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Alcohol consumption and risk of multiple myeloma in the NIH-AARP Diet and Health Study

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Abstract

The epidemiologic evidence regarding the relationship between alcohol consumption and multiple myeloma (MM) risk remains limited and inconsistent, although recent studies suggest a potential protective effect. We prospectively investigated the risk of MM in relation to alcohol consumption frequency among 499,292 participants enrolled in the National Institutes of Health (NIH)-AARP Diet and Health Study in 1995–1996. A total of 1,312 MM cases were identified during follow-up through December 2011. Hazard ratios (HR) and 95% confidence intervals (CI) for categories of alcohol consumption relative to those defined as light drinkers (<1 drink/week) were estimated using multivariate Cox proportional hazard models. Overall, increasing frequency of alcohol consumption was inversely associated with MM (*P*-trend=0.01), with a statistically significant association among those who consumed 2 drinks per day (HR=0.70, 95% CI: 0.50, 0.98); similar but not statistically signifant associations were observed for greater frequency of alcohol consumption. Among women, risk of MM was reduced among those who consumed less that one drink per day (HR=0.73, 95% CI: 0.56, 0.97) and associations with greater frequency of alcohol consumption were inverse although not statistically significant. The findings of this large prospective investigation suggest that moderate alcohol consumption may be associated with reduced future risk of MM.

Keywords

multiple myeloma; alcohol; cohort study

Article category:

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Introduction

Multiple myeloma (MM) is a B-cell malignancy characterized by accumulation of malignant plasma cells in the bone marrow. It is the second most common hematological malignancy,

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and an estimated 24,280 new cases were diagnosed in the US in 2016[1]. Older age, male sex, African ancestry, family history of hematological malignancies, and obesity are established risk factors for MM[2, 3]. Among the potential modifiable risk factors, alcohol consumption has been inconsistently associated with MM. Statistically significant or at least marginal inverse associations between alcohol intake and MM risk have been reported in case-control studies[4–7], including a more recent pooled analysis of six studies[8]; several of these investigations noted somewhat stronger inverse associations with MM for greater frequency of alcohol consumption[6, 7]. However, other case-control studies found no association[9–13]. Evidence from cohort studies is suggestive of an inverse association with MM risk; a prospective investigation in the UK Million women study found that greater frequency of alcohol consumption was associated with a statistically significant reduced risk of MM[14], and another prospective study in Sweden observed a lower risk of MM among individuals with alcohol use disorders[15]. Other cohorts reported non-statistically significant inverse associations with frequency of alcohol consumption[16–18], and one study found an increased risk of MM in light drinkers compared to non-drinkers, but noted an inverse trend with alcohol consumption frequency[19]. To better elucidate the association between alcohol consumption and MM, we prospectively investigated this relationship in the National Institutes of Health (NIH)-AARP Diet and Health Study, a cohort of approximately half a million adults in the United States.

METHODS

Study population

Details of the NIH-AARP Diet and Health Study design have been described[20]. Briefly, a baseline questionnaire was mailed to AARP members who were 50 to 71 years of age and resided in California, Florida, Louisiana, New Jersey, North Carolina, Pennsylvania or two metropolitan areas (Atlanta, Georgia, and Detroit, Michigan). A total of 567,169 satisfactorily completed questionnaires were returned between October 1995 and February 1997.

Records were excluded from our analysis if they met any of the following criteria: the questionnaire was completed in duplicate (n=179), the participant died or moved out of the study area before returning the questionnaire (n= 582), the participant withdrew from the study (n=10), the questionnaire was completed by a proxy (15,760), or the participant had history of cancer as determined by self-report or registry data (n= 51,346). After these exclusions, our final baseline analytical cohort included 499,292 participants (297,823 males and 201,469 females).

