Review: High alcohol intake increases mortality in both men and women

Di Castelnuovo A, Costanzo S, Bagnardi V, et al. **Alcohol dosing and total mortality in men and women: an updated meta-analysis of 34 prospective studies.** Arch Intern Med. 2006;166:2437-45.

Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Gastroenterology ★★★★★☆☆

QUESTION

What is the relation between alcohol intake and mortality in men and women?

METHODS

Data sources: PubMed (to December 2005) and reference lists.

Study selection and assessment: Prospective cohort studies that reported all-cause mortality in adults by level of alcohol intake and separately for men and women. 34 studies met the selection criteria and provided 56 dose-response curves: 37 curves in men (n = 705 596 participants and 78 592 deaths) and 19 curves in women (n = 310 239 participants and 15 941 deaths). The reference category was never-drinkers in 30 curves and may have included occasional or former drinkers in 26 curves. 48 curves were adjusted for such potentially confounding factors as age, social status, and diet. Median duration of follow-up was 11 years (range 5.5 to 26 y).

Outcomes: All-cause mortality.

MAIN RESULTS

The 56 combined curves presented a J-shaped relation between alcohol intake (on the x axis) and mortality (on the y axis), with the mortality rate of the reference groups set at 1.0. A low intake of alcohol (up to 6 g/d or about half a drink/d) resulted in a sharp reduction in mortality of 19% (Table). From that point mortality rates gradually increased with increasing alcohol consumption, until the curve crossed above the line corresponding to the mortality rate of the reference groups at about 4 drinks/d (Table). The 48 curves that were adjusted at least for age gave slightly more conservative results (Table). The maximum protection against mortality and the alcohol intake level at which this occurred were similar in men and women; however, the upward slope of the curve with increasing alcohol intake was sharper in women, such that mortality protection was lost at lower alcohol intake levels in women (about 2 drinks/d) than in men (about 4 drinks/d) (Table). Mortality risk of alcohol drinkers surpassed that of nondrinkers at about 3.5 drinks/d in women and 4.5 drinks/d in men and continued to increase with increasing consumption.

CONCLUSIONS

In both men and women, high alcohol intake increased mortality compared with nondrinkers, whereas moderate alcohol intake is associated with decreased mortality. Maximum protection against mortality occurs when alcohol intake averages half a drink/day.

Source of funding: Italian Ministry of Education, University and Research.

For correspondence: Dr. L. Iacoviello, Catholic University, Campobasso, Italy. E-mail licia.iacoviello@rm.unicatt.it.

All-cause mortality by level of alcohol intake relative to no alcohol intake at median 11 years*

Patient groups	Number of curves (n)	Maximum RRR (99% CI)	Alcoholic drinks/d at maximum RRR (g/d)	Alcoholic drinks at reversion point (g/d)‡
All	56 (1 015 835)	19% (17 to 20)†	0.6 (6)	4.2 (42)
Adjusted at least for age	48 (908 182)	17% (15 to 18)	0.6 (6)	3.7 (37)
Men (adjusted)	32 (622 692)	17% (15 to 19)	0.6 (6)	3.8 (38)
Women (adjusted)	16 (285 490)	18% (13 to 22)	0.5 (5)	1.8 (18)

*Abbreviations defined in Glossary. 1 drink of alcohol was considered equivalent to 10 g of ethanol.
†95% CI.
‡Reversion point is the level of daily alcohol intake at which protection is no longer statistically significant (i.e., where the upper 99% CI of the curve crosses above the line corresponding to the mortality rate of the reference group).

COMMENTARY

The meta-analysis by Di Castelnuovo and colleagues is the latest and largest such analysis and reaffirms the J-shaped association between self-reported alcohol consumption and mortality. I will ignore potential reasons why this finding may be qualitatively incorrect, such as the possibility of publication bias and issues related to the statistical analysis, and accept that, when measured this way, there is a J-shaped association.

The question for primary care practitioners such as myself is whether these data are sufficiently strong to infer a causal relation between alcohol intake and mortality that should change clinical practice. In other words, should we encourage nondrinkers to start consuming 1 drink per day to lower their risk for premature death? I believe there are at least 2 reasons why we should not.

The first reason relates to the measurement of the exposure variable, alcohol intake. An analysis of large surveys with different measures of self-reporting of alcohol consumption showed that "estimated volume was highly sensitive to the number and types of questions upon which it is based (1)," let alone the question of whether self-reporting is an accurate reflection of actual consumption or whether the presence of "binge" drinking is more deleterious and not accounted for in a "daily average." Consequently, I do not have sufficient confidence in the measurement of alcohol consumption in the original studies to conclude that the classification of alcohol intake is accurate.

The second reason has to do with the possibility that moderate alcohol intake is a marker for other healthy lifestyle behaviors. Some of these healthy behaviors are known and could possibly have been adjusted for, but others are probably unknown. The story of hormone therapy in postmenopausal women is a dramatic example of the difficulty even the best observational studies have in controlling for this "healthy behaviors" effect. I suspect that in my professional lifetime we will never have sufficient evidence that moderate drinking is more beneficial than abstinence to recommend that nondrinkers begin moderate drinking. The cause of the J-shaped curve will remain a mystery.

Paul Shekelle, MD, PhD
Greater Los Angeles Veterans Affairs Healthcare System
Santa Monica, California, USA

Reference

1. **Dawson DA.** Volume of ethanol consumption: effects of different approaches to measurement. J Stud Alcohol. 1998;59:191-7.