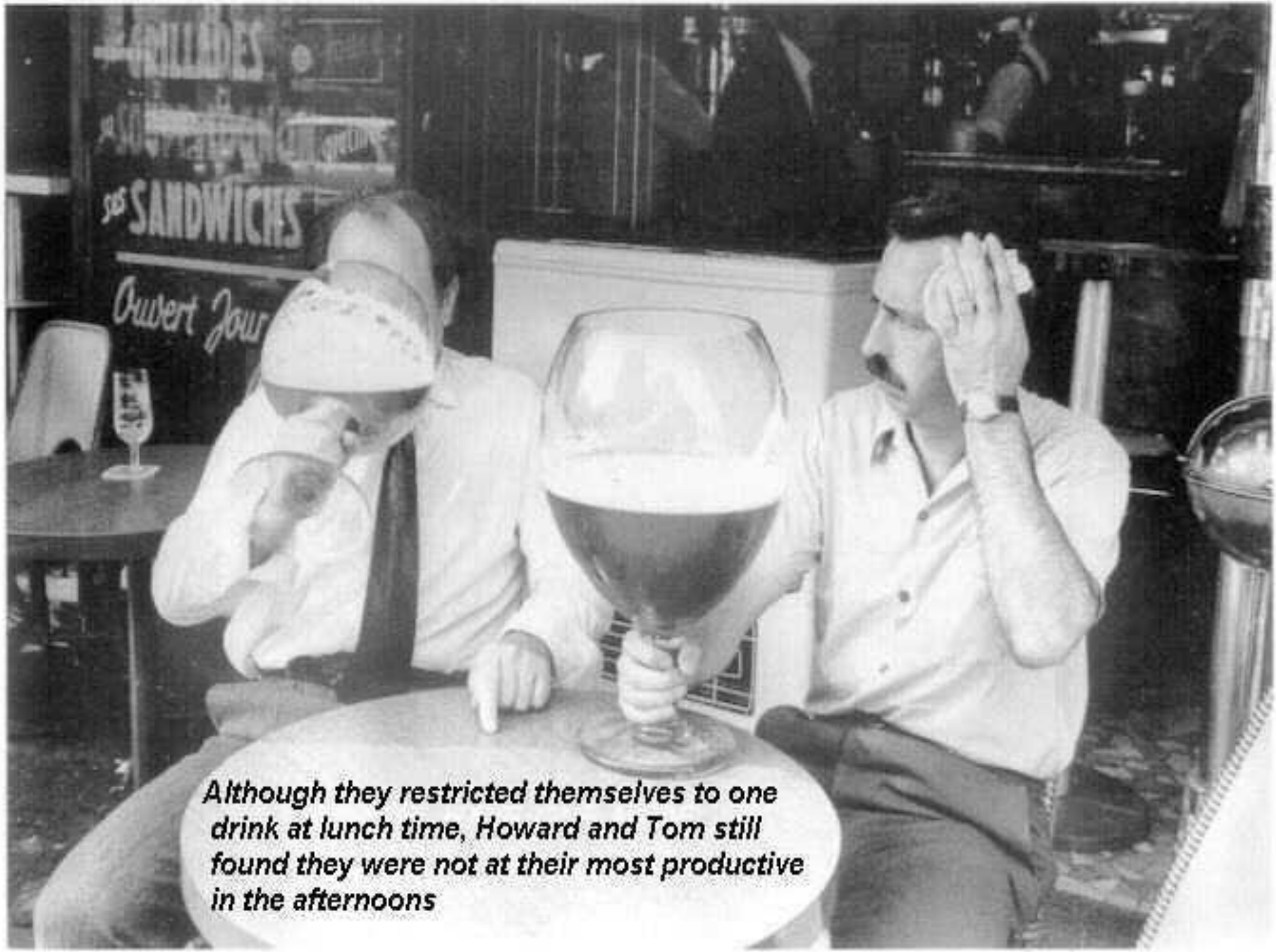

L. Leggi
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Treatment of Alcohol-Associated Liver Disease: The Basics

"Hundreds of years of medical progress, and all you can tell me to do is drink less?"

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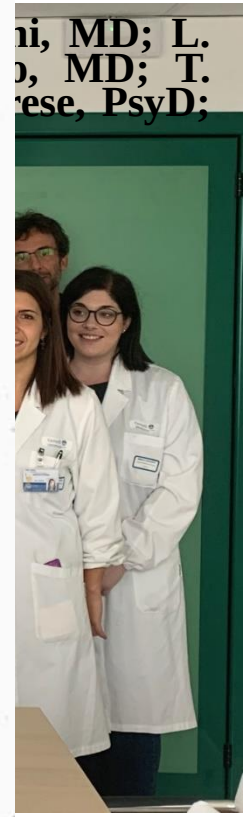

Thank you for your attention