Case ascertainment

Incident cases of MM were identified through linkage to cancer registries in the eight states where recruitment took place, and in three additional states (Arizona, Nevada, and Texas) to capture cases among participants who moved to those areas during follow-up. Case ascertainment has been estimated to be approximately 90% complete[21]. Participants were followed from the date that each questionnaire was received until the first cancer was diagnosed, or until the participant moved out of the study area, died or the follow-up period

ended on December 31, 2011. Vital status was determined through linkage to NDI plus. We defined MM cases as those that were assigned a histology code of 9732 according to the International Classification of Diseases for Oncology, Third Edition. A total of 1,312 cases of MM were identified during 5,910,841 person-years of follow-up.

Exposure assessment

Alcohol consumption in the past 12 months was assessed at baseline with the self-administered questionnaire. Information on the usual frequency and quantity of alcohol consumption was provided by each participant. Servings of alcoholic drinks per day were ascertained for total alcohol consumed and for each type of alcoholic beverage (i.e., beer, wine and liquor). One drink was defined based on the US Department of Agriculture MyPyramid Serving Equivalent Database with one alcoholic drink corresponding to 12 fluid ounces of beer (12.96 g of ethanol), 5 fluid ounces of wine (13.72 g of ethanol), and 1.5 fluid ounces of 80 proof distilled liquor (13.93 g of ethanol). MM risk was assessed according to the frequency of total alcohol consumption: none, <1 drink per week, 1 drink per week to <1 drink per day, 1–1.9 drinks per day, 2–2.9 drinks per day, 3–3.9 drinks per day, and ≥4 drinks per day. We also evaluated alcohol intake as a continuous variable (per 10 g/day increment) and using alternate category cut points based on g/day (none, <5 g/day; ≥5-<10 g/day; ≥10-<20 g/day; ≥20-<30 g/day and ≥30g/day).

Statistical analysis

Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox proportional hazards regression models with person-years as the underlying time metric. Consistent with previous studies including the UK Million Women Study[14, 16, 22–24], for the referent group we selected participants who were light drinkers, defined here as those who consumed less than 1 drink per week. We used this approach to reduce the potential for confounding by unmeasured characteristics, reverse causation, and misclassification of exposure. The questionnaire inquired about alcohol consumption in the past 12 months; it is possible that some participants who abstained from alcohol consumption (non-drinkers) might have had underlying health issues that affected their drinking patterns, whereas others might maintain a generally healthier lifestyle. It is also possible that former drinkers who have recently stopped would be classified as non-drinkers based on their questionnaire responses, however we cannot rule out the possibility that our referent category may include some former heavy drinkers. All statistical models were adjusted for age at study entry, race (non-Hispanic white, non-Hispanic black, Hispanic, other and missing), sex (in the analysis with men and women combined), and BMI (<18.5 kg/m^2, 18.5–24.9 kg/m^2, 25–29.9 kg/m^2, ≥30 kg/m^2, unknown). Additional analyses were performed with further adjustment for smoking status, physical activity and level of education. Tests for linear trend were conducted by modeling alcohol intake as a continuous variable per 10 g/day increment; non-drinkers and high outlying values (defined as alcohol intake >196 g/day) were excluded from the analyses of trend. We also performed analyses stratified by sex and by BMI category; multiplicative interaction was assessed using Wald tests. Sensitivity analyses restricted to non-Hispanic whites, excluding ouliers (alcohol intake >196 g/day) and excluding cases and person-time during the first 2 years of follow-up were conducted.

All the analyses were done using SAS, version 9.4 software (SAS Institute, Inc., Cary, North Carolina). All p-values were considered statistically significant if less than 0.05.

RESULTS

Of the 499,292 participants remaining after exclusions, approximately 91% were non-Hispanic whites, 60% were male, and the median age at baseline was 63 (interquartile range 58–67) years. Over 75% of participants reported consuming alcohol in the past 12 months. As shown in Table 1, non-Hispanic whites were more likely to consume alcohol compared with other racial/ethnic groups, men reported greater frequency of alcohol consumption than women, and the prevalence of overweight or obesity was somewhat lower among moderate drinkers (e.g., 60–61% of those consuming 1 or 2 drinks/day) compared with non-drinkers (67%) and heavy drinkers (68%) with non-missing BMI values.

