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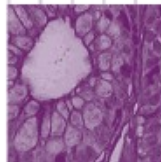
Activities and commitment of the National Institute of Health in the fight against cancer

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ALCOHOL AND TUMORS.

Emanuele Scafato, Alessandra Rossi, Silvia Ghirini, Lucia Galluzzo, Sonia Martire, Lucilla Di Pasquale, Riccardo Scipione, Nicola Parisi, Claudia Gandin
National Center for Epidemiology, Surveillance and Health Promotion, Istituto Superiore di Sanità, Rome

Introduction

In recent years, biological and epidemiological data have been highlighted on which a consensus on alcohol-related carcinogenesis recordable at the level of almost all organs has been achieved. In 2007, the estimate of alcohol-related mortality for Italy showed that 4.4 percent of deaths among men and 2.5 percent among women were related to alcohol consumption, for a total of more than 20,000 deaths that were partially or totally avoidable in the face of correct drinking attitudes. Risky or harmful alcohol consumption, exceeding the Nutritional Guidelines, is now referable to 25% of the male population and about 7.3% of the female population over 11 years of age leading to significant clinical, family and social problems.

The effects of alcohol can be traced and assimilated to those of other drugs: induction of physical and mental dependence, addiction, and behavioral disturbances found at the individual level, among which relevant is compulsivity, *craving*, and at the social level.

The organs damaged by alcohol abuse are numerous, including: heart and vessels, liver, reproductive system, esophagus, stomach, intestines, pancreas, and central nervous system. The pathological conditions most affected by alcohol abuse are: hepatitis, cirrhosis of the liver, reduced fertility, cancer of the esophagus, oropharynx, rectum colon, larynx, liver, breast, esophageal varices. It should also not be forgotten that beyond the possible diseases, alcohol is the leading cause of death from car accidents (1) among young people up to 24 years old with 46% and 18% of cases among men and women respectively.

In this original contribution carried out as part of the epidemiological monitoring responsibilities of the National Alcohol Observatory of the National Center for Epidemiology, Surveillance and Health Promotion, CNESPS, the results of epidemiological studies of alcohol-related mortality, through the estimation of Alcohol Attributable *Fraction* (AAF) and *Alcohol Attributable Death* (AAD), for cancers are described and the results in the population are analyzed. ISTAT, Multiscope-Aspects of Everyday Life data from 2009 and ISTAT mortality data from 2008 were used to assess the impact of alcohol use on health.

Development status

Methodology

The WHO (2) identifies about 60 alcohol-related diseases; risk occurs not only in the face of abuse, but also of simple consumption. The analysis that follows adopts a standardized European and international methodology developed to estimate the effects that t h e use and abuse of alcoholic beverages can lead to and that, in this specific case, was applied to assess the causal impact o f alcohol on mortality in some of the most frequent cancers, particularly those for which deaths from

occurrence in the first aero-digestive tract and liver. Three variables are needed to arrive at the estimate of alcohol-attributable mortality (3) in Italy, the processed data of which are g i v e n b e l o w .

The prevalences of consumers by consumption category were worked out through appropriate algorithms based on data from the ISTAT Multiscopo survey, Aspects of Daily Life 2009, with data referring to the year 2008. Given that the relationship between alcohol consumption and the occurrence of diseases is, in most cases, dose-dependent (4), it is essential to identify the different categories of average daily consumption (Table 1) on the basis of which prevalences can be calculated.

Table 1. Categories of average daily alcohol consumption (g/day) by gender

Categories of consumption	Males	Females
Category 0 (Astemi or light drinkers)	(0-0.25) g/day	(0-0.25) g/day
Category 1	(0.25-40) g/day	(0.25-20) g/day
Category 2	(40-60) g/day	(20-40) g/day
Category 3	(60+) g/day	(40+) g/day

The prevalences of alcohol consumption in grams per day according t o gender and age (11-14, 15-29, 30-44, 45-59, 60-69, 70+) are shown in Figure 1.