Among men and women combined, greater frequency of alcohol consumption was inversely associated with MM risk, with an estimated 4% decrease in risk per 10g/day increase in alcohol intake (p-trend=0.01; Table 2). Compared with light drinkers, we observed a statistically significant reduced risk of MM among those who consumed 2 to 2.9 drinks per day (HR=0.70, 95% CI: 0.50, 0.98), but non-statistically significant reduced risks of MM in other categories of alcohol consumption. A similar pattern of association was observed when alcohol intake was defined in categories of g/day (Supplementary Table 1). Our findings were essentially unchanged after further adjusting for smoking status, level of education and level of physical activity (data not shown) and after exclusion of outliers (alcohol intake > 196 g/day). When we evaluated MM risk in separate analyses of beer, wine and liquor consumption, we found no association between any specific alcohol type and MM risk after adjusting for race, age, sex and other types of alcoholic beverages (data not shown).

The significant associations between alcohol use and MM risk remained in lagged analyses excluding 139 cases diagnosed during the first two years of follow-up; we observed stronger inverse associations with MM risk for consumption of 2 to 2.9 drinks per day (HR=0.67, 95% CI: 0.46, 0.96) or 3 to 3.9 drinks per day (HR=0.63, 95% CI: 0.41, 0.99), with a statistically significant dose-response trend (P-trend=0.016). In sensitivity analyses restricted to non-Hispanic whites, the patterns of association with MM were similar although no longer statistically significant (e.g., 2–2.9 drinks/day vs. <1 drink/week, HR=0.73, 95% CI: 0.52, 1.03; data not shown).

In sex-specific analyses, we observed a statistically significant reduced risk of MM with increasing alcohol consumption among men (HR per 10g/day increase = 0.96; p-trend=0.02). Among women, the dose-response trend per 10g/day increase in alcohol intake was not statistically significant; however, we observed a reduced risk of MM among those who consumed less than 1 drink per day (HR=0.73, 95% CI: 0.56, 0.97) and associations with more frequent alcohol consumption were inverse although not statistically significant. A test of interaction between alcohol consumption and sex was not statistically significant (P-interaction=0.52). When alcohol intake was modeled in categories of g/day, we found that alcohol intake of ≥30 g/day was associated with a reduced risk of MM among men (HR=0.79, 95% CI: 0.63, 0.98), whereas intake of 5-<10 g/day was associated with reduced

MM risk among women (HR=0.53, 95% CI: 0.32, 0.87; Supplementary Table 1). In analyses stratified by BMI, the inverse associations with MM risk for moderate alcohol consumption were more apparent among participants who were overweight (BMI ≥25-<30 kg/m^2: 2–2.9 drinks per day, HR=0.45, 95% CI: 0.25, 0.81; Supplementary Table 2). We noted a similar pattern of association with moderate alcohol consumption among obese individuals, although findings in this group did not achieve statistical significance. A test of interaction between alcohol consumption and BMI was not statistically significant (p-interaction=0.10).

Discussion

In this large prospective investigation in the NIH-AARP Diet and Health Study, we found that moderate frequency of alcohol consumption was associated with a reduced risk of MM development. Our findings are consistent with those from an investigation in the UK Million Women Study noting reduced MM risk with moderate alcohol consumption[14] and evidence from other cohort studies is generally suggestive of inverse associations with MM for increasing frequency of alcohol consumption[15–18]. A recent meta-analysis of results from 10 cohort studies and 16 case-control studies reported a statistically significant inverse association with moderate alcohol consumption (12.5–50 grams of ethanol per day) (pooled RR = 0.87, 95% CI: 0.77, 0.99), whereas there was limited evidence of an association among light drinkers (≤ 12.5 grams per ethanol per day) or heavy drinkers (≥ 50 grams of ethanol per day)[25]. Although our definition of moderate drinking (2–2.9 drinks per day, or approximately 28 to 42 grams of ethanol per day) is narrower than the one in the meta-analysis, our results are consistent with their findings.

Notably, we also observed a statistically significant reduced risk of MM among women who consumed less than 1 drink per day. A similar association with light drinking (3-<7 drinks per week) was observed in the UK Million Women Study[14], and in the recent meta-analysis the protective effect of alcohol consumption on MM risk was more apparent among women compared with men[25]. Taken together, these findings may reflect gender differences in alcohol metabolism that could potentially lead to differences by sex in the relationship between alcohol consumption frequency and MM[26].

The potential biological mechanisms by which alcohol might protect against MM development are not fully understood. It has been shown that high alcohol consumption impairs the immune system and, in turn, increases cancer risk. On the other hand, light and moderate alcohol consumption are hypothesized to improve humoral response[27]. Also, low alcohol consumption improves insulin sensitivity which, in turn, decreases risk of diabetes and other obesity-related disorders[28, 29] and thus, indirectly, may decrease risk of MM. The effect of low alcohol consumption on insulin sensitivity might explain the observed inverse association among overweight individuals. It is possible that overweight individuals have dysregulated hormone levels which induce insulin resistance, making them more sensitive to potential protective effects of moderate alcohol consumption.

Exposure to low doses of ethanol has been associated with inhibition of the mammalian target of rapamycin (mTOR) signaling pathway in *in vitro* and *in vivo* non-Hodgkin lymphoma models[30]. Polyphenols and resveratrol, abundant in red wines, inhibit nuclear

factor-κB (NF-κB) in mononuclear cells and resveratrol induces apoptosis by inhibiting signal transducer and activator of transcription 3 (STAT3) in human MM cells[31–33]. Synergistic cytotoxicity has been shown when resveratrol was combined with bortezomib *in vitro*[32], providing the rationale for clinical trials in humans. A phase 2 clinical trial using SRT501, a resveratrol oral formulation, has demonstrated a high toxicity profile and minimal efficacy[34]. Therefore, *in vitro* molecular studies are needed to better define possible mechanisms of action in MM models.

The strengths of this study include its large sample size, the prospective design, and the ability to control for potential confounding factors and conduct stratified analyses in population subgroups. A limitation of this investigation is that information on alcohol consumption was based on self-report for the 12-month period prior to study enrollment. To account for the possibility that some participants' alcohol consumption habits may have changed as a result of preclinical disease or as yet undiagnosed MM at baseline, we conducted sensitivity analyses excluding the first 2 years of follow-up, but our results did not change.