T h e prevalences of alcohol users according to the four categories show strong gender differences, except for the class below the legal age (11-15). There are 24.2% teetotalers among men, 40.4% consumers in the 1st category, 28.9% consumers in the 2nd category, and 4.4% consumers in the 3rd category; among women 53.5% teetotalers, 36.8% for the 1st category, 6.4% and 1.3% for the 2nd and 3rd categories.

Deaths related to cancers in the ISTAT survey for t h e year 2008, were calculated according to the tenth revision of the International Classification of Diseases (ICD 10) (Table 2), according to the sex and age g r o u p s indicated before.
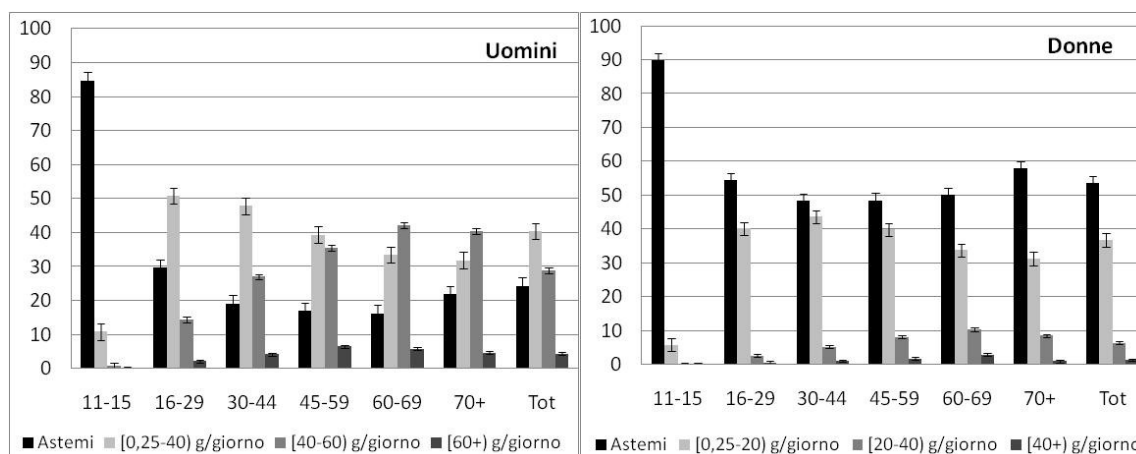

Figure 1. Prevalences of alcohol users according to average daily consumption categories
Source: CNESPS National Alcohol Observatory and *WHO CC Research on Alcohol* elaborations on 2009 ISTAT multiscope data

Table 2. Causes of death according to ICD 10.

Causes of death	ICD 10
Malignant neoplasms	**C00-C97**
Oropharynx	C01-C06, C09-C10, C12-C14
Esophagus	C15
Colon rectum	C18-C21
Larynx	C32
Liver	C22
Mammella	C50
Benign tumors	**D00-D48**

The Relative Risks (RR) (Table 3) are those related to the systematic review of the international literature (5, 6).

The values express the ratio between the probability of developing a disease among subjects exposed t o alcohol (Category 1, Category 2, Category 3), and the probability of developing the same disease in case of abstention (Astemi or light drinkers). In a n u t s h e l l, numerous epidemiological studies have shown that the risk of developing cancer increases a s the amount of alcoholic beverage consumption increases. In the application of RRs, it should be pointed out t h a t, at the population level, up to the age of 29, the effects in terms of mortality on cancers, a classic example of chronic diseases for which a longer time is essential for t h e occurrence of the onset of the specific condition. For this reason, in adopting the RRs produced by epidemiological studies on which it seems congruous to base reliable estimates, 30 years should be considered as the baseline reference age.