In conclusion, the findings of this prospective study – one of the largest of its kind – support a protective effect of alcohol consumption in MM development. Prospective studies with information on long-term alcohol use may help to further elucidate how the timing and amount of alcohol consumption may influence MM risk. Mechanistic studies are also warranted to better understand the potential underlying biological mechanisms, which may help to identify novel molecular targets or therapeutic approaches.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Teras LR, DeSantis CE, Cerhan JR, Morton LM, Jemal A, Flowers CR. 2016 US lymphoid malignancy statistics by World Health Organization subtypes. CA Cancer J Clin 2016.
2. Alexander DD, Mink PJ, Adami HO, Cole P, Mandel JS, Oken MM, Trichopoulos D. Multiple myeloma: a review of the epidemiologic literature. Int J Cancer 2007;120 Suppl 12: 40–61. [PubMed: 17405120]
3. Lauby-Secretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, Straif K, International Agency for Research on Cancer Handbook Working G. Body Fatness and Cancer--Viewpoint of the IARC Working Group. N Engl J Med 2016;375: 794–8. [PubMed: 27557308]
4. Brown LM, Pottern LM, Silverman DT, Schoenberg JB, Schwartz AG, Greenberg RS, Hayes RB, Liff JM, Swanson GM, Hoover R. Multiple myeloma among Blacks and Whites in the United States: role of cigarettes and alcoholic beverages. Cancer Causes Control 1997;8: 610–4. [PubMed: 9242477]
5. Nieters A, Deeg E, Becker N. Tobacco and alcohol consumption and risk of lymphoma: results of a population-based case-control study in Germany. Int J Cancer 2006;118: 422–30. [PubMed: 16080191]
6. Hosgood HD 3rd, Baris D, Zahm, Zheng T, Cross AJ. Diet and risk of multiple myeloma in Connecticut women. Cancer Causes Control 2007;18: 1065–76. [PubMed: 17694422]
7. Gorini G, Stagnaro E, Fontana V, Miligi L, Ramazzotti V, Amadori D, Rodella S, Tumino R, Crosignani P, Vindigni C, Fontana A, Vineis P, et al. Alcohol consumption and risk of Hodgkin's lymphoma and multiple myeloma: a multicentre case-control study. Ann Oncol 2007;18: 143–8. [PubMed: 17047000]
8. Andreotti G, Birmann B, De Roos AJ, Spinelli J, Cozen W, Camp NJ, Moysich K, Chiu B, Steplowski E, Krzystan J, Boffetta P, Benhaim-Luzon V, et al. A pooled analysis of alcohol consumption and risk of multiple myeloma in the international multiple myeloma consortium. Cancer Epidemiol Biomarkers Prev 2013;22: 1620–7. [PubMed: 23964064]
9. Brown LM, Gibson R, Burmeister LF, Schuman LM, Everett GD, Blair A. Alcohol consumption and risk of leukemia, non-Hodgkin's lymphoma, and multiple myeloma. Leuk Res 1992;16: 979–84. [PubMed: 1405712]
10. Tavani A, Pregnolato A, Negri E, Franceschi S, Serraino D, Carbone A, LaVecchia C. Diet and risk of lymphoid neoplasms and soft tissue sarcomas. Nutr Cancer 1997;27: 256–60. [PubMed: 9101555]
11. Linet MS, Harlow SD, Mclaughlin JK. A Case-Control Study of Multiple-Myeloma in Whites - Chronic Antigenic-Stimulation, Occupation, and Drug-Use. Cancer Res 1987;47: 2978–81. [PubMed: 3567914]
12. Deandrea S, Bertuccio P, Chatenoud L, Franceschi S, Serraino D, La Vecchia C. Alcohol consumption and risk of Hodgkin's lymphoma and multiple myeloma: a multicentre case-control study - Reply. Annals of Oncology 2007;18: 1119–21. [PubMed: 17586754]
13. Glass DC, Gray CN, Jolley DJ, Gibbons C, Sim MR, Fritschi L, Adams GG, Bisby JA, Manuell R. Leukemia risk associated with low-level benzene exposure. Epidemiology 2003;14: 569–77. [PubMed: 14501272]
14. Kroll ME, Murphy F, Pirie K, Reeves GK, Green J, Beral V, Million Women Study C. Alcohol drinking, tobacco smoking and subtypes of haematological malignancy in the UK Million Women Study. Br J Cancer 2012;107: 879–87. [PubMed: 22878373]
15. Ji J, Sundquist J, Sundquist K. Alcohol consumption has a protective effect against hematological malignancies: a population-based study in Sweden including 420,489 individuals with alcohol use disorders. Neoplasia 2014;16: 229–34, 34 e1. [PubMed: 24783999]
16. Kanda J, Matsuo K, Inoue M, Iwasaki M, Sawada N, Shimazu T, Yamaji T, Sasazuki S, Tsugane S, Japan Public Health Center-based Prospective Study G. Association of alcohol intake with the risk of malignant lymphoma and plasma cell myeloma in Japanese: a population-based cohort

study (Japan Public Health Center-based Prospective Study). Cancer Epidemiol Biomarkers Prev 2010;19: 429–34. [PubMed: 20086115]

17. Chang ET, Clarke CA, Canchola AJ, Lu Y, Wang SS, Ursin G, West DW, Bernstein L, Horn-Ross PL. Alcohol consumption over time and risk of lymphoid malignancies in the California Teachers Study cohort. Am J Epidemiol 2010;172: 1373–83. [PubMed: 20952595]
18. Troy JD, Hartge P, Weissfeld JL, Oken MM, Colditz GA, Mechanic LE, Morton LM. Associations between anthropometry, cigarette smoking, alcohol consumption, and non-Hodgkin lymphoma in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. Am J Epidemiol 2010;171: 1270–81. [PubMed: 20494998]
19. Heinen MM, Verhage BA, Schouten LJ, Goldbohm RA, Schouten HC, van den Brandt PA. Alcohol consumption and risk of lymphoid and myeloid neoplasms: results of the Netherlands cohort study. Int J Cancer 2013;133: 1701–12. [PubMed: 23553592]
20. Schatzkin A, Subar AF, Thompson FE, Harlan LC, Tangrea J, Hollenbeck AR, Hurwitz PE, Coyle L, Schussler N, Michaud DS, Freedman LS, Brown CC, et al. Design and serendipity in establishing a large cohort with wide dietary intake distributions : the National Institutes of Health-American Association of Retired Persons Diet and Health Study. Am J Epidemiol 2001;154: 1119–25. [PubMed: 11744517]
21. Michaud D, Midthune D, Herman S, Leitzmann M, Harlan LC, Kipnis v, Schatzkin A. Comparison of cancer registry case ascertainment with SEER estimates and self-reporting in a subset of the NIH-AARP Diet and Health Study Journal of Registry Management 2005;32: 70–5.
22. Jiao L, Silverman DT, Schairer C, Thiebaut ACM, Hollenbeck AR, Leitzmann MF, Schatzkin A, Stolzenberg-Solomon RZ. Alcohol Use and Risk of Pancreatic Cancer. American Journal of Epidemiology 2009;169: 1043–51. [PubMed: 19299403]
23. Nieters A, Deeg E, Becker N. Tobacco and alcohol consumption and risk of lymphoma: Results of a population-based case-control study in Germany. International Journal of Cancer 2006;118: 422–30. [PubMed: 16080191]
24. Troy JD, Hartge P, Weissfeld JL, Oken MM, Colditz GA, Mechanic LE, Morton LM. Associations Between Anthropometry, Cigarette Smoking, Alcohol Consumption, and Non-Hodgkin Lymphoma in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. American Journal of Epidemiology 2010;171: 1270–81. [PubMed: 20494998]
25. Psaltopoulou T, Sergentanis TN, Sergentanis IN, Karadimitris A, Terpos E, Dimopoulos MA. Alcohol intake, alcoholic beverage type and multiple myeloma risk: a meta-analysis of 26 observational studies. Leuk Lymphoma 2015;56: 1484–501. [PubMed: 25146435]
26. Baraona E, Abittan CS, Dohmen K, Moretti M, Pozzato G, Chayes ZW, Schaefer C, Lieber CS. Gender differences in pharmacokinetics of alcohol. Alcohol Clin Exp Res 2001;25: 502–7. [PubMed: 11329488]
27. Diaz LE, Montero A, Gonzalez-Gross M, Vallejo AI, Romeo J, Marcos A. Influence of alcohol consumption on immunological status: a review. Eur J Clin Nutr 2002;56 Suppl 3: S50–3.
28. Kato I, Kiyohara Y, Kubo M, Tanizaki Y, Arima H, Iwamoto H, Shinohara N, Nakayama K, Fujishima M. Insulin-mediated effects of alcohol intake on serum lipid levels in a general population: the Hisayama Study. J Clin Epidemiol 2003;56: 196–204. [PubMed: 12654415]
29. Kenkre PV, Lindeman RD, Lillian Yau C, Baumgartner RN, Garry PJ. Serum insulin concentrations in daily drinkers compared with abstainers in the New Mexico elder health survey. J Gerontol A Biol Sci Med Sci 2003;58: M960–3. [PubMed: 14570866]
30. Hagner PR, Mazan-Mamczarz K, Dai B, Corl S, Zhao XF, Gartenhaus RB. Alcohol consumption and decreased risk of non-Hodgkin lymphoma: role of mTOR dysfunction. Blood 2009;113: 5526–35. [PubMed: 19293424]
31. Blanco-Colio LM, Munoz-Garcia B, Martin-Ventura JL, Alvarez-Sala LA, Castilla M, Bustamante A, Lamuela-Raventos RM, Gomez-Gerique J, Fernandez-Cruz A, Millan J, Egido J. Ethanol beverages containing polyphenols decrease nuclear factor kappa-B activation in mononuclear cells and circulating MCP-1 concentrations in healthy volunteers during a fat-enriched diet. Atherosclerosis 2007;192: 335–41. [PubMed: 16970955]
32. Bhardwaj A, Sethi G, Vadhan-Raj S, Bueso-Ramos C, Takada Y, Gaur U, Nair AS, Shishodia S, Aggarwal BB. Resveratrol inhibits proliferation, induces apoptosis, and overcomes