Table 3. RR according to causes of death

Causes of death		Males				Females			
	Age	RR teetotalers 0	RR Cat 1	RR Cat 2	RR Cat 3	RR teetotalers 0	RR Cat 1	RR Cat 2	RR Cat 3
Malignant neoplasms									
Oropharynx	30+	1,00	1,45	1,85	5,39	1,00	1,45	1,85	5,39
Esophagus	30+	1,00	1,80	2,38	4,36	1,00	1,80	2,38	4,36
Colon rectum	30+	1,00	1,00	1,16	1,41	1,00	1,00	1,01	1,41
Larynx	30+	1,00	1,83	3,90	4,93	1,00	1,83	3,90	4,93
Liver	30+	1,00	1,45	3,03	3,60	1,00	1,45	3,03	3,60
Mammella	30-44					1,00	1,15	1,41	1,46
	45+					1,00	1,14	1,38	1,62
Benign tumors	30+	1,00	1,10	1,30	1,70	1,00	1,10	1,30	1,70

Results

Analyses were conducted separately for each sex, analyzing mortality in 2008 initially in the population as a whole (Table 4), then in the population divided by age group (Tables 5 and 6).

Table 4. *Alcohol Attributable Death* (AAD) and *Alcohol Attributable Fraction* (AAF)
according to individual malignancies and benign tumors, ICD10- 2008

		Total age > 15 years		
		AAD	**Deaths**	**AAF%**
Tumor of mouth and oropharynx	Males	543	1.506	36,0
	Females	119	586	20,4
Esophageal cancer	Males	577	1.333	43,3
	Females	123	440	28,0
Colorectal cancer	Males	100	9.869	1,0
	Females	-120	9.869	-1,2
Laryngeal cancer	Males	749	1.554	48,2
	Females	54	153	35,2
Liver cancer	Males	2.151	6.061	35,5
	Females	812	3.368	24,1
Breast cancer	Males	-	.-	-
	Females	761	12.164	6,3
Malignant neoplasms	Males	4.119	93.013	4,4
	Females	1.750	71.061	2,5
Benign tumors	Males	367	4.279	8,6
	Females	151	3.593	4,2
Malignant and benign tumors	Males	4.486	97.292	4,6
	Females	1.900	74.654	2,5

Source: CNESPS National Alcohol Observatory and WHO CC Research on Alcohol elaborations on ISTAT multiscope 2009 and DB mortality 2008 data.

Table 5. *Alcohol Attributable Death* (AAD) *Alcohol Attributable Fraction* (AAF) according
to malignancies, ICD10- 2008

	Age					
	15-29	**30-44**	**45-59**	**60-69**	**70+**	**Total**
Males						
(a) Alcohol-related deaths from malignant neoplasms.	0	53	622	1.164	2.279	4.119
(b) Total deaths from malignant neoplasms.	301	1.498	9.539	19.996	61.679	93.013
AAF% (a)/(b)	0,00%	3,50%	6,50%	5,80%	3,70%	4,40%
(c) Total deaths from malignant and benign tumors.	323	1560	9.779	20.576	65.054	97.292
AAF% (a)/(c)	0,00%	3,40%	6,40%	5,70%	3,50%	4,20%
Females						
(a) Alcohol-related deaths from malignant neoplasms.	0	46	249	355	1.099	1.750
(b) Total deaths from malignant neoplasms.	227	1.814	7.958	11.981	49.081	71.061
AAF% (a)/(b)	0,00%	2,60%	3,10%	3,00%	2,20%	2,50%
(c) Total deaths from malignant and benign tumors.	238	1.853	8.145	12.349	52.069	74.654
AAF% (a)/(c)	0,00%	2,50%	3,10%	2,90%	2,10%	2,30%

(a) AAD; (b) Malignant neoplasms; (c) Malignant and benign tumors.