chemoresistance through down-regulation of STAT3 and nuclear factor-kappaB-regulated antiapoptotic and cell survival gene products in human multiple myeloma cells. Blood 2007;109: 2293–302. [PubMed: 17164350]

33. Boissy P, Andersen TL, Abdallah BM, Kassem M, Plesner T, Delaisse JM. Resveratrol inhibits myeloma cell growth, prevents osteoclast formation, and promotes osteoblast differentiation. Cancer Res 2005;65: 9943–52. [PubMed: 16267019]
34. Popat R, Plesner T, Davies F, Cook G, Cook M, Elliott P, Jacobson E, Gumbleton T, Oakervee H, Cavenagh J. A phase 2 study of SRT501 (resveratrol) with bortezomib for patients with relapsed and or refractory multiple myeloma. Br J Haematol 2013;160: 714–7. [PubMed: 23205612]

What's new

While alcohol consumption is a risk factor for multiple cancer types, epidemiological studies examining specific associations with multiple myeloma have yielded inconsistent results. Here, the authors investigated relationships between alcohol consumption and multiple myeloma risk using data for nearly half-a-million adults enrolled in the National Institutes of Health-AARP Diet and Health Study. Analyses reveal a significant association between reduced multiple myeloma risk and moderate drinking, defined as 2 to 2.9 drinks per day. Further investigation is needed to better understand how alcohol consumption influences multiple myeloma risk.

Table 1

Baseline characteristics of study participants by alcohol intake, NIH-AARP Diet and Health Study, 1995–2011 (n=499,292)

	Alcohol intake[a]													
Characteristic	**None**		**<1 drink/week**		**≥1drink/week-**		**1–1.9 drinks/day**		**2–2.9 drinks/day**		**3–3.9 drinks/day**		**≥4 drinks/day**	
	No.	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**
Age at baseline [b]	62.4	(5.3)	61.9	(5.4)	61.7	(5.4)	62.4	(5.3)	61.9	(5.4)	62.1	(5.3)	62.0	(5.30)
Sex														
Male	62286	(51.0)	61264	(45.8)	85703	(66.5)	41776	(72.2)	13732	(75.9)	10214	(81.5)	22848	(87.7)
Female	59770	(49.0)	72619	(54.2)	43107	(33.5)	16107	(27.8)	4369	(24.1)	2295	(18.4)	3202	(12.3)
Race														
White[c]	106128 (87.0)		120927	(90.3)	119267	(92.6)	54725	(94.5)	17110	(94.5)	11785	(94.2)	24571	(94.3)
Black[c]	7886	(6.5)	5416	(4.1)	3944	(3.1)	1186	(2.1)	396	(2.2)	355	(2.8)	678	(2.6)
Hispanic	2276	(1.9)	2956	(2.2)	2661	(2.1)	920	(1.6)	284	(1.6)	164	(1.3)	361	(1.4)
Other	3135	(2.6)	2701	(2.0)	1539	(1.2)	515	(0.9)	137	(0.8)	82	(0.7)	196	(0.8)
Unknown	2631	(2.2)	1883	(1.4)	1399	(1.1)	537	(0.9)	174	(1.0)	123	(1.0)	244	(1.0)
BMI [d]														
<18.5	1488	(1.2)	1341	(1.0)	1085	(0.8)	601	(1.0)	196	(1.1)	135	(1.1)	246	(0.9)
≥18.5 to <25	37201	(30.5)	44028	(32.9)	44777	(34.8)	22390	(38.7)	6653	(36.8)	4119	(32.9)	7917	(30.4)
≥25 to <30	46993	(38.5)	52652	(39.3)	56092	(43.6)	25357	(43.8)	8075	(44.6)	5818	(46.5)	12198	(49.8)
≥ 30	32131	(26.3)	32579	(24.3)	24368	(18.9)	8497	(14.7)	2845	(15.7)	2207	(17.6)	5151	(19.8)
Unknown	4243	(3.5)	3283	(2.5)	2488	(1.9)	1038	(1.8)	332	(1.8)	230	(1.8)	538	(2.1)

[a] The approximate corresponding values for alcohol intake in grams/day are as follows: <1 drink/week = <2 g/day; ≥1 drink/week - <1 drink/day = ≥2 g/day - <14g/day; 1–1.9 drinks/day = ≥14 - <28 g/day; 2–2.9 drinks/day = ≥28 - <42 g/day; 3–3.9 drinks/day = ≥42 - <56 g/day; ≥4 drinks/day = ≥56 g/day.

[b] mean (standard deviation)

[c] non-Hispanic

[d] Body mass index at baseline in kg/m^2

Table 2

Hazard ratios and 95% CI for the risk of MM in relation to alcohol consumption, NIH-AARP Diet and Health Study, 1995–2011 (n=499,292).

	Men and women combined[a]		Men[b]		Women[b]		
Alcohol consumption[b]	**No$_{cases}$**	**HR (95% CI)**	**No$_{cases}$**	**HR (95% CI)**	**No$_{cases}$**	**HR (95% CI)**	***P*$_{interaction}$**
None	312	0.89 (0.76, 1.03)	177	0.89 (0.73, 1.09)	135	0.89 (0.71, 1.12)	
<1 drink/wk	371	1.00	200	1.00	171	1.00	
<1 drink/day	346	0.91 (0.78, 1.05)	275	0.99 (0.82, 1.19)	71	0.73 (0.56, 0.97)	
1–1.9 drinks/day	156	0.88 (0.73, 1.07)	129	0.93 (0.75, 1.16)	27	0.77 (0.51, 1.16)	
2–2.9 drinks/day	38	0.70 (0.50, 0.98)	32	0.73 (0.50, 1.06)	6	0.66 (0.29, 1.50)	
3–3.9 drinks/day	27	0.72 (0.49, 1.07)	23	0.73 (0.47, 1.12)	4	0.80 (0.30, 2.16)	
>=4 drinks/day	62	0.79 (0.60, 1.04)	57	0.82 (0.61, 1.10)	5	0.76 (0.31, 1.85)	
Per 10g/day increase[c]	987	0.96 (0.93–0.99)	703	0.96 (0.93–0.99)	284	0.93 (0.85–1.03)	
***P*$_{trend}$ [c]**		0.01		0.02		0.17	0.52

[a]Adjusted for race, age (continuous variable), sex, and BMI.

[b]Adjusted for race, age (continuous variable) and BMI.

[c]Among drinkers, excluding high outlying values (>196 g/day), adjusted for race, age (continuous variable), sex, and BMI

[b]The approximate corresponding values for alcohol intake in grams/day are as follows: <1 drink/week = <2 g/day; ≥1 drink/week - <1 drink/day = ≥2 g/day - <14g/day; 1–1.9 drinks/day = ≥14 - <28 g/day; 2–2.9 drinks/day = ≥28 - <42 g/day; 3–3.9 drinks/day = ≥42 - <56 g/day; ≥4 drinks/day = ≥56 g/day.