Table 6. *Alcohol Attributable Death* (AAD) *Alcohol Attributable Fraction* (AAF) according to benign tumors, ICD10- 2008

	Age					
	15-29	30-44	45-59	60-69	70+	Total
Males						
(a) Alcohol-related deaths from benign tumors.	0	6	26	58	278	367
(d) Total deaths from benign tumors.	22	62	240	580	3.375	4.279
AAF% (a)/(d)	0,00%	8,90%	10,70%	10,10%	8,20%	8,60%
(c) Total deaths from malignant and benign tumors.	323	1.560	9.779	20.576	65.054	97.292
AAF% (a)/(c)	0,00%	0,40%	0,30%	0,30%	0,40%	0,40%
Females						
(a) Alcohol-related deaths from benign tumors.	0	2	10	20	118	151
(d) Total deaths from benign tumors.	11	39	187	368	2.988	3.593
AAF% (a)/(d)	0,00%	4,60%	5,60%	5,50%	4,00%	4,20%
(c) Total deaths from malignant and benign tumors.	238	1.853	8.145	12.349	52.069	74.654
AAF% (a)/(c)	0,00%	0,10%	0,10%	0,20%	0,20%	0,20%

(a) AAD; (b) Malignant neoplasms; (c) Malignant and benign tumors; (d) Benign tumors.

In this way, the *Alcohol Attributable Fraction* (AAF), which represents the percentage of the number of deaths attributable to exposure to the factor, and the *Alcohol Attributable Death* (AAD), which estimates the absolute number of deaths that could have been avoided if exposure to the factor had been zero, were estimated.

AAFs for each disease were calculated by combining alcohol exposure and RRs for each category of alcohol consumption.

In 2008, there were 6,386 alcohol-attributable deaths from *cancer*, including 4,486 deaths among men and 1,900 deaths among women, and 4,119 and 1,750 deaths between the two sexes from *malignancies*.

Alcohol is responsible for 4.4% and 2.5% of deaths from *malignant neoplasms*, male and female respectively. The rates of deaths from benign tumors due to alcohol consumption are 8.6% and 4.2% of deaths from benign tumors. Overall, 4.6 percent and 2.5 percent of all *malignant and benign cancers,* respectively, are attributable to alcohol for the two sexes, accounting for 3.7 percent of total *cancer* deaths (171,946, including 97,292 for males and 74,654 for females).

Deaths from *mouth and oropharynx cancer are* determined by alcohol consumption for 36.0% and 20.4% for males and females, respectively. In fact, the risk of developing this type of cancer increases significantly in drinkers of both sexes compared with the reference population consisting of "Astemi or light drinkers."

Esophageal cancers have alcohol-attributable fractions of 43.3% for males and 28.0% for females. *Esophageal cancers* are correlated with alcoholic beverage consumption, with a significant increase in risk. A higher risk has been shown for strong alcoholic beverages, such as hard liquor, than for beer or wine (7).

Colorectal cancer is the only disease affected to a small extent among men, and positively among women by alcohol consumption. The alcohol-attributable fractions are 1.0% for men and -1.2% for women.

The percentage of deaths from *laryngeal cancer* due to alcohol consumption is 48.2% and 35.2% for males and females, respectively. In fact, alcohol has about four and five times higher risk in the second and third categories of drinkers than in those in the reference category ("Astemi or light drinkers").

Alcohol consumption significantly increases the risk of death from *liver cancer* especially for men, who have an alcohol-related mortality rate of 35.5 percent, compared to women's rate of 24.1 percent. In fact, alcohol is recognized as an etiological factor of *liver cancer*.

The percentage of *breast cancer* deaths due to alcohol consumption is 6.3% for women. There is an increased risk of developing *breast cancer* among female alcohol drinkers, and some studies have shown a significant association of alcohol and breast cancer incidence, with a dose-effect proportionality. Since breast cancer is the most frequent cancer in women (12,164 deaths in 2008), even a non-high risk assumes considerable importance, both from a purely scientific point of view and from a public health and prevention perspective.

Malignant neoplasms, which contribute a total of 4.4 percent of male deaths and 2.5 percent of female deaths (a/b), experience a greater alcohol-related impact in the 45-59 and 60-69 age groups, with rates of 6.5 percent and 5.8 percent for males and 3.1 percent and 3.0 percent for females. Considering total cancer deaths (a/d), malignant neoplasms, which have alcohol-attributable rates of 4.2% and 2.3% for males and females respectively, are most affected by alcohol in the 45-59 and 60-69 age groups, with rates of 6.4% and 5.7% for males and 3.1% and 2.9% for females.

The rates of alcohol-attributable deaths from *benign cancers*, overall 8.6 percent and 4.2 percent (w/c), have high values in all ages, and especially among those aged 45-59 and 60-69. The alcohol-attributable fractions in the latter two age groups are 10.7% and 10.1% for males and 5.6% and 5.5% for females. The fractions of alcohol-attribuity to total cancer deaths (a/d) are 0.4% and 0.2% for males and 0.1% and 0.2% for females.

Conclusions

Alcohol causes about 60 different types of pathological conditions and health impairments, including injury, mental and behavioral disorder, cancer, gastrointestinal disease, cardiovascular disease, immunological disease, skeletal system disease, infertility, and prenatal problems. Epidemiological studies have shown that alcohol consumption can significantly increase the risk of developing cancer, particularly in the oral cavity, pharynx, larynx, esophagus, and liver.

Alcohol, use not just abuse, increases the risk of incurring such problems proportionally to the dose of alcohol ingested, with no apparent threshold effect.

Consumption of modest amounts of alcohol (10 g/day) reduces the risk o f heart disease, type 2 diabetes, and a few other conditions although at the same time the same modest amounts increase the risk of numerous diseases and cancers. It can be argued that the risk of alcohol-related death is the result of the balance between the increased risk of disease and injury and the modest reduction in the risk of coronary heart disease, particularly for women and the elderly; in essence, the impact on mortality net of benefits is more than 20,000 deaths per year.

Alcohol is a carcinogen and increases the risk of cancers of the mouth, esophagus, larynx (first tract of the respiratory system), liver, breast, and, to a lesser extent, stomach, colon, and rectum (8). In 2008, there were a total of 6,386 alcohol-attributable cancer deaths, accounting for 3.7 percent of total cancer deaths. This means that in one year such deaths could have been avoided with proper interpretation of drinking.

The annual risk of death from alcohol-related cancers of the mouth, throat, trachea, esophagus, and liver increases significantly among drinkers, particularly among those who use non-moderate (40 g of alcohol) per day. Demonstrating this, the relationship between the volume of alcohol consumed and these types of cancers is characterized by increasing RRs as alcohol volume increases.

There is strong evidence to support that alcohol increases the risk of developing breast cancer (9). The risk at age 80 years increases from 88 per 1,000 nondrinking women to 133 per 1,000 women who consume 6 glasses (60 g) of alcohol per day.

In contrast, the relationship between volume of alcohol consumed and colorectal cancer is very weak, and in the case of women negative.

Mortality impact is an important indicator to take into account in prevention and communication strategies.

The valid and correct public health message should always emphasize that while a glass of wine or beer or any other alcoholic beverage may benefit risk reduction for a specific disease condition, at the same time the same glass significantly increases the risk for all other diseases, such as a good portion of cancers.

The reported data find confirmation in the trends and results identified by the most recent scientific reviews in the literature, which indicate alcohol as one of the leading causes of avoidable death, disease, and disability in all developed nations with stable markets. Extreme caution is therefore to be taken in communicating risk to the population taking care not to generalize unsuitable messages to the youth population that never benefit from alcohol consumption and to emphasize the important differences in risk attributable to the amounts of alcohol consumed according to gender and age differences and that do not allow moderate drinking to be proposed as a health and safety advantage of the person.

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